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Straumann® Emdogain® Application In Conjunction With Minimally Invasive Surgical Technique For Periodontal Disease Treatment: A Split-Mouth Design Study

CR 01/15

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Protocol reviewed and approved by:

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Abbreviations

ADE	Adverse Device Effect
AE	Adverse Event
ASADE	Anticipated Serious Adverse Device Effect
BoP	Bleeding on Probing
CAL	Clinical Attachment Level
CBCT	Cone Beam Computed Tomography
CE	Conformité Européenne
CEJ	Cemento-Enamel Junction
CFR	Code of Federal Regulations
CRF	Case Report Form
DD	Device Deficiencies
DMP	Data Management Plan
EDTA	Ethylenediaminetetraacetic acid, Edetic acid
FDA	Food and Drug Administration
FMPS	Full Mouth Plaque Score
GCP	Good Clinical Practice
GM	Gingival Margin
ICF	Informed Consent Form
ICH	International Conference on Harmonization
IFU	Instructions For Use
IRB	Institutional Review Board
ISO	International Organization for Standardization
ml	Milliliter
mm	Millimeter
MP	Monitoring Plan

PPD	Probing Pocket Depth
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SOP	Standard Operating Procedures
SRP	Scaling and Root Planing
USADE	Unanticipated Serious Adverse Device Effect
VAS	Visual Analog Scale

Note:

- The term Emdogain® used throughout this document refers to the following device: Straumann® Emdogain®
- The term PrefGel® used throughout this document refers to the following device: Straumann® PrefGel®

Synopsis

Study Title	Straumann® Emdogain® Application In Conjunction With Minimally Invasive Surgical Technique For Periodontal Disease Treatment: A Split-Mouth Design
Study Protocol Number	CR 01/15
Study Registration	This protocol will be registered at clinicaltrials.gov before enrollment begins.
Objectives	The aim of this controlled study is to assess the clinical outcomes and patient reported outcomes of using minimally invasive surgical procedure with Straumann® Emdogain® as an adjunct (test treatment) or without Straumann® Emdogain® (control treatment). **Primary Objective:** To evaluate the regenerative potential of Straumann® Emdogain® by looking at differences in Clinical Attachment Level (CAL) between the test and control treatments. **Secondary Objective**: To evaluate the regenerative potential of Straumann® Emdogain® by looking at differences in: • Gingival Margin (GM) • Probing Pocket Depth (PPD) • Full Mouth Plaque Score (FMPS) • Bleeding on Probing (BoP) • Post-surgical pain, and • Root dentin hypersensitivity between the test and control treatments.
Study Design	Post-market, prospective, split-mouth, controlled, multi-center study.
Study Population	The study population will consist of subjects aged 18 to 85 with moderate to severe chronic, generalized periodontitis with pockets of 5 mm – 8 mm probing depth in at least 2 pockets per contralateral quadrants in one arch.
Inclusion Criteria	• Subjects must have voluntarily signed the informed consent form before any study related procedures • Subjects must be males or females who are 18-85 years of age • Subjects must have moderate to severe chronic, generalized periodontitis with pockets of 5 mm – 8 mm probing depth in at least 2 pockets per contralateral quadrants in one arch (study teeth) • Subjects must be committed to the study and the required follow-up visits • Subjects must be in good general health as assessed by the Investigator at time of surgery.
Exclusion Criteria	• Subjects taking or intending to take any medications during the duration of the study that will potentially affect healing and inflammation • Subjects who are currently heavy smokers (defined >10 cigarettes per day or >1 cigar per day) or who use chewing tobacco • Subjects being treated with systemic antibiotics or subjects that were treated with systemic antibiotics within 3 months prior to treatment in this study • Subjects with uncontrolled diabetes

<table>
<tr><td></td><td>

Subjects that are immunocompromised or immunosuppressed
Subjects that cannot provide informed consent
Subjects with drug or alcohol abuse
Subjects that have undergone periodontal root planing or periodontal surgery in the last 6 months
Subjects that are pregnant
Subjects with necrotizing periodontitis or periodontitis related to systemic disease
Teeth with pockets with probing depth ≥ 9 mm will not classify as study teeth
Teeth with pockets or defects with furcation involvement will not classify as study teeth
Teeth with mobility degree > 1 without splint will not classify as study teeth
Subjects with test and control sites in the two quadrants on adjacent teeth
Patients with compromised health conditions such as uncontrolled diabetes or uncontrolled systemic diseases, disorders or treatments that compromise wound healing, chronic high dose steroid therapy, bone metabolic diseases, radiation or immuno-oppressive therapy, and infections or vascular impairment at the surgical site
Subjects with conditions or circumstances, in the opinion of the Investigator , which would prevent completion of study participation or interfere with analysis of study results

</td></tr>
<tr><td>Treatment Plan</td><td>
All eligible patients will receive periodontal therapy consisting of minimally invasive surgery, plaque removal, and post-surgery oral hygiene instructions. Periodontal minimally invasive surgery is performed either alone (control quadrant) or in combination with Straumann® Emdogain® (test quadrant) for the treatment of periodontitis. Following periodontal surgery, control visits are scheduled at 2-3 weeks and at 1-, 3-, 6-, 9- and 12 months for clinical evaluations.
<table>
<tr><th>Visit #</th><th>Visit</th><th>Schedule</th></tr>
<tr><td>Visit 1</td><td>Informed Consent / Screening & Baseline</td><td>Within 14 Days of Enrollment</td></tr>
<tr><td>Visit 2</td><td>Minimally Invasive Scaling and Root Planing (SRP) and Emdogain® First Application</td><td>SURGERY - Point of Enrollment</td></tr>
<tr><td>Visit 3</td><td>Supragingival Plaque Removal and Emdogain® Second Application</td><td>2-3 Weeks after Surgery</td></tr>
<tr><td>Visit 4</td><td>Regular Periodontal Maintenance</td><td>1 Month after Surgery</td></tr>
<tr><td>Visit 5
Visit 6
Visit 7</td><td>Follow-up Visits</td><td>3 Months, 6 Months and 9 Months after Surgery</td></tr>
<tr><td>Visit 8</td><td>Last Follow-up Visit / Study End</td><td>12 Months after Surgery</td></tr>
</table>
</td></tr>
<tr><td>Investigational Device</td><td>Straumann® Emdogain® 0.15 ml, 0.3 ml, or 0.7 ml syringe (30 mg/ml)</td></tr>
<tr><td>Registration Status</td><td>Straumann® Emdogain® used in the study is CE-marked and has received FDA-clearance (PMA approval No. P930021 S013). The investigational device will be used within its cleared indications.</td></tr>
</table>

Primary Analysis	The primary analysis will be conducted after all subjects complete the 12 months post-surgery visit.
Primary Endpoint	• Clinical Attachment Level (CAL) change
Secondary Endpoints	• Change in Gingival Margin (GM) • Change in Probing Pocket Depth (PPD) • Change in Full Mouth Plaque Score (FMPS) • Change in Bleeding on Probing (BoP) • Change in root dentin hypersensitivity • Frequency of successful probing points (PPD < 5 mm) • Number of pockets that would normally be treated surgically that are converted to pockets that do not require surgical intervention.
Interim Analysis	Interim analysis will be done at 3 months post-surgery; optional interim analyses will be performed at 6 months and 9 months post-surgery.
Interim Analysis Endpoints	• Change in Clinical Attachment Level (CAL) • Change in Gingival Margin (GM) • Change in Probing Pocket Depth (PPD) • Change in Bleeding on Probing (BoP) • Change in root dentin hypersensitivity • Frequency of successful probing points (PPD < 5 mm) • Number of pockets that would normally be treated surgically that are converted to pockets that do not require surgical intervention. • Comparison of pain level between treatment groups at 1-2 days, 1 week, and 2 weeks after surgery.
Statistical Consideration	Statistics of the endpoints will be presented for raw values and change from baseline overall and by study center. The planned statistical testing to compare the treatment groups will be outlined in a Statistical Analysis Plan (SAP).
Safety	The patients will be monitored for adverse events by the Investigators until the end of follow-up for each patient. All device complaints and failures will be reported without delay to Straumann.
Countries in which the Study will be performed	United States and Canada
Number of participating centers	4 centers
Principal Investigators at Centers	Dr. Veronique Benhamou, DDS Dr. Jennifer Hirsch Doobrow, DMD Dr. Pamela K. McClain, DDS Prof. Dr. Dr. h.c. Adrian Kasaj, M.Sc
Number of Subjects Planned to be Enrolled	50 subjects

Date of Study Initiation	September 2015
Date of Study Completion	Enrollment through December 2016; Follow-up complete for all subjects by December 2017
Sponsor	Institut Straumann AG
Compliance	This study and any amendments will be performed according to ISO 14155:2011, ICH E6(R1) Guideline on Good Clinical Practice (GCP) 1996, and conformed to the Declaration of Helsinki (last revised Fortaleza 2013). Local legal and regulatory requirements include compliance with 21 CFR 50, 21 CFR 54, and 21 CFR 56.

Table 1 - Schedule of Assessments

Assessments	Visit 1*	Visit 2*	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8
	Informed Consent / Screening & Baseline Visit	**SURGERY** (enrollment) Visit	Treatment Visit	1 Month Follow-Up Visit	3 Month Follow-Up Visit	6-Month Follow-Up Visit	9-Month Follow-Up Visit	12-Month Follow-Up Visit / Study End
	14 - 0 Days before Surgery	**Day 0**	Day 14-21 ± 2-3 days after Surgery	1 Month ±1 Week after Surgery	3 Months ±1 Week after Surgery	6 Months ±2 Weeks after Surgery	9 Months ±2 Weeks after Surgery e	12 Months ±2 Weeks after Surgery
Informed Consent	X							
Medical & Dental History	X							
Demographics	X							
If Female, Pregnancy Test	X							
Initial Perio Exam/ Assessment of Periodontal Status	X							
Inclusion/Exclusion Criteria	X	X						
Identification & Assignment of Quadrants		X						
Full Mouth Plaque Score (FMPS)	X		X					X
Pocket Probing Depth (PPD)	X				X	X	X	X
Gingival Margin (GM)	X				X	X	X	X
Bleeding On Probing (BoP)	X				X	X	X	X
Root Dentin Hypersensitivity		X			X	X	X	X
Randomization		X						
Minimally Invasive Scaling and Root Planing (SRP) + Emdogain® First Application (as indicated by treatment assignment)		X						

Assessments	Visit 1*	Visit 2*	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8
	Informed Consent / Screening & Baseline Visit	**SURGERY** (enrollment) Visit	Treatment Visit	1 Month Follow-Up Visit	3 Month Follow-Up Visit	6-Month Follow-Up Visit	9-Month Follow-Up Visit	12-Month Follow-Up Visit / Study End
	14 - 0 Days before Surgery	**Day 0**	Day 14-21 ± 2-3 days after Surgery	1 Month ±1 Week after Surgery	3 Months ±1 Week after Surgery	6 Months ±2 Weeks after Surgery	9 Months ±2 Weeks after Surgery e	12 Months ±2 Weeks after Surgery
Supragingival Plaque Removal + Emdogain® Second Application (as indicated by treatment assignment)			X					
Pain Scale		X**	X**					
Post-treatment Oral Hygiene Instructions		X	X					
Supragingival Prophylaxis				X				
Regular Periodontal Maintenance					X	X	X	X
Radiographs (according to standard of care)	X							X
Photographs	X	X	X	X	X	X	X	X
Concomitant Medications	X	X	X	X	X	X	X	X
Adverse Events Check	X	X	X	X	X	X	X	X

***Visit 1 and Visit 2 can be conducted at the same office visit**. If Visit 1 and Visit 2 are combined, a set of photographs should be taken pre and post-surgery.

****Pain scale will be sent home with the subject at Visit 2 and completed at 1-2 days, 1 week, and 2 weeks thereafter.**

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1 Background and Rationale

The goal of regenerative periodontal therapy is the reconstruction of lost periodontal structures. Results from preclinical and clinical studies have shown that Emdogain® successfully promotes periodontal wound healing and regeneration, when used in conjunction with periodontal open flap surgery[1]. Although Emdogain® has been proven successful to effectively promote periodontal regeneration as part of surgical procedures attempts to use the product for periodontal regeneration as part of minimally invasive surgery (i.e. flapless) procedures remain inconclusive and controversial or do not allow a definite conclusion on the effectiveness.[1, 2, 3, 4, 5, 6, 7, 8, 9, 10] Although the majority of reports does not support the use of Emdogain® in flapless periodontal procedures, few reports like the one of Wennström et al. indicate a potential effect of the product in flapless periodontal procedures[10]. Specifically the authors have reported that Emdogain® provides an advantage in the early wound healing after flapless periodontal debridement.

A more thorough review of the available literature suggests that all attempts to establish the use of Emdogain® in flapless methods have lacked a systematic and standardized approach. In particular the preconditions as well as the details of the clinical workflow need to be carefully defined in order to analyze the success of regenerative procedures using Emdogain® in a flapless application. With this regards thorough debridement of the root/dentin surface but also removal of granulation tissue might be considered as a precondition for Emdogain® mediated regeneration of the periodontal tissues and periodontal attachment. As a consequence a defined and validated workflow is estimated to be necessary in order to achieve this goal. According to our knowledge such a systematic approach, which is considered to be necessary has not been applied yet to analyze the potential of Emdogain® in flapless periodontal procedures.

Mechanical debridement can be effectively achieved by manual (curettes) and power-driven tools (sonic and ultrasonic instruments) and can be partly combined with fiber optics in power-driven devices to improve the efficiency of root cleaning. In spite of the great efforts in the mechanical surface cleaning process it is well known today that pathogenic bacteria especially remain in the biofilm residues and also inside the tissue and cause reinfection and inflammation. More recent and advanced debridement strategies combine such approaches with laser-therapy, specifically in combination with photosensitizers (= antimicrobial photodynamic therapy, aPDT) to achieve full mechanical and microbiological debridement of the periodontal defect, which cannot be achieved by mechanical strategies alone.

To our knowledge as of today a validated and standardized workflow, which leads to a nearly complete mechanically and microbiologically cleaned root surface as starting point to evaluate the healing potential of Emdogain® in minimally invasive surgery application does not exist. Furthermore the selection criteria for clinical preconditions to allow treatment by the envisaged flapless workflow needs to be defined, such as inclusion criteria related to the type of periodontal defect, i.e. type, depth, width, and amount of granulation tissue, etc.

2 Study Objectives

A concept paper was developed by an independent expert group to identify and define the most important criteria within a clinical workflow using Emdogain® as part of the Scaling and Root Planing (SRP) minimally invasive surgical procedure for periodontal therapy and to standardize the workflow in order to optimize the regenerative potential of Emdogain®. In addition to defining the parameters within the workflow, the authors of the concept paper defined the preconditions and inclusion criteria, as well as exclusion criteria, to help select the appropriate patient population for treatment.

The concept paper is a basis for this study, which aims to provide a clinical assessment of the treatment workflow through a series of controlled cases. The controlled cases in this study will help to further define the workflow and evaluate the workflow based on clinical practicability and usability.

Furthermore this controlled case series will be used to obtain a first indication for the potential of Emdogain® in minimally invasive surgical procedures. Depending on the outcome of this pivotal study future steps in the project will include a defined clinical trial in a larger patient population. This clinical trial will be based on the knowledge gained from these initial controlled cases.

Future steps will also include the transfer of the standardized workflow into daily practice by assessing the conditions under which the workflow can be used and under which it cannot be recommended any more.

The aim of this controlled study is to assess the clinical outcomes and patient reported outcomes of using minimally invasive surgical procedure with Emdogain® as an adjunct (test treatment) or without Emdogain® (control treatment).

2.1 Primary Objective

To evaluate the regenerative potential of Emdogain® by looking at differences in Clinical Attachment Level (CAL) between the test and control treatments.

2.2 Secondary Objectives

To evaluate the regenerative potential of Emdogain® by looking at differences in:

- Gingival Margin (GM)
- Probing Pocket Depth (PPD)
- Full Mouth Plaque Score (FMPS)
- Bleeding on Probing (BoP)
- Post-surgical pain, and
- Root dentin hypersensitivity

between the test and control treatments.

3 Study Design

3.1 Type and Design of Study

This study is a post-market, prospective, split-mouth, controlled, multi-center study. Split-mouth design: each patient receives two treatments that are randomly assigned to either the right or left quadrant of the maxillary or mandibular arches.

- *Test Treatment:* Minimally Invasive Scaling and Root Planing (SRP) and applications of Emdogain®
- *Control Treatment:* Minimally Invasive Scaling and Root Planing (SRP) alone

3.2 Intended Use

Emdogain® is intended as an adjunct to periodontal surgery as a topical application onto exposed root surfaces to provide regeneration of tooth support lost due to periodontal disease or trauma. Emdogain® is indicated for the treatment of the following conditions:

- Intrabony defects due to moderate to severe periodontitis
- Mandibular degree II furcations with minimal interproximal bone loss
- Gingival recession defects in conjunction with surgical coverage procedures such as the coronally advanced flap technique
- Emdogain® is also indicated for use in a minimally invasive surgical technique in esthetic zones to optimize tissue height for intrabony defects only.

This study will be looking at the use of Emdogain® in minimally invasive surgical technique to optimize tissue height for intrabony defects.

PrefGel® is intended for topical application onto exposed root surfaces during periodontal surgery in order to remove the smear layer, prior the application of Emdogain®.

3.3 Study Treatments

The workflow consists of:

Baseline evaluation:

The initial periodontal examination is conducted at the Visit 1 and includes a complete periodontal charting, including Pocket Probing Depth (PPD), Gingival Margin (GM), Bleeding on Probing (BoP), and Full Mouth Plaque Score (FMPS). This examination will be used to determine eligibility for the study based on inclusion/exclusion criteria (Section 3.7.1 and Section 3.7.2). Also, these are the baseline data used for the statistical analysis.

Treatment:

After qualification for the study, the subject will be randomized and treated with minimally invasive Scaling and Root Planing (SRP). An initial application of Emdogain® is performed during the SRP treatment for one quadrant (test). SRP alone will be performed in the contralateral quadrant (control). In addition, PrefGel® is applied on the test quadrant only (prior to the initial application of Emdogain®).

Based on the reported literature on how long Emdogain® remains in periodontal pockets[11,10] a second application will be carried out 2-3 weeks after the initial Emdogain® application for the test quadrant to ensure longer presence of Emdogain® in the defect. Postoperative treatment is detailed in Section 5.2.3.

Re-evaluation and Follow-Up:

At 3 months, 6 months, 9 months, and 12 months after the initial application of Emdogain®, re-evaluations will be carried out in order to identify residual pockets that are indicated for perio-surgery (PPD ≥ 5 mm). This study design, including a dual application of Emdogain®, clearly aims to differentiate this treatment workflow from the approaches that have been reported in the literature.

3.4 Study Endpoints

The primary analysis will be conducted after all subjects complete the 12 months post-surgery visit:

3.4.1 Primary endpoint

- Change in Clinical Attachment Level (CAL)

3.4.2 Secondary endpoints

- Change in Gingival Margin (GM)
- Change in Probing Pocket Depth (PPD)
- Change in Full Mouth Plaque Score (FMPS)
- Change in Bleeding on Probing (BoP)
- Change in root dentin hypersensitivity
- Frequency of successful probing points (PPD < 5 mm)
- Number of pockets that would normally be treated surgically that are converted to pockets that do not require surgical intervention

Additional analysis will be done at 3, 6, 9 months post-surgery:

3.4.3 Additional endpoints

- Change in Clinical Attachment Level (CAL)
- Change in Gingival Margin (GM)
- Change in Probing Pocket Depth (PPD)
- Change in Bleeding on Probing (BoP)
- Change in root dentin hypersensitivity
- Frequency of successful probing points (PPD < 5 mm)
- Number of pockets that would normally be treated surgically that are converted to pockets that do not require surgical intervention
- Comparison of pain level between treatment groups at 1-2 days, 1 week, and 2 weeks after surgery.

3.5 Study Sample Size

The study will enroll 50 subjects at 4 centers.

3.6 Study Duration

The study is expected to enroll up to 50 subjects through December of 2016. The subject's participation in the study is expected to be 12 months and consists of 8 study visits.

3.7 Study Population

The study population will consist of male or female patients aged 18 to 85, with moderate to severe chronic, generalized periodontitis with pockets of 5 mm – 8 mm probing depth in at least 2 pockets per contralateral quadrants in one arch. Subjects will be recruited at the clinics where the Investigators are practicing in the United States and Canada and possibly through referring dentists' offices. Subjects will also be recruited from a University dental clinic in Germany. Each subject will sign a written consent statement prior to any study procedures.

Subjects who provided consent in writing will be evaluated for eligibility during the screening visit and immediately prior to randomization. Patients will be screened based on the inclusion and exclusion criteria presented below.

3.7.1 Inclusion Criteria

All of the inclusion criteria must be met to qualify for this study:

- Subjects must have voluntarily signed the informed consent form before any study related procedures
- Subjects must be males or females who are 18-85 years of age
- Subjects must have moderate to severe chronic, generalized periodontitis with pockets of 5 mm - 8mm probing depth in at least 2 pockets per contralateral quadrants in one arch (study teeth)
- Subjects must be committed to the study and the required follow-up visits
- Subjects must be in good general health as assessed by the Investigator

3.7.2 Exclusion Criteria

If any of the following are met during screening, the subject or teeth must be excluded from the study and will not classify as subjects or study teeth.

- Subjects taking or intending to take any medications during the duration of the study that will potentially affect healing and inflammation
- Subjects who are currently heavy smokers (defined >10 cigarettes per day or >1 cigar per day) or who use chewing tobacco
- Subjects being treated with systemic antibiotics or subjects that were treated with systemic antibiotics within 3 months prior to treatment in this study
- Subjects with uncontrolled diabetes

- Subjects that are immunocompromised or immunosuppressed
- Subjects that cannot provide informed consent
- Subjects with drug or alcohol abuse
- Subjects that have undergone periodontal root planing or periodontal surgery in the last 6 months
- Subjects that are pregnant
- Subjects with necrotizing periodontitis or periodontitis related to systemic disease
- Teeth with pockets with probing depth ≥ 9 mm will not classify as study teeth
- Teeth with pockets or defects with furcation involvement will not classify as study teeth
- Teeth with mobility degree > 1 without splint will not classify as study teeth
- Subjects with test and control sites in the two quadrants on adjacent teeth
- Patients with compromised health conditions such as uncontrolled diabetes or uncontrolled systemic diseases, disorders or treatments that compromise wound healing, chronic high dose steroid therapy, bone metabolic diseases, radiation or immuno-oppressive therapy, and infections or vascular impairment at the surgical site
- Subjects with conditions or circumstances, in the opinion of the Investigator, which would prevent completion of study participation or interfere with analysis of study results

4 Study Products Description

4.1 General Product Information

Emdogain® is the investigational device in this study. PrefGel® is a product applied prior the application of Emdogain® but is not investigated in this study.

Straumann will provide the four centers with the necessary amount of Emdogain® and PrefGel® for the study. These products delivered for the study are to be used only for the subjects enrolled in the study and according to this protocol.

Emdogain® is a resorbable, implantable material for periodontal regeneration. It consists of hydrophobic enamel matrix proteins extracted from developing embryonal enamel of

porcine origin in a propylene glycol alginate carrier. Once applied onto an exposed root surface the protein self assembles into an insoluble three-dimensional matrix. Emdogain® is supplied in pre-filled, ready-to-use sterile, syringes and available in three sizes (0.15 ml, 0.3 ml, 0.7 ml of the gel). The 0.3 ml and 0.7 ml solution are delivered in packs of 1 syringe, while the 0.15 ml solution is delivered in packs of 5 syringes. The gel has a suitable viscosity to facilitate application directly onto root surfaces exposed during periodontal surgery.

The syringe containing 0.15 ml or 0.3 ml is intended for the treatment of one periodontal defect, while the one containing 0.7 ml for the treatment of up to 3 periodontally involved teeth.

PrefGel® 0.6 ml is a neutral Ethylenediaminetetraacetic acid, Edetic acid (EDTA) formulation intended for topical application onto exposed root surfaces during periodontal surgery in order to remove the smear-layer, prior the application of Emdogain®. Mechanical debridement of a root surface inevitably produces a smear-layer, which in turn may prevent or retard periodontal healing. PrefGel® is packaged in single-use sterilized pipettes.

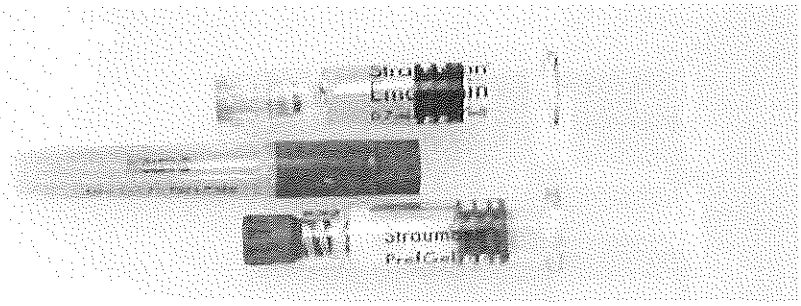

Figure 1: Example of Emdogain® and PrefGel® syringes

4.2 Instructions For Use, Handling and Labeling

Emdogain® and PrefGel® will be used according to the Instructions For Use (Appendix 1 and Appendix 2) containing the approved indications, contraindications, warnings, precautions and sterilization instructions:

- IFU 700019 Emdogain® (US version)
- IFU 701910 Emdogain® (German version)
- IFU 700096 PrefGel®

Emdogain® is CE marked since 1995 (0.3 ml and 0.7 ml syringes) and 2012 (0.15 ml syringe), and received FDA marketing clearance since July 2012 (PMA approval No. P930021 S013). PrefGel® is CE marked since 1997 and subject of cleared 510(k) pre-market notifications K140878 since January 2007.

Emdogain® and PrefGel® will not be used if sterile package is opened or damaged prior to use. The package will be discarded or returned to manufacturer with the enclosed syringe and cannula if this is the case. Each pre-filled syringe is intended for use in one subject only and shall not be re-sterilized or reused. Reuse of single-use devices creates a potential risk of patient or user infection. Contamination of the device may lead to injury or serious illness of the patient.

The products will be **removed from cold storage approximately 30 minutes before use**, applied at ambient temperature and within shelf life.

The plastic top of the syringe will be removed and the supplied application needle will be attached. Emdogain® will be used within 2 hours and any remaining get will be discarded. The syringe and cannula are single use items.

The products must be used within their cleared indications.

All device deficiencies shall be reported by the Investigator to Straumann USA on the Device Deficiency Case Report Form as described under section 7.3.3.

4.3 Storage

The study products should be stored in their original container until used and its access shall be controlled.

Emdogain® and PrefGel® **must be stored in a refrigerator (2 – 8 °C / 36°-46°F)** upon arrival as indicated on the label of the packaging.

Separation of Emdogain® may occur, which is identified as a non-homogeneous gel. Homogenization of the separated material can be achieved by shaking down the gel from the top to the bottom of the syringe, turn around the syringe and repeat the procedure ten to fifteen times until homogenization returns.

4.4 Device Accountability

The Investigator must maintain an accurate and up-to-date accountability record of all study products, Emdogain® and PrefGel®, received, used, discarded (opened, but non-used) and returned during the course of the study. This information shall be recorded in the Device Accountability Record Log.

At each monitoring visit, the monitor will check the investigational device accountability for accuracy and completeness.

At the end of the study, the monitor or Straumann's delegate conducting the closeout visit will perform a final reconciliation of the device accountability (cross check between the Device Record Accountability Log, the shipments delivery notes and the acknowledgement of device receipts).

4.5 Return of Study Device

After treatment of the last subject, any remaining unopened study products at site must be returned to Straumann and acknowledged for receipt. A copy of the acknowledgement of receipt must be filed in the Investigator Site File.

4.6 Risk Analysis, Risk/Benefits

The device risk analysis and risk assessment for Emdogain® and PrefGel® was conducted according to EN ISO 14971, part of the Straumann risk management process which ensures adequate handling of risk analysis, risk evaluation, risk control and evaluation of overall residual risk acceptability. Full results are included in the Risk Management Report for Emdogain®, PrefGel® and Osteogain Version 1.0 dated 1 September 2014.Refer to the Section 7.2.6 of this protocol for a description of the anticipated adverse device effects.

Read carefully the risks associated with the investigational device and the procedures involved in its use listed in Instructions For Use in Appendix 1 and Appendix 2 under Warning and Cautions/ Precautions.

An anticipated benefit of the application of Emdogain® in combination with the minimally invasive surgical technique is the decrease of pain at treatment until 2 weeks after the surgery, as the decrease in root dentin hypersensitivity.

The identified hazards have been mitigated and the overall residual risks for the described medical devices are in the acceptable range.

In conclusion, the risks associated with the use of the Emdogain® and PrefGel® are acceptable when weighed against the benefits to the patient.

5 Study Procedures

5.1 Subject Screening and Baseline Evaluation

5.1.1 Informed Consent

The informed consent process will be conducted at Visit 1. It is the responsibility of the Principal Investigator, or a person designated by the Principal Investigator, to obtain informed consent from each subject participating in this study prior to any study related procedures. As part of the informed consent discussion with a potential subject, the Investigator or designee will provide an adequate explanation of the overall requirements/procedures of the study, purpose of the study, the nature of the planned treatment, any alternative procedures, and possible risks, complications, and benefits of the study. The Investigator or designee will also explain that the subjects are completely free to refuse to enter the study or to withdraw from the study at any time for any reason without prejudice.

The informed consent process will be approved by an Institutional Review Board (IRB) before consenting can begin. The Informed Consent Form (ICF) will be available in the primary language of the subject. This IRB approved consent form will be signed and dated by the subject and the person obtaining consent. Investigators will keep the original signed informed consent document in a secure location and a copy of the signed consent form will be given to the subject.

If new safety information results in significant changes in the risk/benefit assessment, the consent form will be reviewed and updated if necessary. All enrolled subjects will be informed of the new information, given a copy of the revised form and asked to provide consent to continue the study.

5.1.2 Inclusion and Exclusion Criteria

The inclusion and exclusion criteria will be evaluated at the screening visit. Subjects must fulfill all of the inclusion criteria and not meet any of the exclusion criteria. If this condition is not fulfilled, these patients will be considered as screen failures.

5.1.3 Medical and Dental History

Relevant medical history (e.g., allergic reactions, systemic diseases) and current medical conditions will be evaluated by the Investigator based on the information available. The information may be obtained from the subject's general physician or from oral communication with the subject.

Medical History:

If patient needs pre-medication

- Smoker: "yes" or "no"; if "yes", how many
- If patient has been treated with systemic antibiotics, if "yes"; for how long
- If patient has uncontrolled diabetes: "yes" or "no"
- If patient is immunocompromised in anyway
- If patient has history of drug or alcohol abuse
- If patient is pregnant: "yes" or "no"

Dental History:

- If patient has undergone any periodontal root planing or periodontal surgery in the last 6 months

5.1.4 Demographics

Subject demographics, including age, gender, and race/ethnicity, will be documented at the screening visit.

For race, the subject may select American Indian or Alaskan Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, or White. For ethnicity, data will be collected on whether the subject is Hispanic or Latino.

5.1.5 Pregnancy Test

Women of child-bearing potential (women who are not surgically sterile or postmenopausal (defined as amenorrhea for >12 months)) must perform a pregnancy test (validated over-the-counter test) at Visit 1, before taking study required radiographs to confirm that the woman is not pregnant. The test result must be documented in the source data. A woman who is pregnant or planing to become pregnant at any point during the study duration cannot be enrolled in this study.

If a woman becomes pregnant during the study, a protocol deviation form should be completed. The woman should be followed for the duration of the pregnancy, without the study required radiographs, and the outcome of the pregnancy should be documented.

5.1.6 Concomitant Medication

Concomitant medication, procedures, and supportive therapies will be recorded at the screening visit. Any changes in the concomitant medications, procedures, and supportive therapies must be documented at each study visit until the end of the study.

5.1.7 Adverse Event Check

At each visit the Investigator should determine if any adverse events occurred since the last study visit by speaking with the subject and reviewing any dental and medical records. These Adverse Events (AEs), along with any adverse events from the current study visit, should be documented and reported as described in Section 7. of the protocol. In addition the Investigator should evaluate the status of any ongoing adverse events throughout the study as specified in Section 7.4.

5.2 Treatment Procedures

The treatment workflow is graphically presented in Appendix 3 and starts from Visit 2 – Surgery Visit.

5.2.1 Selection and Assignment of Quadrants

The inclusion and exclusion criteria will be reviewed (Section 3.7.1 and 3.7.2). If the subject remains eligible, randomized treatment assignment of a quadrant (test or control), will be done via randomization envelopes. At Visit 2, the Investigator or designee will open a sealed randomization envelope. The randomization envelope will identify the treatment assignment for the right and left quadrants, both in the same arch of the eligible patient. **Randomization envelopes must be open in sequential order.**

5.2.2 Surgery - Minimally Invasive Scaling and Root Planing and Emdogain® First Application

Patients that have been randomized and have scaling and root planing with Emdogain® treatment during Visit 2 are considered enrolled in the studyEach subject will receive local anesthetic and be treated in one visit with a sequence of steps defined by the treatment assignment:

- Test treatment: For the quadrant assigned to scaling and root planing + Emdogain® the following steps should be conducted for treatment: scaling and root planing, control of bleeding, application of PrefGel® (until there is clear overflow from the pocket) to remove any residual smear layer for 2 minutes, irrigation with sterile saline thoroughly, and application of Emdogain® starting apically and advancing coronally until there is clear overflow from the pocket.

- Control treatment: For the contralateral quadrant, assigned to scaling and root planing alone, the following steps should be conducted at the same visit as the test treatment: scaling and root planing and control of bleeding.

Mechanical debridement will be carried out in the manner commonly performed by the clinician (e.g., hand instrumentation, ultrasonic scalers with diamond tips). No antimicrobial agents or techniques (antibiotics or antiseptics, photodynamic therapy) will be applied during treatment. No vasoconstrictors (other than 1:100 000 or 1:200 000 epi in local anesthetic) or hemostatic agents will be used in surrounding soft tissues or pockets. Bleeding will be stopped by conventional techniques as much as possible. No sutures or periodontal dressings will be applied.

In order to standardize treatment across centers, only loupes or a microscope can be used as an assistive visual aid for debridement and removal of calculus from defects.

Other quadrants not being evaluated in the study should be treated according to standard practice.

5.2.3 Plaque Removal and Emdogain® Second Application

After the surgery, all subjects will be given a periodontal cleaning with supragingival plaque removal for both the test and control quadrants at Visit 3. At this visit, Emdogain® will be re-applied to the test quadrant. In detail, this procedure involves no anesthesia, supragingival plaque removal at low power setting, no Prefgel® application, and application of Emdogain® will start apically and advance coronally (as appropriate for treatment assignment group).

Other quadrants not being evaluated in the study should be treated according to standard practice.

5.2.4 Post Treatment Instructions

After both procedures described above, at Visit 2 and 3, the subject will be sent home with post-treatment instructions that includes the use of antiseptic oral rinse (e.g., 0.12% chlorhexidine solution) for one week with no brushing during that time. The subject will also be instructed to refrain from flossing or using a waterpik for one month after the treatment. No local or systemic antibiotics should be prescribed. When brushing, soft brushes are recommended to be used on a 90° angle on the tooth surfaces in order to avoid sulcular brushing.

5.2.5 Supragingival Prophylaxis

Supragingival Prophylaxis includes plaque control and supra-gingival teeth cleaning, with no subgingival instrumentation.

5.2.6 Regular Periodontal Maintenance

At each follow-up visit, regular periodontal maintenance will be provided and may include plaque control, supra-gingival teeth cleaning, or any other necessary therapy that is standard practice at the study center.

5.3 Outcome Assessments

The following measurements will be taken by the same examiner throughout the study.

5.3.1 Pocket Probing Depth (PPD)

Probing Pocket Depth (PPD) will be measured by recording the distance from the gingival margin to the bottom of the probable pocket at 6 sites (mesiofacial, facial, distofacial, distolingual, lingual, mesiolingual) on the teeth in the contralateral quadrants.

Assessment will be done at screening/baseline visit and from the 3-month to the last follow-up visit.

5.3.2 Gingival Margin (GM)

The Gingival Margin (GM) measurements will be performed simultaneously with the PPD measurements. GM will be measured by recording the distance from the Cemento-Enamel Junction (CEJ) to the margin of the gingiva at 6 sites (mesiofacial, facial, distofacial, distolingual, lingual, mesiolingual) on the teeth in the contralateral quadrants.

In periodontal sites with a visible CEJ (see Figure 2), the distance from the CEJ to the margin of the gingiva will be measured as noted in the diagram below.

In periodontal sites with no visible CEJ (see Figure 3), the periodontal probe will be inserted into the periodontal pocket and angulated approximately 45° in order to manually detect the reference line. The depth of insertion into the periodontal pocket will be recorded as the GM.

A negative value for the GM indicates gingival recession. A positive value for the GM indicates the gingiva is covering the CEJ. A zero indicates the gingiva is at the same level as the CEJ.

Assessment will be done at screening/baseline visit and from the 3-month to the last follow-up visit

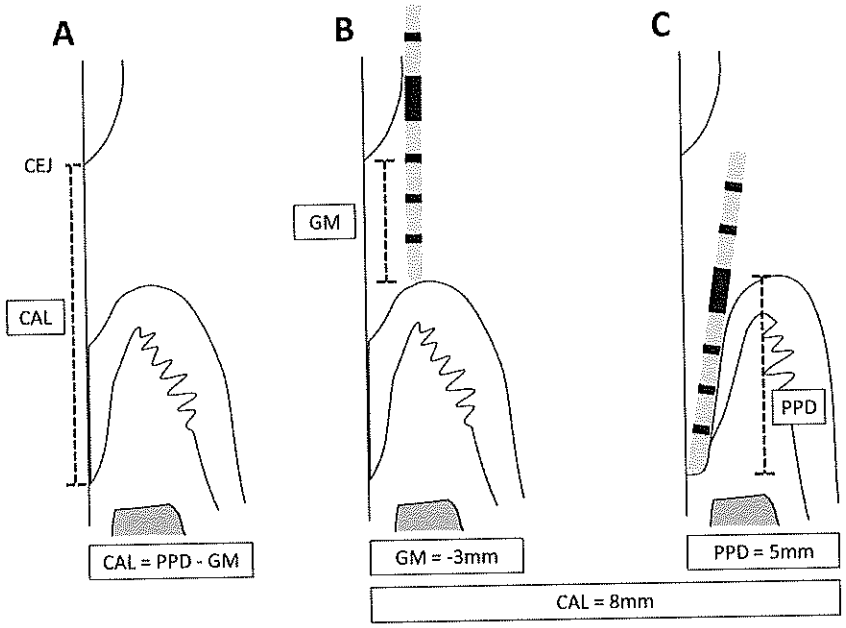

Figure 2: Measurement of the GM when the CEJ is visible.

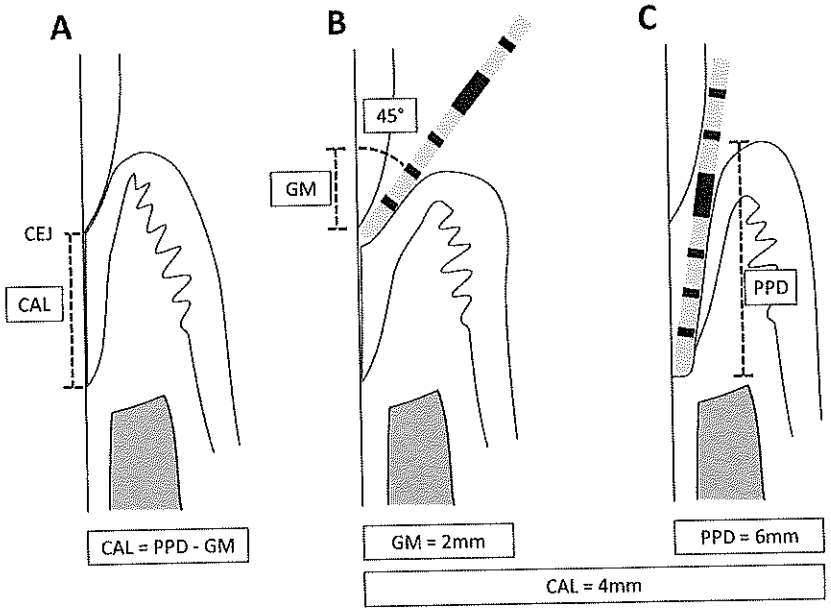

Figure 3: Measurement of the GM when the CEJ is not visible

5.3.3 Clinical Attachment Level (CAL)

Clinical Attachment Level (CAL) measurements will be derived from the PPD and GM measurements as follows:

CAL = PPD - GM

Measurement will be calculated from the PPD and GM values taken at screening/baseline visit and from the 3-month to the last follow-up visit.

5.3.4 Bleeding on Probing (BoP)

Bleeding on probing (BoP) will be measured on the teeth in the contralateral quadrants. The presence of bleeding will be documented as a "yes" or "no" response on 6 sites (mesiofacial, facial, distofacial, distolingual, lingual, mesiolingual).

Assessment will be done at screening/baseline visit and from the 3-month to the last follow-up visit

5.3.5 Full Mouth Plaque Score (FMPS)

The Full Mouth Plaque Score (FMPS) according to O'Leary *et al* should be documented as an indicator for the oral hygiene on each single tooth of the mouth mesial, distal, facial, and lingual.[12] Disclosing agents should not be used to assess plaque.

The FMPS will be assessed with the following formula:

$$\frac{\text{\# of tooth surfaces with plaque}}{\text{total number of tooth surfaces}} \times 100 = \text{FMPS}$$

Assessment will be done at Visit 1, Visit 3 and at the 12-month follow-up visit.

5.3.6 Pain Scale

Postsurgical pain will be measured on a Visual Analog Scale (VAS) (Appendix 4) by asking the patient to assess their pain at three time points after treatment with minimally invasive SRP and Emdogain® application. The three time points will be 1-2 days, 1 week, and 2 weeks after surgery.

Subjects will be given a paper Case Report Form (CRF) to bring home with them and mark their responses on the VAS. The subject will mark a 100 mm scale with a vertical line directly on the CRF. The subject will then return the form to the clinic and a

measurement will be made from the left of the scale to the point of the first marking from the subject to determine the value in mm.

5.3.7 Root Dentin Hypersensitivity

Presence of root dentin hypersensitivity is examined by isolating the neighboring teeth and using a conventional air blast for three seconds on the study tooth. The root dentin hypersensitivity is recorded as "none" (no reaction from the subject), "mild" (sensible with no pain), "moderate" (sensible with slight pain), or "severe" (sensible with pain that persists for a while). Assessment will be done at Visit 2 – Minimally Invasive Scaling and Root Planing and Emdogain® First Application (SURGERY) and from the 3-month to the last follow-up visit.

5.3.8 Radiographs

Peri-apical radiographs, panoramic radiograph, or Cone Beam Computed Tomography (CBCT) of the teeth in the contralateral quadrants will be taken according to the standard practices at the clinic. Ideally images should be taken at screening/baseline visit and at the 12-month visit.

5.3.9 Intra-oral Photographs

Intra-oral photographs will be taken at each study visit to document the initial appearance of the soft tissue and the subsequent healing of the soft tissue after the study treatment. The camera alignment should be perpendicular to the labial surface of the tooth being photographed. Photographs should document all of the treated teeth. A minimum of 5 mm of the marginal soft tissue should be present in the photograph.

Three photographs are required at each visit, including one standard full mouth, and two of the right and left teeth in occlusion. If Visit 1 and Visit 2 are combined, a set of photographs should be taken pre and post-surgery.

Photographs will be labeled for easy identification of the subject and study visit.

5.4 Protocol Related Procedures

5.4.1 Point of Enrollment

The point of enrollment in this study is defined as the moment when the subject is randomized and the investigational device Emdogain® is applied at the study site, during the surgery taking place at Visit 2.

Patients enrolled in the study will be documented in the Patient and Enrollment Log.

5.4.2 Withdrawal Criteria and Procedures

Any subject may withdraw from the study at any time without prejudice and will be offered an alternative treatment for his/her dental condition. Subjects will be advised of the need for the prescribed follow-up visits for their ongoing care, well-being, and collection of any safety data.

- The Investigator may withdraw any subject from the study in the case of:
- Non-compliance with the protocol
- Failure to attend the follow-up visits
- Serious adverse event or adverse event, in the opinion of the Investigator, which prevents the subject's further participation in the study.

The subject withdrawal will be documented on a study termination form and must include the reason for the subject withdrawal. All efforts will be made to capture the primary study endpoint for each subject prior to withdrawal.

If the subject signed consent, but did not meet the inclusion/exclusion criteria, then the subject will be considered a screen failure. This will be documented on the study termination form.

If at any time a subject requires surgery during the course of the study in the region of the mouth being evaluated in the study, then the subject should be withdrawn from the study.

5.4.3 End of Study

Once the subject is seen for the final visit at 12 months post-surgery, the subject will have completed the study. This will be documented on a study completion form.

5.4.4 Subject Replacement Procedures

Subjects that are considered screen failures will be replaced.

Subjects that have been randomized, have scaling and root planing with Emdogain® treatment during Visit 2 are considered enrolled and will not be replaced.

5.4.5 Protocol Deviations

Deviations from the procedures established in the protocol are not permitted. If a deviation occurs, the deviation will be recorded on the Protocol Deviation Log. The sponsor shall be notified immediately of any deviations in informed consent and

inclusion/exclusion criteria (i.e. major deviations), and the IRB shall be notified according to the requirements of the local IRB.

Any deviation from the protocol (including deviations from the expected study visit windows, i.e. minor deviations) may jeopardize the study outcome. Non-compliance of the subjects, as well as of the Investigators, may lead to the closure of the respective study center.

6 Schedule of Assessments

An overview of the schedule of assessments is provided in the Table 1 - "Schedule of Assessments".

6.1 Visit Windows

Subjects need to be seen within the following windows:

Visit #	Visit Name	Visit Window
Visit 1	Informed Consent/Screening & Baseline Visit	14 - 0 Days before enrollment
Visit 2	Final Screening Randomization Minimally Invasive Scaling and Root Planing and Emdogain® First Application	**RANDOMIZATION AND SURGERY** - Point of enrollment **Day 0**
Visit 3	Supragingival Plaque Removal and Emdogain® Second Application	2-3 Weeks ± 2-3 Days
Visit 4	Regular Periodontal Maintenance	1 Month ± 1 Week
Visit 5	3-Month Follow-up Visit	3 Months ± 1 Week
Visit 6	6-Month Follow-up Visit	6 Months ± 2 Weeks
Visit 7	9-Month Follow-up Visit	9 Months ± 2 Weeks
Visit 8	12-Month Follow-up Visit	12 Months ± 2 Weeks

6.2 Visit 1 – Screening & Baseline Visit

This visit should be completed within 14 days prior to the Surgery Visit (Visit 2). An initial evaluation will be conducted to determine whether the subject meets the study inclusion and exclusion criteria.

The following procedures and assessments will be performed and recorded at the screening visit:

- Informed consent
- Medical & Dental history

- Demographics
- Pregnancy Test
- Inclusion/exclusion criteria
- Initial Periodontal Examination and Assessment of Periodontal Status
- Collection of baseline clinical measurements:
    - Pocket Probing Depth
    - Gingival Margin
    - Bleeding on Probing
    - Full Mouth Plaque Score
- Radiographs
- Photographs
- Concomitant Medications
- Adverse Events check

6.3 Visit 2 – Minimally Invasive Scaling and Root Planing and Emdogain® First Application (SURGERY)

Visit 2 needs to be completed within 14 days from the Screening & Baseline Visit. It is possible to conduct Visit 1 and Visit 2 at the same office visit.

The following will be conducted during this visit:

- Final review of inclusion/exclusion criteria and determination of subject eligibility.
- Identification of the contralateral quadrants and treatment assignment
- Root Dentin Hypersensitivity at the study teeth
- Randomization (if subject meets all eligibility criteria).
- Minimally invasive scaling and root planing, control of bleeding, application of PrefGel®, irrigation with sterile saline, and first application of Emdogain® for teeth treated in test quadrant.
- Scaling and root planing and control of bleeding for teeth treated in control quadrant.
- Pain scale completion by the patient

- Post treatment oral hygiene instructions
- Photographs
- Concomitant Medications
- Adverse Events check

6.4 Visit 3 - Supragingival Plaque Removal and Emdogain® Second Application

The patient will be recalled for a visit at 2-3 weeks after the surgery, for a periodontal cleaning with supragingival plaque removal and reapplication of Emdogain® according to the treatment assignment.

In particular, the subject will have the following procedures and/or evaluations performed and documented:

- Supragingival plaque removal for both test and control quadrants
- Emdogain® re-application to teeth treated in test quadrant (no PrefGel® re-application)
- Full Mouth Plaque Score
- Pain scale completion by the patient
- Post treatment oral hygiene instructions
- Photographs
- Concomitant Medications
- Adverse Events check

6.5 Visit 4 – Periodontal Maintenance

The subject will be recalled for a visit at 1 month after Surgery.

In particular, the subject will have the following procedures and/or evaluations performed and documented:

- Supragingival Prophylaxis.
- Photographs
- Concomitant Medications
- Adverse Events check

6.6 Visit 5 – Follow-up Visit 3 Months

Subjects will be recalled at 3 months after Surgery.

The subject will have the following procedures and/or evaluations performed and documented:

- Data Collection including: Pocket Probing Depth, Gingival Margin, Bleeding on Probing, Root Dentin Hypersensitivity at the study teeth
- Regular Periodontal Maintenance
- Photographs
- Concomitant Medications
- Adverse Events check

6.7 Visit 6 – Follow-up Visit 6 Months

Subjects will be recalled at 6 months after Surgery.

The subject will have the following procedures and/or evaluations performed and documented:

- Data Collection including: Pocket Probing Depth, Gingival Margin, Bleeding on Probing, Root Dentin Hypersensitivity at the study teeth
- Regular Periodontal Maintenance
- Photographs
- Concomitant Medications
- Adverse Events check

6.8 Visit 7 – Follow-up Visit 9 Months

Subjects will be recalled at 9 months after Surgery.

The subject will have the following procedures and/or evaluations performed and documented:

- Data Collection including: Pocket Probing Depth, Gingival Margin, Bleeding on Probing, Root Dentin Hypersensitivity at the study teeth
- Regular Periodontal Maintenance
- Photographs

- Concomitant Medications
- Adverse Events check

6.9 Visit 8 – Follow-up Visit 12 Months / Study End

Subjects will be recalled at 12 months after Surgery.

The subject will have the following procedures and/or evaluations performed and documented:

- Data Collection including: Pocket Probing Depth, Gingival Margin, Bleeding on Probing, Root Dentin Hypersensitivity at the study teeth, with addition of Full Mouth Plaque Score (FMPS)
- Regular Periodontal Maintenance
- Radiographs
- Photographs
- Concomitant Medications
- Adverse Events check

7 Evaluation of Adverse Events

For the avoidance of doubt, ***all*** AE/SAEs as defined below should be collected for all subjects from the time of screening (Visit 1).

7.1 Definitions

7.1.1 Adverse Event (AE)

An AE is defined as any untoward medical occurrence, unintended disease or injury, or any untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device. This definition includes events related to the investigational medical device or the comparator, or events related to the procedures involved. For users or other persons, this definition is restricted to events related to investigational medical devices.

7.1.2 Serious Adverse Event (SAE)

Any adverse event that:

- led to a death
- led to a serious deterioration in the health of the subject, that either resulted in

- a life-threatening illness or injury, or
- a permanent impairment of a body structure or a body function, or
- in-patient or prolonged hospitalization, or
- medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function,

- led to fetal distress, fetal death, or a congenital abnormality or birth defect

A planned hospitalization for a pre-existing condition, or a procedure required by the protocol, without serious deterioration in health, is not considered to be a serious adverse event.

7.1.3 Device Deficiency (DD)

A device deficiency is an inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance. Device deficiencies include malfunctions, use errors and inadequate labeling.

7.1.4 Adverse Device Effect (ADE)

An ADE is an adverse event related to the use of an investigational medical device. This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device. This definition includes any event resulting from use error or from intentional misuse of the investigational medical device. ***Any adverse event which the clinical Investigator believes has even a possible relationship to the device, the event will be classified as and ADE.***

7.1.5 Serious Adverse Device Effect (SADE)

An SADE is an adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

7.1.6 Unanticipated Serious Adverse Device Effect (USADE)

An USADE is a serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report.

7.1.7 Anticipated Serious Adverse Device Effect (ASADE)

An ASADE is a serious adverse device effect which by its nature, incidence, severity or outcome has been identified in the risk analysis report.

Summary of the classification for adverse events:

Adverse events	Non-device related	Device or procedure related	
Non-serious	Adverse Event (AE)	Adverse Device Effect (ADE)	
Serious	Serious Adverse Event (SAE)	Serious Adverse Device Effect (SADE)	
		Anticipated Anticipated Serious Adverse Device Effect (ASADE)	Unanticipated Unanticipated Serious Adverse Device Effect (USADE)

7.2 Assessment of Adverse Events

In the event of an adverse event, the Investigator or another suitably qualified clinician who is trained in recording and reporting AEs and have been delegated to this role (such delegation must be captured in the study site delegation log) must review all documentation (e.g., hospital notes, laboratory and diagnostic reports) relevant to the event.

Each adverse event should be assessed for seriousness, relationship to the study device or the procedure, severity and expectedness, as described below, by the Investigator.

7.2.1 Seriousness

An adverse event will be described as serious if it meets the definition in Section 7.1.2. The rationale for the assessment shall be provided in a short narrative.

7.2.2 Relationship to the Study Device

The Investigator should assess the relationship of the adverse event to the study product and study procedure. The relationship should be assessed using the following categories:

- **Definitely Related** – There is a reasonable causal and temporal relationship between the treatment with the study device and the adverse event.
- **Possibly Related** – The relationship between the treatment with the study device and the adverse event is less likely; however, the determination that there is no relationship cannot be made.
- **Not related** – No relationship between treatment with the study device and the adverse event is obvious

NOTE: Device deficiencies that might have led to an SAE are always related to the medical device.

The Investigator shall provide rationale for the assessment of the expectedness in a short narrative on the AE/ADE Report Form.

7.2.3 Relationship to the Procedure

The Investigator should assess the relationship of the adverse event to the surgical procedure (i.e. application or reapplication of Emdogain®). The relationship should be assessed using the categories described in Section 7.2.2.

The Investigator shall provide rationale for the assessment of the expectedness in a short narrative on the AE/ADE Report Form.

7.2.4 Severity

Each adverse event should be assessed for its severity, or the intensity of an event experienced by a subject, using the following:

- **Mild** – events are usually transient, requiring no special treatment, and do not interfere with the subjects daily activities.
- **Moderate** – events that introduce a low level of inconvenience or concern to the subject and may interfere with daily activities, but are usually ameliorated by simple therapeutic measures
- **Severe** – events interrupt a subject's usual daily activity and traditionally require systemic drug therapy or other treatment

The maximum severity observed is to be recorded, except if there is a significant worsening in an AE/ADE severity after device intake, then the change will be tracked as a new AE/ADE record as follows:

- The same wording describing the original AE/ADE must be used.
- Outcome of the initial entry should be designated as 'worsened'.
- The end date of the previous AE/ADE must equal the start date of the new AE/ADE.

7.2.5 Outcome

The outcome should reflect the status of the adverse event at the moment of recording.

- **Resolved without sequelae**- The subject fully recovered from the event without any sequelae. This option also applies when it is unknown whether there are sequelae.
- **Resolved with sequelae** - The subject's condition stabilized despite the persistence of sequelae (e.g., lesion or medical condition which is a consequence of the event). This option does not apply to irreversible congenital anomalies (see under "ongoing").
- **Ongoing** – The subject has not yet recovered from the event. By convention, in the case of an irreversible congenital anomaly, the "Ongoing" option should be chosen and understood as "Not recovered/Not resolved". The same applies to conditions that are not yet resolved, but are controlled by medication (e.g., diabetes, epilepsy) and therefore may not have any symptoms.
- **Worsened** - The severity of the AE/ADE increased.
- **Fatal** – The event is related to a death; whether it caused death or contributed to it. If the subject died of a different cause, prior to resolution of the AE/ADE, the outcome of this AE/ADE should designated "Ongoing", and not "Fatal", and an end date should not be specified.
- **Unknown:** Knowledge of the current status of the AE/ADE is truly not available to the Investigator (i.e. event was ongoing at last observation, but no further contact with the subject could be established). However, all efforts should be made to determine the outcome of any AE, especially that of an SAE/SADE.

7.2.6 Expectedness

If the adverse event is judged to be related to the device, the Investigator will make an assessment of expectedness based on knowledge of the reaction and any relevant product information as documented in the IFU and current protocol. The event will be classed as either;

- **Expected**: the reaction is consistent with the effects of the device listed in the IFU and protocol;
- **Unexpected**: the reaction is not consistent with the effects listed in the IFU and protocol.

The Investigator shall provide rationale for the assessment of the expectedness in a short narrative on the AE/ADE Report Form.

Potential expected adverse events following the application of Emdogain® by type and in order of severity, observed in the clinical trials, are listed below:

Adverse Event type	Adverse Event description
Sensitization	*Low rate of sensitization to Emdogain® as a result of repeated use.*
Local soft tissue reactions	*Local redness, inflammation soreness, gingival irritation, hematoma/ecchymosis, oral candidiasis, tissue necrosis/cratering, angulitis, herpes-like blisters, hypoesthesia (burning and itching reaction on the tongue), oral mucosal reaction, fibrin layer, discoloration.*
Local tooth-related reactions	*Increased tooth mobility, hypersensitive root surfaces (root sensitivity), pain.*
General reactions	*Urticaria, itching skin reaction, gastrointestinal disturbances, urogenital disturbances.*

Potential expected adverse device effects following the application of PrefGel®: Reversible and short duration procedure-related dentin hypersensitivity may occasionally occur.

7.3 Procedure for Reporting Adverse Events

Adverse event reporting will begin at the time a subject provides written informed consent and ends after a subject withdraws from the study or completes the final study visit.

For screen failure subjects, any AEs, ADEs, and DDs that occur from the time of informed consent up until the date on which the subject is deemed ineligible for the study will be recorded on a case report form.

Only one AE/ADE Report Form or SAE/SADE Report Form should be completed per event.

To ensure patient confidentiality, the following reports will include the patient number only.

7.3.1 AE Reporting

In the occurrence of an adverse event (AE), the AE/ADE Report Form should be completed in a timely manner. Safety reporting to the Institutional Review Board (IRB) should occur according to the requirements of the local IRB.

7.3.2 SAE Reporting

In the occurrence of a serious adverse event (SAE), expedited reporting requirements are followed. The SAE/SADE Report Form should be completed within 24 hours of awareness of the event and sent to Straumann by fax or email.

Safety reporting to the Institutional Review Board (IRB) should occur according to the requirements of the local IRB.

It is recognized that in many cases SAEs will be treated in a medical rather than a dental environment and the Investigator may not have immediate knowledge of the event. The Investigator should report an SAE as soon as he/she has knowledge of the event within the above time frame irrespective of when the actual event occurred.

7.3.3 DD Reporting

The Investigator should report all Device Deficiencies (DD) by completing the Device Deficiency Case Report Form.

When a device deficiency leads to a potential AE (e.g. bleeding, pain, swelling, infection, peri-implantitis), the AE/ADE Report Form needs to be additionally completed in a timely manner.

Moreover, device deficiencies with SADE potential (e.g. nerve encroachment, sinus perforation, etc.) must be recorded in the SAE/SADE Report Form and follow the expedited reporting requirements (within 24 hours).

7.3.4 ADE Reporting

Adverse device effects (ADE) must be recorded and submitted to Straumann by completing the AE/ADE Report Form in a timely manner. Safety reporting to the Institutional Review Board (IRB) should occur according to the requirements of the local IRB.

7.3.5 SADE Reporting

In the occurrence of a serious adverse device effect (SADE), expedited reporting requirements are followed. The SAE/SADE Report Form should be completed within 24 hours of awareness of the event and sent to Straumann by fax or email.

7.3.6 Additional Safety Reporting

Straumann will report additional safety information to the centers that is relevant to the protocol or study device and may affect the risk/benefit ratio, the rights, safety or welfare of subjects, or the integrity of the study. Such reports may include notification of any changes to the Instructions for Use, any publications or interim reports, or any product recalls.

7.4 Monitoring of Subjects with Adverse Events

Any AE that occurs during the course of this study must be monitored and followed-up by the Investigator until one or more of the following have occurred:

- The AE is resolved,
- Pathological laboratory findings have returned to normal,
- Steady state has been achieved, or
- It has been shown to be unrelated to the study products

It is the responsibility of the sponsor to cooperate with the Investigator to assure that any necessary additional therapeutic measures and follow-up procedures are performed.

8 Statistical Analysis Procedures

The statistical analysis principles described below will be supplemented by a detailed Statistical Analysis Plan (SAP).

8.1 Sample Size Calculation

This is a pilot study with a goal to create a standardized treatment workflow that can later be tested in further studies to show that Emdogain® can effectively promote periodontal regeneration as part of the minimally invasive surgical procedure. This study will help to define the selection criteria for clinical preconditions to allow treatment via the envisaged surgical treatment workflow. A sample size of 50 subjects will be adequate for this pilot phase considering a possible dropout rate of up to 15%.

8.2 General Statistical Methods

A qualified statistician using validated statistical software will perform all statistical analysis according to the planned statistical testing provided in the Statistical Analysis Plan (SAP).

95% confidence intervals will be calculated based on the SAP to support the descriptive statistics, where necessary.

Unless otherwise specified, the data will be summarized for non-missing subjects in tables listing the number of subjects, and the mean, 25% percentile, median, 75% percentile minimum, maximum, standard deviation in each treatment group for continuous data (e.g., PPD, GM, CAL, FMPS and pain), or number of subjects and percentage in each treatment group for categorical data (e.g., Bleeding on Probing, Root Dentin Hypersensitivity), as appropriate. In general the denominator for the percentage calculation will be based upon the total number of subjects (N) in the study population, unless otherwise specified.

8.2.1 Baseline Characteristics

The baseline data are presented on the basis of all screened subjects. They are collected at the Visit 1 and include: Medical & Dental History, Demographics, Inclusion & Exclusion Criteria, Concomitant Medications, Adverse Event Check, PPD, GM, CAL, FMPS, and Pain (see details in Section 5.1 and 5.3).

To assess balance in baseline characteristics, the distribution of each baseline variable of interest will be compared between the two treatment groups, i.e. test and control quadrants of the same arch. Continuous variables will be summarized using mean, median, standard deviation, 95% confidence interval, and range; testing between the two groups will be based on a two-sample t-test (or Wilcoxon rank-sum test as appropriate). Categorical variables will be summarized using counts and percentages, and differences between treatment groups will be assessed using a Chi-square test (or Fisher's exact test as appropriate).

8.2.2 Treatment Procedures

The treatment procedures data is presented on the basis of all enrolled patients. They are performed at Visit 2 and 3 (see details in Section 5.2).

Summaries of treatment procedures and supportive measures will be presented by assigned treatment group (test and control). Detailed information regarding the treatment procedures will be presented in listings (i.e. details per patient).

8.2.3 Other Data Summaries

Protocol deviations will be summarized by deviation type and study center.

Concomitant medications will be presented in listings and also summarized by drug category.

Adverse events will be presented in listings and also summarized by event category.

8.2.4 Subject Disposition

A description of subject disposition falling in various subgroups of interest, such as consented, screen failures, enrolled, withdrawn early, completed study, will be provided by study center. Moreover, a detailed description providing the reason of any screen failures or early withdrawal by subgroup will be done.

8.2.5 Missing Data

Every effort will be made to minimize the amount of missing data. If subjects drop out of the study prior to completing their primary endpoint assessment, every effort will be made to measure their primary endpoint immediately prior to discontinuation if possible.

Techniques for handling missing data and the presence of outliers will be provided in the Statistical Analysis Plan.

8.3 Planned Statistical Analysis

Two analyses will be performed: A primary analysis at 12 months and an interim analysis at 3 months post-surgery. An optional interim analysis at 6 and 9 months post-surgery may also be performed. Descriptive summary statistics will be computed for all endpoints of the primary and interim analysis.

The data of the four study centers will be pooled. Pooling is justified by applying a high degree of standardization of study procedures and investigator training.

8.3.1 Primary Analysis of Primary Endpoint

Change in Clinical Attachment Level (CAL) between the surgery and 12 months post-surgery will be measured as the primary endpoint.

Statistics of the primary endpoint will present the seven-point scales (mean, standard deviation, minimum, 25% percentile, median, 75% percentile and maximum) of the change in CAL on the site of interest for each treatment group.

8.3.2 Primary Analysis of Secondary Endpoints

Statistics of the secondary endpoints will present the seven-point scales of the change in GM and PPD on the site of interest for each treatment group, and the change in

FMPS. Additionally, the percentage of Bleeding on Probing and Root Dentin Hypersensitivity on the site of interest will be presented by treatment group.

Investigator's assessment on the number of pockets that would normally be treated surgically that are converted to pockets that do not require surgical intervention will be presented.

The influence of pocket size as a factor impacting outcomes will also be evaluated with pocket size being categorized into two groups: 5 - 6 mm pockets and 6 - 8 mm pockets. Other covariates may be considered in the exploratory analysis.

8.3.3 Interim Analysis of Endpoints

Interim analysis will be performed for all above endpoints between the surgery and 3 months post-surgery. Optional interim analyses will be performed at 6 months and 9 months post-surgery, as applicable.

In addition, the seven-point scales (mean, standard deviation, minimum, 25% percentile, median, 75% percentile and maximum) of the change in pain for each treatment group will be presented at 1-2 days, 1 week and 2 weeks after surgery.

9 Data Management

The general data management procedures are described below, details can be found in the separate Data Management Plan (DMP).

Required clinical data for this study will be collected and recorded in the clinical database using a paper Case Report Form (CRF) for all study subjects from whom informed consent is obtained. Site numbers and subject numbers will be used to track subject information throughout the registry. The Principal Investigator or authorized designee is responsible for the timely completion and signature of all CRFs.

All original CRFs will be retrieved from the site by the study monitor and sent to the data management. Double data entry and computer programmed error checks will be carried out by data management personnel for inconsistent, illogical and/or missing data. If validation of data leads to discrepancies, data management will generate queries. The timely resolution of the queries is under the responsibility of the monitor and the Investigators at site. The query process is an ongoing process starting with the first data entered into the database.

The electronic clinical database used for this study has a security system that prevents unauthorized access to the data and any deletion of data (audit and edit trail). All above mentioned tasks will be carried out according to Straumann Standard Operating Procedures,

except for those tasks performed by Straumann contracted Contract Research Organizations (CRO), where the CRO procedures shall be used.

10 Obligations of the Principal Investigator

10.1 Investigator Compliance

The Investigators must work according to standard ethical practice as laid down by their professional body and insert the product according to what is described in the handling procedures and the IFU for the products investigated in this clinical study. In addition they must work in accordance with the "Declaration of Helsinki" (last revision Fortaleza 2013, Appendix 5), the ISO 14155:2011, GCP, and with local legal and regulatory requirements.

The Investigators will ensure that the study is conducted in compliance with this protocol and the Clinical Study Agreement. Furthermore, they are responsible of conducting the informed consent process (section 5.5.1).

11 Study Management

11.1 Regulatory and Ethical Requirements

11.1.1 Informed Consent

Written informed consent will be obtained from all subjects prior to study participation as described in Section 5.1.1.

11.1.2 Institutional Review Board

Prior to initiation of any study procedures, the protocol and informed consent will be submitted to each local Institutional Review Board (IRB) for review and approval. In addition, any amendments to the protocol or informed consent will be reviewed and approved (if necessary) by the IRB. The study will not begin until the required approval from the IRB has been obtained. Any additional requirements imposed by the IRB shall be followed.

The Investigator will provide the appropriate reports to the IRB during the course of the clinical study including the following:

- Informing the IRB of the study progress periodically as required, but at a minimum annually
- Reporting any unanticipated serious adverse device effects within 10 working days of becoming aware of the event

- Reporting any deviations from the protocol that adversely affect the risk/benefit ratio, the rights, safety, or welfare of the participants, or integrity of the study
- Providing any other reports requested by the IRB

11.1.3 Study registration

This protocol will be registered at clinicaltrials.gov at the study start.

11.2 Record Management

The following will be required from the Investigator prior to the initiation of the study:

- A signed confidentiality agreement
- Signed and dated curriculum vitae of the Investigator (s) and a copy of his/her dental license
- Signed Financial Disclosure
- A signed copy of the final protocol and any amendments
- A signed copy of the clinical study agreement with the sponsor
- IRB approval letter and IRB approved informed consent document

11.2.1 Case Report Forms

Required clinical data for this study will be collected using a paper CRF for all study patients from whom informed consent is obtained. Site numbers and patient numbers will be used to track patient information throughout the study to respect confidentiality.

The Principal Investigator or authorized designee will be responsible for the accuracy of the data entered on the CRFs from source documents, query resolution and signature of all CRFs. The Investigator will also allow a Straumann representative and/or regulatory bodies to review the data reported on the CRFs with the source documents as far as is permitted by local regulations.

11.2.2 Source Documents

Source documents are defined as the original point of entry of a specific data point. Source documents will include, but are not limited to, progress notes, electronic data, computer printouts, radiographs, and recorded data from automated instruments. All source documents pertaining to this study will be maintained by the Investigator and made available for inspection by authorized persons.

11.2.3 Records/Data Retention

Original radiographs, photographs, and study documents will be maintained at the study center in a file established for this study. All study documentation needs to be stored at the study center for at least twenty (20) years following the completion of the study, as specified by the sponsor. The Investigator should have access to the study documents in order to answer any queries associated with the study. All other study records will be kept by Straumann once the study has been completed. These records will be maintained at Straumann according to Straumann's Standard Operating Procedures (SOP).

11.3 Monitoring

Straumann will assign a qualified individual to monitor the study.

The study specific monitoring procedures for performing site visits, frequency, data verification, data corrections, adverse event reporting and tracking, device accountability, regulatory documents review, visit communication and reporting are described in the separate Monitoring Plan.

11.3.1 Pre-Study Meetings

After selection of all Investigators, Pre-Study Meetings were conducted during the preparation phase for the study, at congresses, to explain the study requirements and ensure the sites are fully capable and equipped to participate in the study.

11.3.2 Study Initiation Visit

Once a site receives IRB approval and before enrollment in the study starts, the monitor will schedule a site initiation visit in order to make sure all study documents are in place and that all the site personnel that will participate in the study are trained on the study procedures. The monitor will ensure during the study initiation that the Investigator clearly understands and accepts the responsibilities and obligations of conducting a clinical study:

- Understands the clinical protocol and relevant items outlined in the protocol (including inclusion/exclusion criteria, AE and SAE reporting requirements)
- Understands and accepts the obligations to obtain informed consent
- Understands how to document study data (especially the importance of having supporting documentation for AE assessment)

- Understands the information outlined in the Investigator 's brochure, including proper device usage
- Understands aspects of study device accountability (i.e. how to obtain the device, how to store the device, how to document device receipt, usage and return)
- Understands and accepts the obligation to obtain IRB review and approval of the protocol and informed consent, and to ensure continuing review of the study by the IRB
- Has adequate facilities and access to an adequate number of suitable subjects to conduct the study

11.3.3 Routine Monitoring Visits

Monitoring visits will be scheduled and conducted periodically during the course of the study to supervise study procedures as defined in the Monitoring Plan, but at a minimum annually to review the following:

- The study is in compliance with the currently approved protocol/ amendment(s); deviations will be discussed with the responsible Investigator, documented, and reported to the sponsor and IRB (according to the IRB policy).
- The study is in compliance with Good Clinical Practice (GCP) and with the applicable regulatory requirements
- Only authorized Investigators/ clinical personnel are participating in the clinical investigation
- Device accountability including adequate supply at center, proper storage, and documentation of device traceability.
- The reported study data entered on CRFs are accurate, complete, and verifiable from source documents
- All adverse events and serious adverse events are reported correctly. In cases where there is missing information about an adverse event or missing evidence to support the Investigator's assessment, a monitor will review and discuss the adverse event with the responsible Investigator.
- The reason for a subject's withdrawal has been documented

The Investigator is providing to the sponsor the necessary study records for a thorough review of the study's progress.

11.3.4 Study Closeout Visit

After the last subject has completed the study, all the data have been collected (there are no more outstanding AEs/SAEs & all outstanding Queries/data clarification forms have been resolved appropriately), the database is locked and ready for statistical analysis, the closeout visit will be conducted at the center. The following tasks should be completed at the last visit by Straumann or the monitor:

- Ensure that device accountability is complete
- Ensure that the documentation and clinical investigation requirements were met
- Collect outstanding documents (original signed tracking logs) and ensure that the Site Files are complete
- Ensure that adverse events were reported to the IRB according to the IRB's policy and that the IRB was notified in writing of the study completion
- Review any outstanding questions from the Clinical Investigation Report and organize the signature process
- Organize the archiving of all study-related documents and remind the Investigator of the obligation to retain the records and to notify Straumann in case the site is informed of an inspection by a regulatory authority.

11.4 Study Termination or Premature Termination

At study termination, a Clinical Investigation Report will be prepared by the sponsor, even if the study was terminated prematurely. The report will contain a summary of the study results and made available to the participating Investigators.

The study can be terminated earlier at the discretion of the Investigator or the sponsor in the case of any of the following:

- Occurrence of adverse device effects unknown at the start of the study with respect to their nature, severity, and duration, or the unexpected excessive incidence of known adverse device effects
- New scientific knowledge obtained after the start of the study showing the ethical claim of the study is no longer valid

Patients will be advised of the need for follow-up visits for their ongoing care and well-being.

11.4.1 Study Discontinuation

The study Center will be closed and the study terminated under the following circumstances:

- The Center is not recruiting a sufficient number of subjects or is unlikely to recruit a sufficient number of subjects
- The Center does not respond to study management requests
- Repeated protocol violations have been discovered that affect the integrity of the study or the study data.

11.5 Protocol Amendments

Once the first subject has entered the study, any part of this study plan can be amended upon agreement of the sponsor and the participating Principal Investigators throughout the clinical investigation. Protocol changes will be kept to a minimum. Only those changes that are deemed essential to the successful completion of the protocol will be considered.

The reasons and justifications for the amendment will be included with each amended section of the document, and the amendment will include a version number and date. Once the Investigator and the sponsor have accepted the changes, a written amendment to the protocol will be sent to the Investigator for signature.

All significant protocol changes affecting the scientific soundness of the study or the rights, safety, or welfare of subjects which occur after the initial IRB approval, must be submitted for approval by each center to the IRB as an amendment to the original protocol before the changes can be implemented by the Investigator. Each investigational center will send a copy of the IRB approval letter for the amendment to Straumann.

Requests for clarification statements to the protocol shall be discussed with the study monitor. The clarification statements will be sent to each Investigator and will be kept in the appropriate file.

11.6 Publications

Analysis of data will be conducted by Straumann and the final report will be prepared by Straumann with input from the Investigators. Any publications or presentations utilizing the

data from this study must be reviewed by Straumann prior to submission according to the time frame specified in the Clinical Study Agreement.

12 Protocol Signature Page

Protocol: CR 01/15

Study Title: Straumann® Emdogain® Application In Conjunction With Minimally Invasive Surgical Technique For Periodontal Disease Treatment: A Split-Mouth Design Study.

Version: Version 5.0; Date: 29-Mar-2018

I have read the foregoing protocol and agree to conduct the study as outlined. I agree that the examinations and follow-up visits required by the study protocol are in accordance with the standard treatment plan for dental implant subjects.

Signature:

Clinical Center Name	Clinical Center Number	
Printed Name of Investigator	Signature of Investigator	Date

Received by Sponsor:

Printed Name of Study Manager	Signature of Study Manager	Date

13 References

[1] Gutierrez MA, Mellonig JT, Cochran DL. Evaluation of enamel matrix derivative as an adjunct to non-surgical periodontal therapy. J Clin Periodontol. 2003 Aug;30(8):739-45.

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[3] Harrel SK, Wilson TG, Nunn ME. Prospective assessment of the use of enamel matrix proteins with minimally invasive surgery. J Periodontol. 2005 Mar;76(3):380-4.

[4] Mombelli A, Brochut P, Plagnat D, Casagni F, Giannopoulou C. Enamel matrix proteins and systemic antibiotics as adjuncts to non-surgical periodontal treatment: clinical effects. J Clin Periodontol. 2005 Mar;32(3):225-30.

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[10] Wennström JL, Lindhe J. Some effects of enamel matrix proteins on wound healing in the dento-gingival region. J Clin Periodontol. 2002 Jan;29(1):9-14.

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Appendix 1 – Instructions For Use IFU 700019 (US version) - Emdogain®

V 07/12 700019-8
D 07/12

straumann

Straumann® Emdogain (0.15, 0.3 and 0.7 ml) 30 mg/ml

Presentation: Straumann® Emdogain, Enamel Matrix Derivative 30 mg/ml, Propylene Glycol Alginate in aqueous solution.

Manufactured by: Institut Straumann AG, CH-4002 Basel/Schweiz, www.straumann.com

Distributed by: Straumann USA, LLC, 60 Minuteman Road, Andover, MA 01810 USA, Phone: 800/448 8168

Emdogain Instructions for Use
Straumann® Emdogain is a resorbable, implantable material for periodontal regeneration. It consists of hydrophobic enamel matrix proteins extracted from developing embryonal enamel of porcine origin in a propylene glycol alginate carrier. Once applied onto an exposed root surface the protein self assembles into an insoluble three-dimensional matrix. Emdogain is supplied in a pre-filled, ready-to-use sterile, syringe. The gel has a suitable viscosity to facilitate application directly onto root surfaces exposed during periodontal surgery.

Indications for Use
Emdogain is intended as an adjunct to periodontal surgery as a topical application onto exposed root surfaces. Emdogain is indicated for the treatment of the following conditions:

- Intrabony defects due to moderate or severe periodontitis
- Mandibular degree II furcations with minimal interproximal bone loss
- Gingival recession defects in conjunction with surgical coverage procedures such as the coronally advanced flap technique
- Emdogain is also indicated for use in a minimally invasive surgical technique in esthetic zones to optimize tissue height for intrabony defects only.

In cases of wide defects or where soft tissue support is desired, Straumann® Emdogain can be used in conjunction with a bone graft material. For further information on the use of Emdogain with bone graft materials, please refer to **"For Straumann® Emdogain in Conjunction with Bone Graft Material in Wide Defects"** in the Clinical Procedure Section of these Instructions.

Contraindications
Emdogain should not be used in patients with disorders or conditions including, but not limited to the following: uncontrolled diabetes or other uncontrolled systemic diseases, disorders or treatments that compromise wound healing, chronic high dose steroid therapy, bone metabolic diseases, radiation or other immuno-oppressive therapy and infections or vascular impairment at the surgical site.

Warnings

- Immunological studies suggest that a small number of patients may become sensitized to Emdogain as a result of repeated use. Please use caution in patients predisposed to allergic reactions and follow patients receiving repeated use closely. Post-market experience has indicated that the sensitization adverse reaction rate is low. Required treatment has ranged from no intervention needed to analgesics and/or antihistamines.
- The safety and effectiveness of Emdogain has not been established in patients undergoing anticoagulant therapy. Careful consideration should be given before using Emdogain for these patients.
- Emdogain is intended for application around teeth only. Gain of tooth support occurs only to the level on the root surface covered by the repositioned oral soft tissue. Therefore, Emdogain should be used in areas where there is adequate tissue for root coverage. Emdogain should be used only after plaque and calculus have been removed from the diseased site.

Precautions

- Appropriate oral hygiene is necessary for proper healing to take place. Please refer to the "Clinical Considerations" section for additional information.
- Clinical and radiographic evaluation should be performed before treatment.
- It is important to maintain asepsis during surgery.

Clinical Considerations

Periodontal devices should only be used by those practitioners familiar with current periodontal therapy and periodontal surgical procedures. Improper technique may yield suboptimal results. Preclinical and radiographic surgical evaluation is imperative. Special effort to maintain asepsis during surgery is most important. To prevent postoperative infection and to optimize healing, the use of an antiseptic mouth rinse is recommended for a period of 3 to 6 weeks post-surgery. Antibiotics may be used if deemed appropriate based on the nature of the severity of the disease/defect and the clinician's judgment.

Since maintenance of a stable wound is a critical factor for success, the patient should be instructed not to brush in the area where surgery has been performed until 6 weeks postoperatively. However, consistent with conventional post-surgical care, the patient should be subjected to "professional tooth-cleaning" as needed. Recommendations for appropriate oral hygiene measures, including methods for interproximal cleaning, should be based on the clinician's judgment, due to the need for extended wound stability, and the awareness that regain of clinical attachment and alveolar bone has been shown to continue for more than a year following treatment with Emdogain. In addition, clinicians have reported on enhanced wound healing in cases treated with Emdogain while patients report less post-surgical discomfort following the use of Emdogain.

Clinical studies with Emdogain demonstrated clinical attachment gain and alveolar bone gain in intrabony defects associated with moderate to severe periodontitis and in mandibular degree II furcations with an interproximal bone level at or above the fornix of the furcation. Radiographic evidence of new bone gain provided the primary support for the use of Emdogain in intrabony defects, while horizontal furcation depth as assessed during re-entry was the primary outcome parameter when evaluating the use of Emdogain in mandibular degree II furcation involvements. Adjunctive use of Emdogain in the treatment of recession type defects has demonstrated equal or better root coverage compared to conventional treatments, as well as an increase in the amount of keratinized tissue.

Histological studies have demonstrated periodontal regeneration (newly formed cementum, periodontal ligament, and alveolar bone). Clinical data demonstrates the long-term stability of regenerated tissue. As in any periodontal surgical therapy, defect morphology, surgical technique and host response are important parameters for successful outcomes.

The following table presents results from three clinical trials evaluating the use of Emdogain in intrabony defects. The data is reported as the difference between the clinical measurements taken at baseline before the initial operation and the clinical measurements taken at the designated follow-up periods. For the clinical parameters of pocket depth reduction and clinical attachment gain, the data are also expressed as the percent difference between the results of the surgical procedure alone and treatment with Emdogain. Radiographic bone gain is reported as the linear measurement and as the percentage of the initial bone loss that was regained.

Adverse Reactions/Complications
A distinction of adverse events seen due to the use of Emdogain alone could not be performed because Emdogain is labeled for use in conjunction with conventional periodontal surgery for which there are associated risks. The adverse events by type and in order of severity, observed in the clinical trials, are listed below.

Local Soft Tissue Reactions
Local redness, inflammation soreness, gingival irritation, hematoma/ecchymosis, oral candidiasis, tissue necrosis/ cratering, angulitis, herpes-like blisters, hypoesthesia (burning and itching reaction on the tongue), oral mucosal reaction, fibrin layer, discoloration.

Local Tooth-related Reactions
Increased tooth mobility, hypersensitive root surfaces (root sensitivity), pain.

General Reactions
Urticaria, itching skin reaction, gastrointestinal disturbances, urogenital disturbances

The following additional adverse events and surgical complications, although not observed in the studies, may be related to this type of surgical procedure and have the potential to occur: postoperative hemorrhage, infection, would dehiscence, sloughing of tissue, paresthesia, bleeding, loosening of sutures.

Directions for Use
Do not use if sterile package is opened or damaged prior to use. To prevent possible contamination, discard or return damaged package with the enclosed syringe and cannula.

Each pre-filled syringe is intended for use in one patient only.

The syringe containing 0.15 ml and 0.3 ml are intended for the treatment of one periodontal defect.
The syringe containing 0.7 ml is intended for the treatment of up to three periodontally involved teeth.

1. Take out the Emdogain from cold storage approx. 30 minutes before use and allow it to assume ambient temperature.

2. Remove the plastic top of the syringe.

3. Carefully attach the supplied application needle.

4. Use Emdogain within 2 hours and discard any remaining gel.

Syringe and cannula are single use items. Do not re-sterilize or re-use syringe or application needle.
Be aware that bending the needle may cause breakage.

Storage
The product should be stored in a refrigerator (36°–46°F) upon arrival.

Separation of Straumann Emdogain may occur. Separation of Straumann Emdogain is identified as a non-homogeneous gel. Homogenization of the separated material can be achieved by shaking down the gel from the top to the bottom of the syringe, turn around the syringe and repeat the procedure ten to fifteen times until homogenization returns.

Clinical Procedure

For Straumann® Emdogain in Conjunction with Periodontal Flap Surgery

1. Anesthetize the area selected for surgery by block and/or infiltration anesthesia. Avoid injection of local anesthetic with a vasoconstrictor into the interdental papilla or marginal gingiva.

2. Make intra-crevicular incisions. Then, if judged appropriate, make one or two vertical releasing incisions extending out into the alveolar mucosa. Raise full-thickness (mucoperiosteal) flaps on the buccal and palatal/lingual surfaces of the teeth. Preserve as much of the gingival connective tissue in the flap as possible. Maintain viability of periodontal cells by hydration of the soft tissue with saline.

3. Only remove the granulation tissue adherent to the alveolar bone and any associated osseous defects necessary to provide full access and visibility to the root surfaces.

4. Remove subgingival plaque and calculus.

5. Remove remaining smear layer by cleansing the root surface with Straumann® PrefGel (EDTA) for 2 minutes. Rinse thoroughly with sterile saline. Avoid contamination of the cleaned root surfaces with saliva or blood after the final rinse.

6. Immediately apply Emdogain onto the exposed root surfaces, starting at the most apical bone level. Apply Emdogain to fully cover the exposed root surface areas. Overflow of surplus material during suturing should occur.

7. Complete coverage of the interproximal area and optimal soft tissue adaptation are essential. If deemed appropriate, a periosteal fenestration at the base of the flap may be used to facilitate coronal repositioning of the soft tissue. Suture materials appropriate for extended stable closure are preferred.

8. The patient should be advised to rinse daily with an antiseptic mouth rinse (e.g. 0.1–0.2 % chlorhexidine solution) until 3–6 weeks post-surgery. Antibiotics may also be used if deemed appropriate based on the clinician's judgment.

9. Sutures may be removed when clinical healing of flaps and the root/soft tissue interface are stable or when they no longer add to the stability of the healing wound.

10. The patient should be instructed not to brush in the area where surgery has been performed until 6 weeks postoperatively. However, "professional tooth-cleaning" should be performed as needed. After the initial healing period, patients are instructed in appropriate tooth cleaning measures, including methods for interproximal cleaning. Recommendations for oral hygiene should be based on the need to maintain extended would stability.

Clinical Procedure

For Straumann® Emdogain in Conjunction with a Minimally Invasive Surgical Technique

1. Anesthetize the area selected for surgery by block and/or infiltration anesthesia. Avoid injection of local anesthetic with a vasoconstrictor into the interdental papilla or marginal gingival.

2. Remove subgingival plaque and calculus from the root surface. Following mechanical debridement, the epithelial lining of the pocket is removed. Apply pressure to the site with a gauze sponge for 1 minute to stop bleeding. Thoroughly rinse the area with sterile saline to remove any blood and or saliva.

3. Remove remaining smear layer by cleansing the root surface with Straumann® PrefGel™ (EDTA) for 2 minutes. Rinse thoroughly with sterile saline. Avoid contamination of the conditioned root surface with saliva or blood after the final rinse.

4. Immediately apply Emdogain onto the root surface, starting at the bottom of the periodontal defect. Apply Emdogain to fully cover the root surface until an overflow of material occurs.

5. Optimal soft tissue adaptation is essential. Sutures can be used to closely adapt the soft tissues to the tooth surfaces.

6. The patient should be advised to rinse daily with an antiseptic mouth rinse (e.g. 0.1–0.2 % chlorhexidine solution) until 3–6 weeks post-surgery. Antibiotics may also be used if deemed appropriate based on the clinician's judgment.

7. Sutures may be removed when clinical healing and the root/soft tissue are stable.

8. The patient should be instructed not to brush in the area where surgery has been performed until 6 weeks post-operatively. However, "professional tooth-cleaning" should be performed as needed. After the initial healing period, patients are instructed in appropriate tooth cleaning measures, including methods for interproximal cleaning. Recommendations for oral hygiene should be based on the need to maintain extended would stability.

Clinical Procedure

For Straumann® Emdogain in Conjunction with Coronally Advanced Flap for Treatment of Recession Type Defects

1. Anesthetize the area selected for surgery by infiltration and, if needed block anesthesia. Avoid injection of local anesthetic with a vasoconstrictor into the interdental papilla or marginal gingival.

2. Scale and plan the exposed root surface to remove plaque, calculus, root surface irregularities and, if judged appropriate, to reduce prominence.

3. Make a sulcular incision at the site of the recession. Extend the incision horizontally into the adjacent interdental area slightly coronal to the level of the soft tissue margin of the recession.

4. Make two vertical divergent releasing incisions at the mesial and distal line angle connected to the horizontal incision.

5. Raise a full-thickness (mucoperiosteal) flap until the mucogingival junction is passed.

6. Make a cut through the periosteum and continue to raise a split-thickness flap by means of a blunt dissection. The aim is to eliminate any muscle tension on the flap margins and allow for a passive and tension-free coronal positioning of the flap at the level of the CEJ.

7. De-epithelialize the buccal aspect of the interdental papilla to create a connective tissue bed for suturing the coronally advanced flap.

8. Remove remaining smear layer by cleansing the root surface with Straumann® PrefGel (EDTA) for 2 minutes. Rinse thoroughly with sterile saline. Avoid contamination of the conditioned root surface with saliva or blood after the final rinse.

9. Immediately apply Emdogain to fully cover the exposed and conditioned root surface.

10. Coronally position the flap and secure it at the level of the CEJ by suturing the flap into the recipient bed, i.e. the de-epithelialized papilla. Also close the vertical incisions with lateral sutures. Use suture materials for extended stable closure. No pressure should be applied to the flap after suturing.

11. The patient should be advised to rinse daily with an antiseptic mouth rinse (e.g. 0.1–0.2 % chlorhexidine solution) until 4 weeks post-surgery. Patients should also be instructed to avoid muscle traction or other trauma to the treated area for the same period.

12. Sutures may be removed when clinical healing of the flap is stable or when they no longer add to the stability of the healing wound.

13. The patient should be instructed not to brush in the area where surgery has been performed until 4 weeks postoperatively. However, "professional tooth-cleaning" should be performed as needed. After the initial healing period, patients are instructed in a tooth cleaning technique, which minimizes apically directed trauma on the gingival margin/soft tissues of the treated tooth.

Clinical Procedure

For Straumann® Emdogain in Conjunction with Bone Graft Material in Wide Defects

The use of bone graft materials in wide defects may be necessary in order to prevent tissue prolapse and interference in the bone-healing process. The performance of Emdogain with various bone grafting substitutes had not been evaluated in the original marketing application. Straumann conducted a review of the published dental literature to learn of the safety and effectiveness of combining Emdogain with various bone substitutes. A meta analysis of the published literature (see references listed below) concluded that Emdogain, whether combined with autograft, allograft, bone derived xenograft, ß-Tricalcium phosphate, or Bioactive Glass, or implanted by itself, produced an improvement in average CAL gain, average PD reduction, and average recession gain over baseline values. These results demonstrated that the combination of Emdogain and any one of the bone graft materials studied did not adversely affect wound healing outcomes. Therefore, in cases of wide defects or where soft tissue support is desired, Straumann® Emdogain can be used in conjunction with a bone graft material.

It is important to note that due to the nature of the Meta analysis process and variation in study protocols evaluated, Meta analyses can introduce confounding variables affecting conclusions drawn from them. This Meta analysis of the use of Emdogain with bone grafting materials does not constitute a complete or rigorous evaluation of the use of Emdogain in combination with bone graft materials.

In the case where a bone grafting substitute is desired, it is recommended to prepare and condition the root surface as described elsewhere within these instructions, followed by application of Straumann® Emdogain onto the root surface, avoiding an overflow of the material. The remaining Straumann Emdogain may be used to moisten the bone substitute material.

Alternatively, the bone substitute material may be moistened using a medium described in the instructions from the bone substitute manufacturer. The moistened bone substitute is then applied to fill the defect to the highest level of bone loss before closing the flap.

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Prospective Clinical Study Results with Emdogain Compared to Surgical Treatment Alone

Design	Eval. Period (Mon.)	Number of Patients	Radiographic Bone Gain (mm) [Range: Min, Max]					Clinical Attachment Gain (mm) [Range: Min, Max]				Pocket Depth Reduction (mm) [Range: Min, Max]			
			Emdogain®	Control	Diff.	% of Initial Bone Loss Regained		Emdogain®	Control	Diff.	% Diff. of Control	Emdogain®	Control	Diff.	% Diff. of Control
						Emdogain®	Control								
Parallel groups 1-, 2- and 3-wall Control: Surgery	8	107 T 33 C	1.2 [-2.1, +4.8]	0.3 [-1.1, +3.1]	0.9*	15%	4%	3.1 [-1.0, +11.0]	2.6 [0, +5.0]	0.5	19%	4.3 [+0.5, +12.5]	3.7 [+1.0, +7.0]	0.6*	16%
	36	45 T 21 T	2.4 [-0.6, +5.4]	0 [-1.4, +2.5]	2.4***	31%	0%	2.9 [+0.5, +7.5]	2.2 [0, +4.5]	0.7*	32%	3.8 [+0.5, +8.5]	3.2 [0, +8.0]	0.6	19%
Splitmouth[1] 1- or 2-wall Control: Surgery	8	26	0.7 [-0.6, +1.8]	0.1 [-1.3, +2.1]	0.6*	12%	0%	2.1 [-1.0, +5.5]	1.8 [-1.0, +4.0]	0.3	16%	3.3 [-0.5, +7.0]	3.1 [0, +6.0]	0.2	6%
		10[2]	0.8 [0, +1.5]	0 [-0.9, +1.9]	0.8**	8%	0%	3.5 [+1.5, +5.5]	2.2 [0, +4.0]	1.3*	59%	3.6 [+1.5, +5.5]	3.6 [0, +7.0]	0	0%
Splitmouth[1] 1- or 2-wall Control: Surgery	8	34	0.9 [-0.3, +2.1]	-0.1 [-1.0, +0.9]	1.0**	13%	-2%	2.1 [-0.5, +5.5]	1.5 [-1.0, +3.5]	0.6**	40%	3.3 [+0.5, +6.5]	2.6 [0, +5.0]	0.7**	27%
	16	31	2.2 [-0.4, +6.0]	-0.2 [-1.2, +1.4]	2.4***	31%	-4%	2.3 [-1.0, +5.0]	1.7 [-1.0, +4.5]	0.6**	35%	3.3 [+0.5, +6.5]	2.6 [-1.0, +4.5]	0.7**	27%
	36	27	2.6 [+0.1, +7.1]	0 [-1.1, +1.5]	2.6***	36%	0%	2.2 [0, +4.5]	1.7 [-1.0, +3.5]	0.5**	30%	3.1 [+1.0, +6.0]	2.3 [-0.5, +4.5]	0.8***	35%

[1] The split mouth design indicates that the patient serves as his/her own control
[2] Patient with deepest baseline pocket exceeding 8 mm

T, C Test and control patients, respectively
*, **, *** p <0.05, p <0.01, p <0.001, p = 0.08, respectively

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Please note
Practitioners must have appropriate knowledge and instruction in the handling of the Straumann product described herein ("Straumann Product") for using the Straumann Product safely and properly in accordance with these instructions for use.

The Straumann Product must be used in accordance with the instructions for use provided by the manufacturer. It is the practitioner's responsibility to use the device in accordance with these instructions for use and to determine, if the device fits to the individual patient situation.

CE 0123 Straumann Products with the CE mark fulfil the requirements of the Medical Devices Directive 93/42 EEC

LOT Batch code

Temperature limitation (2°C–8°C/36°F–46°F)

Caution, consult accompanying documents

Validity
Upon publication of these instructions for use, all previous versions are superseded.

Do not re-use

Rx only U.S. Federal law restricts this device to sale by or on the order of a licensed dentist

STERILE A Sterilized using aseptic processing techniques

REF Catalogue number

Use by date

Manufacturer

straumann

Appendix II - Instructions For Use IFU 701910 (German version) - Emdogain®

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simply doing more

CE 0124

Manufacturer / Hersteller / Fabricant /
Produttore / Fabricante / Fabricante

Institut Straumann AG, Peter Merian-Weg 12
CH-4002 Basel/Switzerland, www.straumann.com

701910/B/01 02/15

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English Instructions for use: Straumann® Emdogain®

CAUTION: U.S. federal law restricts this device to sale by or on the order of a dental professional.

1. Product Description

Straumann® Emdogain® is a resorbable, implantable material and supports periodontal regeneration, which takes place over more than a year. It consists of hydrophobic enamel matrix proteins extracted from developing embryonal enamel of porcine origin in a propylene glycol alginate carrier. The gel has a suitable viscosity to facilitate application directly onto root surfaces exposed during periodontal surgery. Once applied onto an exposed root surface the protein self assembles into an insoluble three-dimensional matrix and creates a suitable environment for selective periodontal cell migration and attachment, which re-establishes lost tooth supporting tissues. Subsequent to formation of new attachment, alveolar bone can also be regenerated due to the osteogenic capacity of the restored periodontal ligament. Emdogain® is degraded by enzymatic processes of normal wound healing.

Straumann® Emdogain® is supplied in pre-filled, ready-to-use sterile syringes and available in three sizes (0.15 ml, 0.3 ml, 0.7 ml of the gel). The different filling sizes allow adapting the amount to the size and number of defects in one single patient as part of one surgical session. Each (pre-filled) syringe is meant for single use in one patient only.

The following procedure packs are offered for customer convenience:

- Straumann® Emdogain® Multipack: combination of 3 syringes with Emdogain® (either 0.3 ml or 0.7 ml filling volume) together with 3 syringes of Straumann® PrefGel®

2. Intended use

Emdogain® is intended for topical application in conjunction with periodontal surgery to provide for regeneration of tooth support lost to periodontal disease or trauma.

Straumann® Emdogain® may be used to support the soft tissue wound healing processes as part of oral surgical procedures.

3. Indications

- Emdogain® has been shown to be effective in sites with periodontal pockets more than 6 mm associated with vertical bone loss on radiograph greater than 3 mm.
- Emdogain® has also been shown to be effective with furcation involvements exceeding 2 mm but not through-and-through defects.
- Emdogain® used in recession defects has been shown to offer a potential for improved root coverage compared to the use of a coronally advanced flap alone, good aesthetic outcome, a gain in keratinized tissue and a potential for regeneration of attachment.
- Emdogain® is indicated to support healing of clean and non-inflamed wounds of the gingiva and oral mucosa resulting from surgical incisions (e.g. mucoperiosteal flaps).

4. Contraindications

Based on the results of the risk analysis the following patient population are contraindicated: patients with disorders or conditions including, but not limited to the following: uncontrolled diabetes or other uncontrolled systemic diseases, disorders or treatments that compromise wound healing, chronic high dose steroid therapy, bone metabolic diseases, radiation or other immuno-oppressive therapy and infections or vascular impairment at the surgical site.

5. Side effects, interactions and precautions; complications with Straumann products

In rare cases, clinical studies have reported the occurrence of general, procedure-related adverse events including but not limited to gingival bleeding, hematoma, infection, root (hyper)sensitivity, small wound dehiscence, mucosal irritation (soreness, pain, swelling) and aphta-like lesions.

6. Warnings

Immunological studies suggest that a small number of patients may become sensitized to Emdogain® as a result of repeated use. Please use caution in patients predisposed to allergic reactions and follow patients receiving repeated use closely. Post-market experience has indicated that the sensitization adverse reaction rate is low. Required treatment has ranged from no intervention needed to analgesics and/or antihistamines. The safety and effectiveness of Emdogain® has not been established in patients undergoing anticoagulant therapy. Careful consideration should be given before using Emdogain® for these patients. Emdogain® is intended for application around teeth only. Gain of tooth support occurs only to the level of the root surface covered by the repositioned oral soft tissue. Therefore, Emdogain® should be used in areas where there is adequate tissue for root coverage. Emdogain® should be used only after plaque and calculus have been removed from the diseased site.

7. Caution/Precautions

- Do not use if sterile package is opened or damaged. To prevent possible cross contamination discard or return damaged package and the enclosed device.
- Syringe and application device are single use items. Do not re-sterilize or reuse syringe or application device. Each (pre-filled) syringe is intended for use in one patient only. Reuse of single-use devices creates a potential risk of patient or user infections. Contamination of the device may lead to injury or serious illness of the patient.
- The product should be stored at 2 - 8 °C upon arrival.
- Site-specific anatomy, surgical management, wound stabilization during healing, and post-surgical oral hygiene are critical factors for success.
- Be aware that bending the cannula when it is attached to the syringe may cause breakage of the syringe.

8. Note

Separation of Straumann® Emdogain® may occur. Separation of Straumann® Emdogain® is identified as a non-homogeneous gel. Homogenization of the separated material can be achieved by shaking down the gel from the top to the bottom of the syringe, turn around the syringe and repeat the procedure ten to fifteen times until homogenization returns.

9. Procedure

1. Take out Emdogain® from cold storage approx. 30 minutes before use and allow it to assume ambient temperature.
2. Carefully attach the supplied application cannula.
3. Use the Emdogain® within 2 hours and discard any remaining gel.

In conjunction with conventional periodontal surgery:

1. Anaesthetize the area selected for surgery by block and/or infiltration anesthesia. Avoid injection with a vasoconstrictor into the interdental papilla or marginal gingiva.
2. Make intracrevicular incisions. Then, if judged appropriate, make one or two vertical releasing incisions extending out into the alveolar mucosa. Raise full-thickness (mucoperiosteal) flaps on the buccal and palatal/lingual surfaces of the teeth. Preserve as much of the gingival connective tissue in the flap as possible. Maintain viability of periodontal cells by hydration of the soft tissue with saline.
3. Only remove the granulation tissue adherent to the alveolar bone and any associated osseous defects necessary to provide full access and visibility to the root surfaces. Remove subgin-

gival plaque and calculus. Remove remaining smear layer by a quick surface cleaning with Straumann® PrefGel® (EDTA) for 2 min or 15 s with citric or phosphoric acid. Rinse thoroughly with sterile saline. Avoid contamination of the surgical area with saliva or blood after the final rinse.

4. Immediately apply Emdogain® onto the exposed root surfaces, starting at the most apical bone level. Apply Emdogain® to fully cover the exposed root surface areas. (Overflow of surplus material during suturing should occur).
5. Complete coverage of the interproximal area and optimal soft tissue adaptation is essential. If deemed appropriate, a periosteal fenestration at the base of the flap may be used to facilitate coronal repositioning of the soft tissue. Suture materials appropriate for extended stable closure should be preferred. Wound stability is critical to the outcome of a regeneration procedure using Emdogain®. If the linkage between the root surface and the healing connective tissues is broken, the periodontal defect will readily epithelialize resulting in a clinical failure.
6. The patients should be advised to rinse daily with an antiseptic mouth rinse (e.g. 0.1–0.2% chlorhexidine solution) until 3–6 weeks post-surgery. Antibiotics may also be used if deemed appropriate based on the clinician's judgement.
7. The patient should be instructed not to brush in the area where surgery has been performed until 3 weeks postoperatively. Then only gentle brushing on buccal and lingual surfaces using the "roll-stroke" method is recommended. No sulcular or interproximal tooth cleaning must be performed until 6 weeks postoperatively.
8. Sutures may be removed when the flaps and the root/soft tissue interface are stable, usually within 2–3 weeks. Consistent with conventional post-surgical care all patients should be re-instructed in proper oral hygiene measures as needed. Healing of clinical attachment and alveolar bone has been shown to continue for more than a year, and care should be taken not to interfere with this process.

In conjunction with coronally advanced flap for treatment of recession type Defects:

1. Anesthetize the area selected for surgery by infiltration and, if needed, block anesthesia. Avoid injection of local anesthetic with vasoconstrictor into the interdental papillas or marginal gingiva.
2. Plan and scale the exposed root surface to remove plaque, calculus, root surface irregularities and, if judged appropriate, to reduce prominence.
3. Make a sulcular incision at the site of the recession. Extend the incision horizontally into the adjacent interdental area slightly coronal to the CEJ.
4. Make two vertical divergent releasing incisions at the mesial and distal line angles connected to the horizontal incision.
5. Raise a full-thickness (mucoperiosteal) flap until the mucogingival junction is passed.
6. Make a cut through the periosteum and continue to raise a split-thickness flap by means of a blunt dissection. The aim is to eliminate any muscle tension on the flap margins and allow for a passive and tension-free coronal positioning of the flap at the level of the CEJ.
7. De-epithelialize the buccal aspect of the interdental papillas to create a connective tissue bed for suturing the coronally advanced flap.
8. Condition the exposed root surface with Straumann® PrefGel® (EDTA) for 2 min. or 15 s with citric or phosphoric acid. Rinse thoroughly with sterile saline. Avoid contamination of the conditioned root surface with saliva or blood after the final rinse.
9. Immediately apply Emdogain® to fully cover the exposed and conditioned root surface.
10. Coronally position the flap and secure it at the level of the CEJ by suturing the flap into the recipient bed, i.e. the de-epithelialized papillas. Also close the vertical incisions with lateral sutures. Use suture materials for extended stable closure. No pressure should be applied to the flap after suturing.
11. The patient should be advised not to brush in the area, but rinse daily with an antiseptic mouth rinse (e.g. 0.1–0.2% chlorhexidine solution) until 3 weeks post-surgery. Patients should also be instructed to avoid muscle traction or other trauma to the treated area for the same period.
12. Sutures are removed when clinical healing of the flap is stable and sutures no longer add to wound stability.
13. After the initial healing period, patients are instructed in a tooth cleaning technique, which minimizes apically directed trauma on the gingival margin/soft tissues of the treated tooth. After 4–6 weeks patients can gradually return to normal tooth cleaning measures.

In conjunction with oral surgical procedures to improve soft tissue wound healing:

- In conjunction with oral surgical procedures to improve soft tissue wound healing Emdogain® can be used to support soft tissue wound healing of surgical wounds as part of typical oral surgical procedures such as flap surgery, dental implantation procedures, soft tissue grafting procedures and gingivectomy procedures. In these procedures Emdogain® is applied on the complete wound area and wound margins of the surgical wound before flap closure and final suturing. Residual Emdogain® can be used to be applied on the wound margins after wound closure. Emdogain® gel oozing out of the wound margins can be removed if considered necessary.
- In case of gingivectomy procedures like tissue graft procedures or periodontal gingivectomy procedures that may not require suturing Emdogain® can be applied on the wound margins to facilitate wound healing as the final step of the procedure.
- Suture materials should be used for extended stable closure. No pressure should be applied to the flap after suturing. The patient should be advised not to brush in the area, but rinse daily with an antiseptic mouth rinse (e.g. 0.1–0.2% chlorhexidine solution) until 3 weeks post-surgery. Patients should also be instructed to avoid muscle traction or other trauma to the treated area for the same period.
- Sutures are removed when clinical healing of the flap is stable and sutures no longer add to wound stability.

In Conjunction with Bone Graft Material:

In cases of wide defects or where soft tissue support is desired, Straumann® Emdogain® can be used in conjunction with a bone graft material.

- When combined with bone graft materials Straumann® Emdogain® is added drop-wise to the bone substitute and the resulting product is mixed with a spatula or other instruments suited for mixing until the mix gets a paste-like/wet coarse sand consistency that is suited for the application.
- The defect should be filled as completely as possible with the resulting mixture. Overaugmentation should be prevented. The bone graft should be gently compacted in the defect to ensure mechanical stability against compression. Too much pressure that would result in crushing the bone graft particles should be avoided.
- To improve soft tissue wound healing a layer of Straumann® Emdogain® is applied on top of the bone graft augmentate immediately before final wound closure.
- In case of periodontal root surface treatments Straumann® Emdogain® should be applied on the root surface prior to the application of the bone graft or bone graft/Straumann® Emdogain® mixture to ensure proper coverage of the root surface with Straumann® Emdogain®.

10. Healing phase

Please refer to the specific procedure part at section 9.

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11. Further Information
Please refer to Straumann website for additional information

12. Please note
Practitioners must have knowledge of Periodontology and instruction in the handling of the Straumann product described herein ("Straumann Product") for using the Straumann Product safely and properly in accordance with these instructions for use.
The Straumann Product must be used in accordance with the instructions for use provided by the manufacturer. It is the practitioner's responsibility to use the device in accordance with these instructions for use and to determine if the device fits to the individual patient situation.

The Straumann Product is part of an overall concept and must be used only in conjunction with the corresponding original components and instruments distributed by Institut Straumann AG, its ultimate parent company and all affiliates or subsidiaries of such parent company ("Straumann"), except if stated otherwise for the respective Straumann Product. If use of products made by third parties is not recommended by Straumann, any such use will void any warranty or other obligation, express or implied, of Straumann.

13. Validity
Upon publication of these instructions for use, all previous versions are superseded.

14. Availability
Some items of the Straumann® regenerative portfolio are not available in all countries.

CE 0344 — Straumann Products with the CE mark fulfil the requirements of the Medical Devices Directive 93/42 EEC

LOT — Batch code

Temperature limitation (2 °C – 8 °C/36 °F – 46 °F)

REF — Catalogue number

Use by date

Caution, consult accompanying documents

STERILE A — Sterilized using aseptic processing techniques

Do not re-use

Rx only — Caution: U.S. federal law restricts this device to sale by or on the order of a dental professional.

Manufacturer

straumann

Deutsch Gebrauchsanweisung Straumann® Emdogain®

1. Produktbeschreibung

Straumann® Emdogain® ist ein resorbierbares, implantierbares Material, das die parodontale Regeneration unterstützt, die sich über die Dauer von mehr als einem Jahr fortsetzt. Es besteht aus hydrophoben Schmelzmatrixproteinen, die aus embryonalen porcinen Zähnen gewonnen werden und in eine Propylenglykolalginat-Trägersubstanz eingebettet sind. Die spezifische Viskosität des Gels erleichtert die direkte Applikation auf die im Rahmen eines parodontalchirurgischen Eingriffs freigelegten Wurzeloberflächen. Nach der Applikation auf eine freigelegte Wurzeloberfläche schliesst sich das Protein selbsttätig zu einer unlöslichen dreidimensionalen Matrix zusammen und schafft so ein günstiges Umfeld für eine selektive parodontale Zellmigration und das Reattachment, sodass verloren gegangenes Zahnstützgewebe wiederhergestellt wird. Dank der osteogenen Wirkung des regenerierten parodontalen Ligaments kann nach erfolgtem Reattachment des Bindegewebes auch Alveolarknochen neu gebildet werden. Emdogain® wird im Rahmen der enzymatischen Prozesse der physiologischen Wundheilung abgebaut.

Straumann® Emdogain® wird in vorgefüllten, gebrauchsfertigen, sterilen Spritzen geliefert und ist in drei Grössen (mit 0,15 ml, 0,3 ml oder 0,7 ml Gel) erhältlich. Die verschiedenen Füllgrössen erleichtern die Wahl der zu verwendenden Menge entsprechend der Grösse und Anzahl der während einer Operation zu behandelnden parodontalen Defekte. Die (vorgefüllten) Spritzen sind Einmalartikel, jede Spritze darf nur für einen Patienten verwendet werden.

Die nachstehenden praktischen Behandlungskits stehen zur Verfügung:

- Straumann® Emdogain® Multipack. Diese Kombipackung enthält 3 Spritzen Emdogain® (entweder 0,3 ml oder 0,7 ml Füllvolumen) plus 3 Spritzen Straumann® PrefGel®

2. Vorgesehene Verwendung

Emdogain® ist zur topischen Applikation bei parodontalchirurgischen Eingriffen vorgesehen, um die Regeneration des Zahnstützgewebes zu fördern, das infolge einer Parodontalerkrankung oder einer Verletzung verloren gegangen ist.

Straumann® Emdogain® kann zur Unterstützung der Wundheilungsprozesse der oralen Weichgewebe bei oralchirurgischen Eingriffen eingesetzt werden.

3. Indikationen

- Klinische Studien haben die Wirksamkeit von Emdogain® bei der Behandlung von Parodontaltaschen mit mehr als 6 mm Tiefe und röntgenologisch bestätigtem vertikalem Knochenverlust von über 3 mm gezeigt.
- Zudem wurde die Wirksamkeit von Emdogain® bei der Behandlung von Furkationsdefekten mit einer Defekthöhe von mehr als 2 mm nachgewiesen, ausgenommen durchgängige Defekte.
- Bei Rezessionsdefekten kann Emdogain® gegenüber der alleinigen Rezessionsdeckung mit koronalen Verschiebelappen nachweislich eine verbesserte Abdeckung der Zahnwurzeln erreichen sowie gute ästhetische Resultate, eine Zunahme der keratinisierten Gingiva und potenziell ein Reattachment erzielen.
- Emdogain® ist indiziert, um die Heilung von sauberen, nicht entzündeten inzisionsbedingten Wunden (z. B. bei der chirurgischen Bildung von Mukoperiostlappen) der Gingiva und Mundschleimhaut zu unterstützen.

4. Kontraindikationen

Basierend auf den Ergebnissen der Risikoanalyse ist die Anwendung von Emdogain® bei den folgenden Patientenpopulationen kontraindiziert: Patienten, die unter den nachstehenden (ohne darauf beschränkt zu sein) Erkrankungen oder Störungen leiden: unkontrollierter Diabetes oder andere unkontrollierte systemische Erkrankungen, Störungen oder Behandlungen, die die Wundheilung beeinträchtigen; Langzeitbehandlung mit hochdosierten Steroiden, Störungen des Knochenmetabolismus, Strahlentherapie oder sonstige immunsuppressive Therapie sowie Infektionen oder vaskuläre Störungen in der zu behandelnden Region.

5. Nebenwirkungen, Wechselwirkungen, Vorsichtsmassnahmen und mit Straumann-Produkten assoziierte Komplikationen

In klinischen Studien wurde in seltenen Fällen von allgemeinen, eingriffsbedingten unerwünschten Ereignissen berichtet, darunter (ohne darauf beschränkt zu sein) Zahnfleischblutung, Hämatom, Infektion, (Hyper-)Sensibilität der Zahnwurzeln, kleine Wunddehiszenzen, Schleimhautreizung (Wundheit, Schmerzen, Schwellung) und aphthoide Läsionen.

6. Warnhinweise

Die Ergebnisse immunologischer Studien deuten darauf hin, dass in wenigen Fällen nach wiederholter Anwendung eine Sensibilisierung gegenüber Emdogain® auftreten kann. Gehen Sie daher bei Patienten mit Prädisposition für allergische Reaktionen mit besonderer Vorsicht vor und sorgen Sie bei wiederholter Anwendung für eine engmaschige Nachbeobachtung der Patienten. Aus den Anwendungsbeobachtungen nach dem Inverkehrbringen geht hervor, dass die Rate der Sensibilisierungen als unerwünschte Nebenwirkung der Behandlung niedrig ist. In den Fällen, in denen eine Sensibilisierung auftrat, war entweder gar keine Intervention erforderlich oder die Gabe von Analgetika und/oder Antihistaminika. Zur Sicherheit und Wirksamkeit von Emdogain® bei Patienten unter Antikoagulationstherapie liegen bis dato keine belastbaren Daten vor. Bei dieser Patientengruppe sollte Emdogain® nur nach sorgfältiger Abwägung angewendet werden. Emdogain® ist ausschliesslich für die Applikation in der Zahnumgebung vorgesehen. Die Neubildung von Zahnstützgewebe erfolgt nur bis auf die Höhe der Wurzeloberfläche, die mit dem repositionierten oralen Weichteilgewebe bedeckt ist. Emdogain® sollte daher nur in solchen Bereichen angewendet werden, in denen adäquates Gewebe für die Wurzeldeckung zur Verfügung steht. Emdogain® erst anwenden, nachdem die erkrankte Stelle von Plaque und Zahnstein befreit wurde.

7. Vorsichtsmassnahmen

- Bei beschädigter oder geöffneter Sterilverpackung das Produkt nicht verwenden. Um eine mögliche Kreuzkontamination zu vermeiden, die beschädigte Verpackung und den Packungsinhalt entsorgen oder zurücksenden.
- Spritze und Applikationskanüle sind Einmalartikel. Spritze und Applikationskanüle dürfen nicht resterilisiert oder wiederverwendet werden. Jede (vorgefüllte) Spritze darf nur für einen Patienten verwendet werden. Die Wiederverwendung von Einmalprodukten schafft ein potenzielles Infektionsrisiko für Patienten und Anwender. Eine Verunreinigung des Produkts kann zu Verletzungen, schwerer Erkrankung oder Tod des Patienten führen.
- Nach Wareneingang sollte das Produkt bei ca. 2 – 8 °C gelagert werden.
- Die defektspezifische Anatomie, das chirurgische Vorgehen, die Wundstabilisation während der Heilung und die postoperative Mundhygiene sind entscheidend für den Erfolg der Behandlung.
- Es ist zu beachten, dass ein Verbiegen der Applikationskanüle, wenn diese bereits an der Spritze befestigt ist, zum Bruch der Spritze führen kann.

8. Hinweis

Es kann zu einer Phasenseparation (Entmischung) von Straumann® Emdogain® kommen. Eine Phasenseparation zeigt sich durch Inhomogenität des Straumann® Emdogain® Gels. Für eine erneute Homogenisierung des entmischten Materials das Gel vom oberen Teil zum Boden der Spritze schütteln, die Spritze umdrehen und diesen Vorgang 10 bis

15 Mal wiederholen, bis erneut ein homogenes Gel vorliegt.

9. Verfahren

1. Entnehmen Sie Emdogain® ca. 30 Minuten vor der geplanten Verwendung aus dem Kühlschrank und lassen Sie es auf Raumtemperatur anwärmen.
2. Befestigen Sie die im Lieferumfang enthaltene Applikationskanüle sorgfältig an der Spritze.
3. Verwenden Sie Emdogain® innerhalb von 2 Stunden, entsorgen Sie mögliche Restmengen des Gels.

In Verbindung mit konventioneller Parodontalchirurgie:

1. Betäuben Sie den geplanten Operationsbereich mittels Leitungs- und/oder Infiltrationsanästhesie. Vermeiden Sie die Injektion eines Anästhetikums mit einem Vasokonstriktor in die interdentalpapille oder in die marginale Gingiva.
2. Legen Sie intrakrevikuläre Hautinzisionen und, sofern angezeigt, eine oder zwei bis in die Alveolarschleimhaut reichende vertikale Entlastungsinzisionen an. An den bukkalen und palatinalen bzw. lingualen Zahnflächen präparieren und mobilisieren Sie Vollschichtlappen (Mukoperiostlappen). Erhalten Sie so viel gingivales Bindegewebe im Lappen wie möglich. Halten Sie das Weichgewebe mit steriler Kochsalzlösung feucht, um die Lebensfähigkeit der parodontalen Zellen zu bewahren.
3. Entfernen Sie das dem Alveolarknochen aufsitzende und im Knochendefekt vorhandene Granulationsgewebe nur so weit wie erforderlich, um vollständigen Zugang sowie eine gute Sicht auf die Wurzeloberflächen zu erhalten. Entfernen Sie subgingivale Plaque und Zahnstein. Zur Entfernung der verbleibenden Schmierschicht (Smear Layer) konditionieren Sie die Wurzeloberfläche ca. 2 Min. lang mit Straumann® PrefGel® (EDTA) oder 15 Sek. lang mit Zitronen- oder Phosphorsäure. Spülen Sie anschliessend gründlich mit steriler Kochsalzlösung. Vermeiden Sie nach dem abschliessenden Spülen eine Kontaminierung der konditionierten Wurzeloberfläche durch Speichel oder Blut.
4. Applizieren Sie Emdogain® unmittelbar danach auf die freigelegten Wurzeloberflächen. Beginnen Sie dabei am apikalsten Punkt. Tragen Sie Emdogain® so auf, dass die exponierten Wurzeloberflächen vollständig bedeckt sind. (Überschüssiges Material fliesst während des Wundverschlusses ab.)
5. Die vollständige Abdeckung im Approximalraum und eine optimale Weichgewebsadaptation sind von entscheidender Bedeutung. Sofern es angezeigt erscheint, kann eine Periostschlitzung an der Lappenbasis vorgenommen werden, um die koronale Verschiebung des Weichgewebes zu erleichtern. Verwenden Sie Nahtmaterial, das einen stabilen Verschluss über einen längeren Zeitraum gewährleistet. Adäquate Wundstabilität ist entscheidend für den Erfolg der gesteuerten Regeneration mit Emdogain®. Wird die Verbindung zwischen Wurzeloberfläche und einheilendem Bindegewebe unterbrochen, kommt es leicht zu einer Epithelisierung des parodontalen Defekts und damit zum klinischem Misserfolg.
6. Der Patient sollte angewiesen werden, nach der Operation 3 bis 6 Wochen lang täglich mit einer antiseptischen Mundspülung (z. B. Chlorhexidin 0,1 % – 0,2 %) zu spülen. Sofern nach klinischer Einschätzung des Arztes angezeigt, können zusätzlich Antibiotika verabreicht werden.
7. Der Patient sollte angewiesen werden, den operierten Bereich während der ersten 3 Wochen postoperativ nicht mit einer Bürste zu reinigen. Danach wird empfohlen, die bukkalen und lingualen Oberflächen mit sanft kreisenden Bewegungen mit einer weichen Bürste zu reinigen. Bis 6 Wochen postoperativ darf keine subkulare oder interproximale Zahnreinigung durchgeführt werden.
8. Die Nähte können entfernt werden, sobald die Lappen und die Verbindung Wurzeloberfläche/Weichgewebe stabil sind, in der Regel nach 2 – 3 Wochen. Bei Bedarf sollte wie im Rahmen der herkömmlichen postoperativen Nachsorge eine erneute Unterweisung in der korrekten Mundhygiene und Zahnpflege erfolgen. Der klinische Attachmentgewinn und die Aushellung des Alveolarknochens setzen sich erwiesenermassen über die Dauer von mehr als einem Jahr fort. Es ist sorgsam darauf zu achten, dass dieser Prozess nicht gestört wird.

In Verbindung mit einem koronalen Verschiebelappen für die Behandlung von Rezessionsdefekten:

1. Betäuben Sie den geplanten Operationsbereich mittels Infiltrations- und, sofern erforderlich, Leitungsanästhesie. Vermeiden Sie die Injektion eines Lokalanasthetikums mit einem Vasokonstriktor in die Interdentalpapillen oder in die marginale Gingiva.
2. Glätten und scalen Sie die freigelegte Wurzeloberfläche, um Plaque, Zahnstein sowie Unregelmässigkeiten der Wurzeloberfläche zu entfernen, und, sofern angezeigt, eventuelle Vorsprünge zu reduzieren.
3. Legen Sie an der Rezessionsstelle eine subkulare Inzision an. Verlängern Sie den Schnitt horizontal bis in den Approximalraum, etwas koronal der Schmelz-Zement-Grenze.
4. Ausgehend von diesem Horizontalschnitt legen Sie mesial und distal zwei vertikal divergierende Entlastungsinzisionen an.
5. Präparieren und mobilisieren Sie einen Vollschichtlappen (Mukoperiostlappen) bis über die Mukogingivalgrenze hinaus.
6. Führen Sie einen horizontalen Schnitt in das Periost aus und bilden Sie durch stumpfe Präparation einen Spaltlappen. An den Lappenrändern darf keine Muskelspannung mehr vorhanden sein, sodass der Lappen bei der Rezessionsdeckung absolut spannungsfrei bleibt und passiv nach koronal bis an die Schmelz-Zement-Grenze verschoben werden kann.
7. Deepithelisieren Sie den bukkalen Aspekt der Interdentalpapillen und schaffen Sie ein Bindegewebsbett für das Vernähen des koronal verschobenen Lappens.
8. Konditionieren Sie die freigelegte Wurzeloberfläche ca. 2 Min. lang mit Straumann® PrefGel® (EDTA) oder 15 Sek. lang mit Zitronen- oder Phosphorsäure. Spülen Sie anschliessend gründlich mit steriler Kochsalzlösung. Vermeiden Sie nach dem abschliessenden Spülen eine Kontaminierung der konditionierten Wurzeloberfläche durch Speichel oder Blut.
9. Applizieren Sie Emdogain® unmittelbar danach auf die freigelegten und konditionierten Wurzeloberflächen. Achten Sie auf vollständige Abdeckung.
10. Verschieben Sie den Lappen nach koronal und vernähen Sie ihn auf Höhe der Schmelz-Zement-Grenze in dem durch Deepithelisierung im Papillenbereich geschaffenen Bindegewebsbett. Verschliessen Sie anschliessend die vertikalen Inzisionen mit lateralen Nähten. Verwenden Sie Nahtmaterial, das einen stabilen Verschluss über einen längeren Zeitraum gewährleistet. Nach dem Nahtverschluss sollte Druck auf den Gewebelappen vermieden werden.
11. Der Patient sollte angewiesen werden, während der ersten 3 Wochen postoperativ keine Bürste zur Reinigung des betroffenen Bereichs zu verwenden, sondern täglich mit einer antiseptischen Mundspülung (z. B. Chlorhexidin 0,1 % 0,2 %) zu spülen. Der Patient sollte zudem angewiesen werden, während des genannten Zeitraums starke Muskeltraktionen oder sonstige Verletzungen des betroffenen Bereichs zu vermeiden.
12. Nach stabiler klinischer Einheilung des Lappens und sobald die Nähte nicht länger zur Stabilität der Wundversorgung beitragen, werden die Nahtfäden entfernt.
13. Um nach apikal gerichtete Verletzungen des Zahnfleischsaums/der Weichgewebe des behandelten Zahns auf ein Minimum zu reduzieren, werden die Patienten im Anschluss

an die initiale Heilungsphase in einer speziellen Zahnpflegetechnik unterwiesen. Nach 4 – 6 Wochen können die Patienten allmählich wieder zur normalen Zahnpflege übergehen.

In Verbindung mit oralchirurgischen Verfahren zur Optimierung der Weichgewebeheilung:

- In Verbindung mit oralchirurgischen Verfahren zur Optimierung der Weichgewebeheilung kann Emdogain® eingesetzt werden, um die Weichgewebewundheilung im Rahmen typischer oralchirurgischer Verfahren, z. B. bei Eingriffen mit Lappenbildung, Implantatbehandlungen, Weichgewebetransplantationen und Gingivektomien, zu unterstützen. Applizieren Sie Emdogain® vor dem endgültigen Vernähen des Lappens auf den kompletten Wundbereich und die Wundränder. Restmengen von Emdogain® können nach dem Wundverschluss auf die Wundränder appliziert werden. Sofern als nötig erachtet, kann überschüssiges Emdogain® Gel, das aus den Wundrändern sickert, entfernt werden.
- Bei einem chirurgischen Eingriff am Zahnfleisch, z. B. einer Weichgewebetransplantation oder parodontalen Gingivektomie, bei der gegebenenfalls kein Nahtverschluss nötig ist, kann Emdogain® im letzten Operationsschritt auf die Wundränder appliziert werden, um die Wundheilung zu fördern.
- Verwenden Sie Nahtmaterial, das einen stabilen Verschluss über einen längeren Zeitraum gewährleistet. Nach dem Nahtverschluss sollte Druck auf den Gewebelappen vermieden werden. Der Patient sollte angewiesen werden, während der ersten 3 Wochen postoperativ keine Bürste zur Reinigung der betroffenen Mundregion zu verwenden, sondern täglich mit einer antiseptischen Mundspülung (z. B. Chlorhexidin 0,1% – 0,2 %) zu spülen. Der Patient sollte zudem angewiesen werden, während des genannten Zeitraums starke Muskelfraktionen oder sonstige Verletzungen des betroffenen Bereichs zu vermeiden.
- Nach stabiler klinischer Einheilung des Lappens und sobald die Nähte nicht länger zur Stabilität der Wundversorgung beitragen, werden die Nahtfäden entfernt.

In Verbindung mit Knochentransplantat/ Knochenersatzmaterial:

Bei ausgedehnten Defekten oder wenn Weichgewebeabstützung gewünscht ist, kann Straumann® Emdogain® in Verbindung mit Knochentransplantat/Knochenersatzmaterial verwendet werden.

- Geben Sie Straumann® Emdogain® tropfenweise in den Behälter mit Knochentransplantat/ Knochenersatzmaterial und verwenden Sie einen Spatel oder ein anderes geeignetes Instrument, um die Produkte zu vermischen, bis die geeignete Konsistenz (Paste/feuchter grobkörniger Sand) für die Applikation erreicht ist.
- Füllen Sie den Defekt so vollständig wie möglich auf. Eine übermässige Augmentation ist zu vermeiden. Das Augmentationsmaterial sollte behutsam im Defekt verdichtet werden, um eine gute Druckstabilität zu erreichen. Vermeiden Sie zu hohen Kraftaufwand, um ein Zerdrücken der Augmentationsmaterialpartikel zu vermeiden.
- Um die Wundheilung der Weichgewebe zu fördern, bringen Sie unmittelbar bevor Sie die Wunde endgültig verschliessen eine Schicht Straumann® Emdogain® auf das Augmentationsmaterial auf.
- Bei parodontalen Wurzeloberflächenbehandlungen sollte Straumann® Emdogain® vor der Anlagerung des Gemisches aus Knochentransplantat oder Knochenersatzmaterial und Straumann® Emdogain® auf die Wurzeloberflächen appliziert werden, um eine adäquate Abdeckung der Wurzeloberfläche mit Straumann® Emdogain® zu gewährleisten.

10. Einheilphase

Einzelheiten siehe die spezifischen Verfahren in Abschnitt 9.

11. Weitere Informationen

Weitergehende Informationen finden Sie auf der Straumann-Website.

12. Hinweise:

Zahnärzte müssen über entsprechende Kenntnisse auf dem Gebiet der Parodontologie verfügen und in der Handhabung des in diesem Dokument beschriebenen Straumann-Produkts („Straumann-Produkt") geschult sein, um das Straumann-Produkt sicher und fachgerecht gemäss Gebrauchsanweisung zu verwenden.

Das Straumann-Produkt ist gemäss der vom Hersteller bereitgestellten Gebrauchsanweisung zu verwenden. Es liegt in der Verantwortung des Zahnarztes, das Produkt gemäss Gebrauchsanweisung zu verwenden und in jedem Einzelfall zu prüfen, ob das Produkt für die individuelle Situation des Patienten geeignet ist.

Straumann-Produkte sind Teil eines Gesamtkonzepts und ausschliesslich zusammen mit den entsprechenden Originalteilen und -instrumenten zu verwenden, die von der Institut Straumann AG, deren Muttergesellschaft und sämtlichen verbundenen Unternehmen oder Tochtergesellschaften dieser Muttergesellschaft („Straumann") vertrieben werden, es sei denn, die Gebrauchsanweisung für das entsprechende Straumann®-Produkt enthält anderslautende Angaben. Wird die Verwendung von Produkten, die von Drittherstellern stammen, von Straumann nicht empfohlen, führt eine solche Verwendung zum Verlust jeder expliziten oder impliziten Garantie oder zum Erlöschen jeder sonstigen Verpflichtung von Straumann.

13. Gültigkeit

Mit der Veröffentlichung dieser Gebrauchsanweisung verlieren alle vorherigen Versionen ihre Gültigkeit.

14. Verfügbarkeit

Einige Artikel des regenerativen Portfolios von Straumann® sind nicht in allen Ländern verfügbar.

CE 0123 Straumann® Produkte mit dem CE-Zeichen erfüllen die Anforderungen der Medizingeräte-Richtlinie 93/42 EWG.

LOT Chargennummer

Temperaturgrenzen (2 °C – 8 °C/36 °F – 46 °F)

REF Katalognummer

Verfallsdatum

Achtung! Begleitdokumentate beachten

STERILE A Sterilisiert mittels aseptischer Verarbeitungstechniken

Nicht wiederverwenden

Hersteller

straumann

Français Mode d'emploi : Straumann® Emdogain®

1. Description du produit

Straumann® Emdogain® est un matériau implantable, résorbable qui favorise la régénération parodontale, celle-ci pouvant durer plus d'un an. Il se compose de protéines dérivées de la matrice amélaire, extraites d'émail embryonnaire en développement d'origine porcine, dans un vecteur à base d'alginate de propylène glycol. Le gel présente une viscosité adéquate pour faciliter l'application directement sur les surfaces radiculaires exposées au cours de la chirurgie parodontale. Une fois appliquées sur une surface radiculaire exposée, les protéines se rassemblent spontanément en une matrice tridimensionnelle insoluble et créent un environnement favorable à la migration et à l'adhésion sélectives des cellules parodontales, ce qui rétablit les tissus de soutien de la dent manquante. Après la formation d'une nouvelle attache, l'os alvéolaire peut être aussi régénéré du fait de la capacité ostéogénique du ligament parodontal restauré. Emdogain® se dégrade sous l'effet de processus enzymatiques normaux dans la cicatrisation.

Straumann® Emdogain® est fourni sous forme de seringues stériles préremplies et prêtes à l'emploi et disponible en trois contenances (0,15 ml, 0,3 ml, 0,7 ml de gel). Les différentes tailles de remplissage permettent d'adapter la quantité à la taille et au nombre de défauts chez un seul patient dans le cadre d'une procédure chirurgicale. Chaque seringue (préremplie) est réservée à un usage unique chez un seul patient.

Les packs pour procédure suivants sont proposés au client par souci de praticité :

- Straumann® Emdogain® Multipack : lot de 3 seringues avec Emdogain® (volume de remplissage de 0,3 ml ou de 0,7 ml) et de 3 seringues de Straumann® PrefGel®

2. Utilisation prévue

Emdogain® est indiqué en application locale associé à une chirurgie parodontale pour assurer la régénération des tissus de soutien délabrés du fait d'une maladie parodontale ou d'un traumatisme.

Straumann® Emdogain® peut être utilisé pour favoriser les processus de cicatrisation des tissus mous dans les procédures de chirurgie buccale.

3. Indications

- Il a été démontré qu'Emdogain® est efficace dans le traitement des poches parodontales de plus de 6 mm associées à une perte osseuse verticale de plus de 3 mm à la radiographie.
- L'efficacité d'Emdogain® a également été démontrée dans des défauts de furcation de plus de 2 mm, mais pas sur des lésions de part en part.
- Il a été démontré qu'utilisé dans les lésions de type récession, Emdogain® permet d'améliorer la couverture de la racine comparativement à l'utilisation d'un lambeau repositionné coronairement, un bon résultat esthétique, un gain de tissu kératinisé et une possibilité de régénération ligamentaire.
- Emdogain® est indiqué pour favoriser la cicatrisation des plaies d'incisions chirurgicales propres et ne présentant aucune inflammation au niveau de la gencive et de la muqueuse buccale (p. ex. lambeaux muco-périostés).

4. Contre-indications

D'après les résultats de l'analyse des risques, le produit est contre-indiqué chez le patient s'il est atteint, notamment mais pas seulement, des affections ou des pathologies suivantes : diabète non régulé ou autre maladie systémique non contrôlée, affection ou traitement compromettant la cicatrisation des plaies, stéroïdothérapie chronique à hautes doses, maladie métabolique osseuse, radiothérapie ou autre traitement immunosuppresseur, et infection ou lésion vasculaire au site chirurgical.

5. Effets secondaires, interactions et précautions : complications avec les produits Straumann

Dans des cas rares, les études cliniques ont signalé l'occurrence d'événements indésirables associés à la procédure, par exemple mais pas seulement, les saignements gingivaux, les hématomes, l'infection, la sensibilité/hypersensibilité radiculaire, une légère déhiscence de la plaie, l'irritation de la muqueuse (endolorissement, douleur, gonflement) et des lésions pseudo-aphteuses.

6. Mise en garde

Les études immunologiques montrent qu'un petit nombre de patients peut devenir sensible à Emdogain® à la suite d'une utilisation répétée. Utiliser le gel avec prudence chez les patients prédisposés aux réactions allergiques, et suivre étroitement les patients chez qui le produit est administré de manière répétée. Les données de pharmacovigilance indiquent que le taux des réactions de sensibilisation indésirables est faible. Une telle situation ne requiert généralement pas d'intervention, ou l'administration d'antalgiques et/ou d'antihistaminiques. La sécurité et l'efficacité d'Emdogain® n'ont pas été établies chez les patients sous anticoagulothérapie. L'administration d'Emdogain® chez cette catégorie de patients doit d'abord faire l'objet d'une réflexion sérieuse avant d'être envisagée. Emdogain® est un produit destiné à être appliqué autour des dents seulement. Le gain de consolidation dentaire ne se produit qu'au niveau de la surface radiculaire couverte par le tissu mou repositionné. Le gel Emdogain® ne doit donc être appliqué que dans les zones où la quantité de tissu de couverture est suffisante. Emdogain® ne doit être utilisé qu'après élimination de la plaque et du tartre du site touché.

7. Mise en garde/Précautions

- Ne pas utiliser si l'emballage stérile est ouvert ou endommagé. Pour éviter une éventuelle contamination croisée, il convient de jeter ou de renvoyer l'emballage endommagé et le dispositif qu'il contient.
- La seringue et le dispositif d'application sont à usage unique. Ne pas restériliser ni réutiliser la seringue ou le dispositif d'application. Chaque seringue (préremplie) est destinée à être utilisée chez un seul patient. La réutilisation de dispositifs à usage unique crée un risque potentiel d'infection chez le patient ou l'utilisateur. La contamination du dispositif peut être à l'origine de blessures ou de maladies graves du patient.
- Le produit doit être conservé à une température de 2 à 8 °C après réception.
- L'anatomie du site, la gestion chirurgicale, la stabilisation de la plaie pendant la cicatrisation et l'hygiène buccale postopératoire sont des facteurs critiques de réussite.
- Il faut savoir que la flexion de la canule lorsqu'elle est attachée à la seringue peut provoquer une rupture de la seringue.

8. Remarque

Une séparation de Straumann® Emdogain® est possible. S'il a subi une séparation, le gel Straumann® Emdogain® n'est plus homogène. Le cas échéant, il est possible de ré-homogénéiser le matériau en agitant le gel de haut en bas dans la seringue, en retournant la seringue et en répétant cette procédure dix à quinze fois jusqu'à homogénéisation complète du matériau.

9. Procédure

1. Sortir Emdogain® de son lieu de conservation au froid environ 30 minutes avant utilisation, afin qu'il puisse revenir à température ambiante.
2. Fixer avec précaution la canule d'application fournie.
3. Utiliser Emdogain® dans les 2 heures et jeter tout gel restant.

En association avec une procédure parodontale classique :

1. Anesthésier la zone sélectionnée pour la chirurgie par anesthésie tronculaire et/ou par

infiltration. Éviter toute injection d'anesthésique local avec un vasoconstricteur dans les papilles interdentaires ou la gencive marginale.

2. Pratiquer des incisions intracréviculaires. Puis, si cela est jugé approprié, pratiquer une ou deux incisions de relâchement vertical se prolongeant jusque dans la muqueuse alvéolaire. Prélever un lambeau muco-périosté de pleine épaisseur sur les surfaces vestibulaire et palatine/linguale des dents. Préserver autant de tissu conjonctif gingival que possible dans le lambeau. Maintenir la viabilité des cellules parodontales en hydratant les tissus mous avec une solution physiologique.
3. Retirer uniquement les tissus de granulation adhérant à l'os alvéolaire ainsi que tout défaut osseux associé qui sont nécessaires pour obtenir un accès total aux surfaces radiculaires et une parfaite visibilité. Éliminer la plaque et le tartre sous-gingivaux. Éliminer la couche de boue dentinaire résiduelle en effectuant un rapide nettoyage de surface avec Straumann® PrefGel® (EDTA) pendant 2 min ou 15 s avec de l'acide citrique ou phosphorique. Rincer abondamment avec une solution saline stérile. Après ce rinçage final éviter tout contact avec la salive ou du sang.
4. Appliquer immédiatement l'Emdogain® sur les surfaces radiculaires exposées, en commençant par la zone osseuse la plus apicale. Appliquer l'Emdogain® pour recouvrir entièrement les surfaces radiculaires exposées. (Il doit se produire un débordement du gel en excès lors de la fermeture du site.)
5. Une couverture totale de la zone interproximale et une adaptation optimale des tissus mous sont essentielles. Si cela est jugé approprié, il est possible d'utiliser une fenestration périostée à la base du lambeau afin de faciliter le repositionnement coronaire de ces tissus mous. Privilégier les matériaux de suture assurant une fermeture stable prolongée. La stabilité de la plaie est essentielle pour l'issue d'une procédure de régénération utilisant l'Emdogain®. Si le lien est rompu entre la surface radiculaire et les tissus conjonctifs en cours de cicatrisation, la lésion parodontale s'épithélialisera rapidement, entraînant un échec clinique.
6. Donner au patient la consigne de se rincer quotidiennement la bouche à l'aide d'un bain de bouche antiseptique (p. ex. une solution de chlorhexidine à 0,1– 0,2%) pendant 3 à 6 semaines postopératoires. Des antibiotiques peuvent également être utilisés si un médecin le juge approprié.
7. Il faut conseiller au patient de ne pas brosser le ou les sites traités pendant 3 semaines après l'intervention. Il est ensuite recommandé de brosser doucement uniquement les surfaces vestibulaires ou linguales en utilisant la méthode « du rouleau ». Il ne faut procéder à aucun brossage interproximal ou sulculaire pendant les 6 semaines suivant l'opération.
8. Les fils de suture peuvent être enlevés lorsque les lambeaux et l'interface racine/tissu mou sont stables, ce qui est habituellement le cas après 2 à 3 semaines. En accord avec les soins postopératoires classiques, les bonnes pratiques d'hygiène bucco-dentaire doivent être rappelées à tous les patients. Il a été démontré que la cicatrisation de l'attache clinique et de l'os alvéolaire continue pendant plus d'un an, et toutes les précautions doivent être prises pour ne pas interférer avec ce processus.

Conjointement à un lambeau repositionné coronairement pour le traitement des lésions de type récession :

1. Anesthésier le secteur sélectionné pour l'intervention chirurgicale à l'aide d'une infiltration et, si nécessaire, d'un bloc anesthésique. Ne pas injecter d'anesthésique local avec vasoconstricteur dans les papilles interdentaires ou dans la gencive marginale.
2. Surfacer et détartrer la surface radiculaire exposée afin d'éliminer la plaque, le tartre, les irrégularités de la surface radiculaire et, si on le juge approprié, pour réduire une proéminence.
3. Pratiquer une incision sulculaire à l'endroit de la récession. Prolonger l'incision horizontalement dans la zone interdentaire adjacente, légèrement en direction coronaire jusqu'à la jonction cément-émail (JCE).
4. Pratiquer aux angles mésial et distal de la ligne deux incisions verticales divergentes de relâchement reliées à l'incision horizontale.
5. Prélever un lambeau (muco-périosté) de pleine épaisseur jusqu'au-delà de la jonction muco-gingivale.
6. Pratiquer une incision dans le périoste et prélever un lambeau d'épaisseur partielle par dissection délicate. Le but est d'éliminer toute tension musculaire sur les bords du lambeau et de permettre un positionnement coronaire passif et sans tension du lambeau au niveau de la JCE.
7. Désépithélialiser la face buccale des papilles interdentaires afin de créer un lit de tissu conjonctif pour suturer le lambeau repositionné coronairement.
8. Traiter la surface radiculaire exposée au Straumann® PrefGel (EDTA) pendant 2 minutes ou 15 secondes avec de l'acide citrique ou phosphorique. Rincer abondamment avec une solution saline stérile. Éviter toute contamination de la surface radiculaire traitée par de la salive ou du sang après le rinçage final.
9. Appliquer immédiatement Emdogain® pour recouvrir complètement la surface radiculaire traitée.
10. Repositionner le lambeau coronairement et le fixer au niveau de la JCE en le suturant dans le lit receveur, à savoir les papilles désépithélialisées. Refermer également les incisions verticales par des sutures latérales. Utiliser du matériel de suture pour fermeture stable prolongée. Aucune pression ne doit être exercée sur le lambeau après la suture.
11. Il faut conseiller au patient de ne pas brosser la zone, mais de la rincer quotidiennement avec un bain de bouche antiseptique (par ex., une solution de chlorhexidine à 0,1–0,2%) pendant environ 3 semaines suivant l'intervention. Les patients doivent également être informés d'éviter toute traction musculaire ou d'autres traumatismes au niveau de la zone traitée pendant la même période.
12. Les sutures sont supprimées lorsque la cicatrisation clinique du lambeau est stable et les sutures ne participent plus à la stabilité de la plaie.
13. Après la période de cicatrisation initiale, il faut recommander aux patients une technique de nettoyage des dents qui minimise le traumatisme en direction apicale sur le bord de la gencive/des tissus mous de la dent traitée. Après 4 à 6 semaines, les patients peuvent progressivement revenir à des mesures normales de brossage des dents.

En association avec les procédures de chirurgie buccale pour améliorer la cicatrisation :

- En association avec les procédures chirurgicales buccales pour améliorer la cicatrisation des tissus mous Emdogain® peut être utilisé pour favoriser la cicatrisation des tissus mous des plaies chirurgicales dans le cadre de procédures de chirurgie buccale classiques telles qu'une procédure chirurgicale par lambeau, des procédures d'implantation dentaire, des procédures de greffes de tissus mous et des procédures de gingivectomie. Dans ces procédures Emdogain® est appliqué sur toute la surface et les berges de la plaie chirurgicale avant la fermeture des lambeaux et la suture finale. L'Emdogain® résiduel peut être utilisé pour une application sur les berges de la plaie après la fermeture de la plaie. Le gel d'Emdogain® qui coule des berges de la plaie peut être éliminé en cas de nécessité.
- En cas de procédures de gingivectomie comme des procédures de greffe de tissu ou des procédures de gingivectomie parodontales qui peuvent ne pas nécessiter de suture, Emdogain® peut être appliqué sur les berges de la plaie pour faciliter la cicatrisation comme étape finale de la procédure.
- Les matériaux de suture doivent être utilisés

pour les longues fermetures stables. Aucune pression ne doit être exercée sur le lambeau après la suture. Le patient doit être averti de ne pas brosser dans la zone opérée, mais de rincer quotidiennement avec un rince-bouche antiseptique (p. ex. une solution de chlorhexidine 0,1 - 0,2%) jusqu'à 3 semaines post-chirurgie. Les patients doivent également être informés d'éviter toute traction musculaire ou d'autres traumatismes au niveau de la zone traitée pendant la même période.

- Les sutures sont supprimées lorsque la cicatrisation clinique du lambeau est stable et les sutures ne participent plus à la stabilité de la plaie.

En association avec un matériau de greffe osseuse :
En cas de défauts importants ou là où le soutien des tissus mous est souhaité, Straumann® Emdogain® peut être utilisé en association avec un matériau de greffe osseuse.

- En association avec une greffe osseuse, Straumann® Emdogain® est ajouté goutte à goutte au substitut osseux et le produit qui en résulte est mélangé avec une spatule ou d'autres instruments permettant d'effectuer un mélange jusqu'à ce que le mélange est une consistance grossière sableuse humide/pâteuse adaptée à l'application.
- Le défaut doit être rempli aussi complètement que possible avec le mélange résultant. Une sur-augmentation doit être évitée. La greffe osseuse doit être compactée en douceur dans le défaut afin d'assurer une stabilité mécanique contre la compression. Une pression trop forte qui se traduirait par un écrasement des particules de greffe osseuse doit être évitée.
- Pour améliorer la cicatrisation des tissus mous, une couche de Straumann® Emdogain® est appliquée sur la greffe osseuse et augmente immédiatement avant la fermeture finale de la plaie.
- Dans les cas de traitements parodontaux de la surface des racines Straumann® Emdogain® doit être appliqué sur la surface de la racine avant l'application de la greffe osseuse ou du mélange greffe osseuse/Straumann® Emdogain® pour assurer une couverture adéquate de la surface de la racine avec Straumann® Emdogain®.

10. Phase de cicatrisation
Se référer à la partie spécifique de la procédure à la rubrique 9.

11. Informations complémentaires
Pour des informations complémentaires, consulter le site internet de Straumann.

12. Remarque
Les praticiens doivent avoir acquis les connaissances en parodontologie et la formation nécessaire à la manipulation du produit Straumann® décrit dans le présent document (« Produits Straumann »), afin d'utiliser les Produits Straumann® en toute sécurité et de manière appropriée, conformément au mode d'emploi.
Le produit Straumann doit être utilisé conformément au mode d'emploi fourni par le fabricant. Il appartient au praticien d'utiliser le dispositif conformément à ce mode d'emploi et de déterminer si le dispositif est adapté à la situation d'un patient donné.

Le produit Straumann relève d'un concept global et ne doit être utilisé qu'avec les composants et les instruments d'origine correspondants distribués par Institut Straumann AG, sa société mère ultime et toutes les filiales de cette société mère (« Straumann »), sauf mention contraire pour le produit Straumann respectif. Si l'utilisation de produits fabriqués par des tiers n'est pas recommandée par Straumann, aura pour effet d'annuler toute garantie ou toute autre obligation, expresse ou implicite, de Straumann.

13. Validité
La parution de ce mode d'emploi annule et remplace toutes les versions antérieures.

14. Disponibilité
Certains articles de la gamme Straumann® Regenerative ne sont pas disponibles dans tous les pays.

CE 0123 Les produits Straumann portant la marque CE sont conformes aux exigences de la Directive 93 /42 EEC relative au Matériel Médical.

LOT Numéro de lot

Limite de température (2°C – 8°C/36°F – 46°F)

REF Référence du catalogue

Date limite d'utilisation

Attention, lire les documents joints

STERILE A Stérilisé en utilisant des techniques aseptisées

Ne pas réutiliser

Fabricant

straumann

Italiano Istruzioni per l'uso: Straumann® Emdogain®

1. Descrizione del prodotto

Straumann® Emdogain® è un materiale riassorbibile e impiantabile che supporta la rigenerazione parodontale, un processo che richiede oltre un anno. È costituito da proteine idrofobe della matrice dello smalto estratte da smalto embrionale in sviluppo di origine suina, in propilene glicole alginato come vettore. Questo gel ha una viscosità adatta a facilitare l'applicazione direttamente sulle superfici radicolari esposte, durante la chirurgia parodontale. Una volta applicato su una superficie radicolare esposta, la proteina si auto-assembla in una matrice insolubile tridimensionale, creando un ambiente idoneo per la migrazione cellulare parodontale selettiva e l'attacco, che ripristina i tessuti di supporto del dente compromesso. In seguito alla formazione di nuovo attacco, anche l'osso alveolare può essere rigenerato grazie alla capacità osteogenica del legamento parodontale rigenerato. Emdogain® si degrada attraverso i processi enzimatici connessi al normale processo di guarigione delle ferite.

Straumann® Emdogain è disponibile in siringhe sterili preriempite e pronte all'uso, in tre formati: 0,15 ml, 0,3 ml e 0,7 ml di gel. I diversi formati consentono l'adattamento della quantità alla dimensione e al numero di difetti per un singolo paziente, come parte di un'unica sessione chirurgica. Ogni siringa (pre-riempita) deve essere utilizzata su un solo paziente.

Per agevolarne l'uso, sono disponibili le seguenti confezioni di trattamento:

- Straumann® Emdogain Multipack: set di 3 siringhe con Emdogain® (da 0,3 o 0,7 ml di volume) con 3 siringhe di Straumann® PrefGel®.

2. Uso previsto

Emdogain® è indicato per applicazione topica associata a chirurgia parodontale per fornire la rigenerazione dell'apparato di sostegno del dente perso a causa della malattia parodontale o da trauma.

Straumann® Emdogain® può essere usato a supporto del processo di guarigione delle ferite del tessuto molle nell'ambito di interventi di chirurgia orale.

3. Indicazioni

- Emdogain® si è rivelato efficace nei siti con tasche parodontali di oltre 6 mm associati a perdita ossea verticale superiore a 3 mm, evidenziata da esame radiologico.
- Emdogain® si è rivelato efficace anche nei casi di difetti di forcazione superiori a 7 mm, ma non nel caso di difetti passanti.
- Emdogain® utilizzato nei difetti di recessione ha mostrato di offrire una migliore copertura radicolare rispetto alla tecnica del lembo avanzato coronalmente utilizzata da sola, buoni esiti estetici, un guadagno di tessuto cheratinizzato e la capacità di rigenerare l'attacco.
- Emdogain® è indicato per supportare la guarigione di ferite pulite non infiammate della gengiva e della mucosa orale derivanti da incisioni chirurgiche (ad es. lembi mucoperiostei).

4. Controindicazioni

Sulla base dei risultati dell'analisi dei rischi, la seguente popolazione di pazienti è risultata controindicata: pazienti con disturbi o stati patologici, ivi compresi, a titolo esemplificativo ma non esaustivo, i seguenti: diabete non controllato o altre patologie sistemiche non controllate, disturbi o trattamenti che compromettono la guarigione delle ferite, terapie steroidee croniche ad alte dosi, malattie metaboliche dell'osso, radiazioni o altre terapie immunosoppressive e infezioni o compromissione vascolare in prossimità del sito chirurgico.

5. Effetti collaterali, interazioni e precauzioni; complicazioni con i prodotti Straumann

Studi clinici hanno rilevato in casi rari l'insorgenza di eventi avversi generici correlati alla procedura, ivi compresi, a titolo esemplificativo ma non esaustivo, emorragie gengivali, ematomi, infezioni, (iper)sensibilità della radice, lievi deiscenze della ferita, irritazioni della mucosa (indolenzimento, dolore, gonfiore) e lesioni simili ad afte.

6. Avvertenze

Studi immunologici suggeriscono che un numero limitato di pazienti potrebbe sviluppare sensibilizzazione a Emdogain® in seguito a uso ripetuto. Prestare attenzione nei pazienti con predisposizione a reazioni allergiche e seguire attentamente i pazienti trattati con uso ripetuto ravvicinato. L'esperienza post-commercializzazione ha indicato che la percentuale di reazioni avverse per sensibilizzazione è bassa. Il trattamento richiesto poteva variare dall'assenza di intervento richiesto alla somministrazione di analgesici e/o antistaminici. La sicurezza e l'efficacia di Emdogain® non sono state stabilite in pazienti sottoposti a terapia anticoagulante. L'utilizzo di Emdogain® in questi pazienti deve essere attentamente valutato. Emdogain è destinato a essere applicato unicamente intorno ai denti. Il guadagno di supporto dentale si verifica solo a livello della superficie radicolare coperta dai tessuti molli orali riposizionati. Pertanto, Emdogain® deve essere utilizzato nelle aree in cui è presente tessuto adeguato per la copertura della radice. Emdogain® deve essere utilizzato solo dopo che placca e tartaro sono stati rimossi dal sito malato.

7. Attenzione/Precauzioni

- Non utilizzare se la confezione sterile è aperta o danneggiata. Per evitare possibili contaminazioni incrociate, eliminare o restituire la confezione danneggiata e il dispositivo contenuto.
- La siringa e il dispositivo applicatore sono articoli monouso. Non risterilizzare né riutilizzare la siringa o il dispositivo applicatore. Ogni siringa (pre-riempita) deve essere utilizzata su un solo paziente. Il riutilizzo di dispositivi monouso crea un potenziale rischio di infezioni per il paziente o l'utilizzatore. La contaminazione del dispositivo può causare lesioni o gravi patologie al paziente.
- Al ricevimento il prodotto deve essere conservato a una temperatura compresa tra 2 e 8 °C.
- L'anatomia specifica del sito, la gestione chirurgica, la stabilizzazione della ferita durante la guarigione e l'igiene orale post-chirurgica sono fattori critici per il successo.
- Si noti che piegare l'ago montato sulla siringa può provocare la rottura della siringa.

8. Nota

Straumann® Emdogain può andare incontro a separazione, che si può osservare quando il prodotto si presenta sotto forma di gel non omogeneo. Per omogeneizzare nuovamente il prodotto separato, è sufficiente scuotere la siringa facendo scendere il gel dall'alto in basso e capovolgerla (per 10–15 volte) fino a ottenere il risultato desiderato.

9. Procedura

1. Togliere Emdogain® dall'ambiente freddo in cui era conservato circa 30 minuti prima dell'utilizzo, riportandolo a temperatura ambiente.
2. Attaccare attentamente l'ago di applicazione fornito.
3. Utilizzare Emdogain® entro 2 ore, gettando l'eventuale gel rimasto.

Associato a chirurgia parodontale convenzionale

1. Anestetizzare la zona operatoria mediante anestesia di blocco e/o di infiltrazione. Evitare di iniettare un vasocostrittore nella papilla interdentale o nella gengiva marginale.
2. Praticare incisioni intracrevicolari e, se opportuno, una o due incisioni verticali di scarico fino a raggiungere la mucosa alveolare. Sollevare i lembi a spessore totale (mucoperiostei) sulle superfici buccali e palatali/linguali dei denti. Preservare nel lembo il maggior quantitativo possibile di tessuto connettivo gengivale. Mantenere la vitalità delle cellule parodontali idratando il tessuto molle con soluzione salina.

3. Rimuovere solo il tessuto di granulazione aderente all'osso alveolare ed eventuali difetti ossei associati per poter accedere completamente alle superfici radicolari e ottenere un'eccellente visibilità. Rimuovere la placca subgengivale e il tartaro. Asportare il fango dentinale rimanente pulendo velocemente la superficie con applicazione di Straumann® PrefGel (EDTA) per 2 minuti o acido citrico o fosforico per 15 secondi. Sciacquare accuratamente con soluzione fisiologica sterile. Dopo l'ultimo risciacquo, evitare di contaminare con sangue o saliva la zona operatoria.
4. Applicare immediatamente Emdogain® sulla superficie radicolare esposta, partendo dal livello apicale. Emdogain® va applicato in modo da coprire l'intera superficie della radice. (Durante la sutura può verificarsi un traboccamento del materiale in eccedenza).
5. La copertura completa dell'area interprossimale e l'adattamento ottimale dei tessuti molli sono fattori essenziali. Se lo si ritiene necessario, per facilitare il riposizionamento coronale dei tessuti molli è possibile praticare un'incisione nel periostio alla base del lembo. Utilizzare materiali di sutura appropriati per chiusure stabili ed estese. La stabilità della ferita è estremamente importante per il buon esito di una procedura di rigenerazione con Emdogain®. Se il collegamento tra la superficie radicolare e i tessuti connettivi di guarigione si interrompe, il difetto parodontale si epitelizza rapidamente, portando ad un insuccesso clinico.
6. Informare i pazienti di fare degli sciacqui giornalieri con un collutorio antisettico (ad es. clorexidina allo 0,1–0,2%) per 3–6 settimane dopo l'intervento. Se il medico lo ritiene necessario, è possibile somministrare antibiotici.
7. Istruire il paziente a non spazzolare la zona operatoria per 3 settimane dopo l'intervento. Solo successivamente spazzolare delicatamente le superfici buccali e linguali, evitando il solco gengivale. La pulizia del solco gengivale o interprossimale può essere ripresa dopo 6 settimane dall'intervento.
8. Le suture possono essere rimosse quando i lembi e la radice/interfaccia del tessuto molle sono stabili, generalmente entro 2–3 settimane, in linea con le cure convenzionali post-intervento. Tutti i pazienti devono essere nuovamente istruiti sulle idonee misure di igiene orale. Si è visto che la guarigione dell'attacco clinico e dell'osso alveolare continua per oltre un anno. Pertanto fare attenzione a non interferire con questo processo.

Associato alla tecnica del lembo avanzato coronalmente nel trattamento dei difetti di recessione:

1. Anestetizzare la zona operatoria mediante anestesia di blocco e/o di infiltrazione. Evitare di iniettare un vasocostrittore nella papilla interdentale o nella gengiva marginale.
2. Eseguire lo scaling e la levigatura della superficie radicolare esposta per rimuovere placca, tartaro, irregolarità superficiali e, se ritenuto opportuno, per ridurre l'eventuale prominenza.
3. Praticare un'incisione nel solco in corrispondenza del sito della recessione. Estendere orizzontalmente l'incisione fino alle adiacenti zone interdentali, in direzione leggermente coronale verso la giunzione smalto-cemento (CEJ).
4. Eseguire due incisioni divergenti verticali di scarico partendo dalle estremità laterali mesiali e distali delle incisioni orizzontali.
5. Sollevare un lembo a spessore totale (mucoperiosteo) fino a oltrepassare la giunzione mucogengivale.
6. Praticare un taglio attraverso il periosteo e continuare a sollevare un lembo a spessore parziale mediante dissezione smussata, al fine di eliminare eventuali tensioni muscolari sui margini del lembo e agevolare il posizionamento coronale passivo e privo di tensione del lembo a livello della CEJ.
7. Isolare dall'epitelio la superficie buccale della papilla interdentale per creare un letto di tessuto connettivo per la sutura del lembo avanzato in direzione coronale.
8. Applicare per 2 minuti Straumann® PrefGel (EDTA) sulla superficie radicolare esposta, oppure dell'acido citrico o fosforico per 15 secondi. Sciacquare accuratamente con soluzione fisiologica sterile. Dopo l'ultimo risciacquo, evitare di contaminare con sangue o saliva la superficie radicolare condizionata.
9. Applicare immediatamente Emdogain® in modo da coprire completamente la superficie radicolare esposta e condizionata.
10. Fare avanzare il lembo in direzione coronale e fissarlo a livello della giunzione smalto-cemento, suturandolo nel letto ricevente, vale a dire la papilla de-epitelizzata. Chiudere anche le incisioni verticali con suture laterali. Utilizzare materiali di sutura per chiusure stabili ed estese. Dopo la sutura non deve essere applicata alcuna pressione sul lembo.
11. Informare il paziente di non spazzolare l'area interessata, preferendo sciacqui quotidiani con un collutorio antisettico (ad es. clorexidina allo 0,1–0,2%) per 3 settimane dopo l'intervento. I pazienti devono inoltre essere istruiti ad evitare trazione muscolare o altro trauma alla zona trattata per lo stesso periodo.
12. Le suture devono essere rimosse quando la guarigione clinica del lembo è stabile e le suture non aggiungono più stabilità alla ferita.
13. Dopo il periodo di guarigione iniziale, ai pazienti viene insegnato come spazzolare i denti riducendo al minimo il trauma in direzione apicale sui tessuti marginali della gengiva/tessuti molli del dente trattato. Dopo 4–6 settimane i pazienti possono gradualmente tornare a spazzolare i denti in modo normale.

Associato a procedure chirurgiche orali per migliorare la guarigione di ferite dei tessuti molli:

- Associato a interventi chirurgici orali per migliorare la guarigione di ferite dei tessuti molli, Emdogain® può essere usato per supportare la guarigione delle ferite dei tessuti molli in tipici interventi di chirurgia orale quali flap surgery, impianti odontoiatrici, innesti di tessuto molle e procedure di gengivectomia. In queste procedure Emdogain® si applica sull'intera regione della ferita e sui margini della ferita chirurgica, poco prima della chiusura del lembo e della sutura definitiva. I residui di Emdogain® possono essere applicati sui margini della ferita dopo la chiusura definitiva. Il gel Emdogain® fuoriuscito dai margini della ferita può essere rimosso se lo si ritiene necessario.
- Nel caso di procedure di gengivectomia, quali procedure di innesto di tessuto molle o procedure di gengivectomia parodontale che potrebbero non richiedere sutura, Emdogain® può essere applicato sui margini della ferita, come passaggio finale della procedura, per facilitarne la guarigione.
- Devono essere utilizzati materiali di sutura per una chiusura stabile ed estesa. Dopo la sutura non deve essere applicata alcuna pressione sul lembo. Avvisare il paziente di non spazzolare l'area interessata, preferendo sciacqui quotidiani con un collutorio antisettico (ad es. soluzione di clorexidina allo 0,1-0,2%) per 3 settimane dopo l'intervento. I pazienti devono inoltre essere avvisati di evitare trazione muscolare o altro trauma alla zona trattata per lo stesso periodo.
- Le suture devono essere rimosse quando la guarigione clinica del lembo è stabile e le suture non aggiungono più stabilità alla ferita.

Associato a materiale per innesto osseo:

Nel caso di ampi difetti o in cui si desideri un sostegno per i tessuti molli, Straumann® Emdogain® può essere utilizzato associato a materiale per innesto osseo.

- Associato a materiali per innesto osseo, Straumann® Emdogain® deve essere aggiunto al sostituto osseo goccia a goccia mescolando il prodotto con una spatola o altri strumenti idonei alla miscelazione fino a ottenere una consistenza granulosa umida e pastosa idonea per l'applicazione.
- Il difetto deve essere riempito nel modo più completo possibile con la miscela ottenuta. Evitare

di eccedere con il materiale di innesto. L'innesto osseo deve essere compattato delicatamente nel difetto per garantire la stabilità meccanica per compressione. Evitare un'eccessiva pressione che potrebbe frantumare le particelle di innesto osseo.
- Per migliorare la guarigione di ferite dei tessuti molli applicare uno strato di Straumann® Emdogain® sopra al sostituto di innesto osseo immediatamente prima della chiusura definitiva della ferita.
- Nel caso di trattamenti della superficie radicolare parodontale, Straumann® Emdogain® deve essere applicato sulla superficie radicolare prima dell'innesto osseo o della miscela di innesto osseo/Straumann® Emdogain® per garantire una corretta copertura della superficie radicolare con Straumann® Emdogain®.

10. Fase di guarigione
Fare riferimento alle specifiche procedure riportate alla sezione 9.

11. Ulteriori informazioni
Per ulteriori informazioni consultare il sito web Straumann.

12. Importante
I medici che utilizzano il presente prodotto Straumann ("Prodotto Straumann") devono essere in possesso delle necessarie competenze nell'ambito della parodontologia e delle istruzioni sul suo utilizzo, al fine di garantirne l'impiego sicuro e adeguato, in conformità con le presenti istruzioni per l'uso.
Il prodotto Straumann deve essere utilizzato in conformità con le istruzioni per l'uso fornite dal produttore. È responsabilità del medico utilizzare il dispositivo in conformità con le presenti istruzioni per l'uso, nonché valutare se il suo impiego è indicato per il singolo paziente.

Il prodotto Straumann fa parte di un progetto globale e deve essere utilizzato solo in combinazione con i relativi componenti e strumenti originali distribuiti dall'Institut Straumann AG, dalla casa madre e da tutte le affiliate o consociate della stessa ("Straumann"), salvo diversamente specificato per il relativo prodotto Straumann. L'uso di prodotti fabbricati da terzi, e non distribuiti da Straumann, fa decadere qualsiasi garanzia o altro obbligo implicito o esplicito di Straumann.

13. Validità
Al momento della pubblicazione delle presenti istruzioni per l'uso tutte le versioni precedenti sono superate.

Straumann® e/o altri marchi commerciali e loghi di Straumann® citati nel presente documento sono marchi commerciali o marchi commerciali registrati di Straumann Holding AG e/o sue affiliate.

14. Disponibilità
Alcuni articoli della linea Straumann® regenerative non sono disponibili in tutti i paesi.

CE 0344	I prodotti Straumann sono provvisti di marchio CE e soddisfano i requisiti della Direttiva sui Prodotti Medicali 93/42 CEE.
LOT	Numero di lotto
	Limiti di temperatura (2 °C – 8 °C/36 °F – 46 °F)
REF	Numero di catalogo
	Usare entro
	Attenzione, consultare la documentazione di accompagnamento
STERILE A	Sterilizzato mediante tecniche di processamento asettiche
	Non riutilizzare
	Produttore

straumann

Español Instrucciones de uso: Straumann® Emdogain®

1. Descripción del producto

Straumann® Emdogain® es un material implantable reabsorbible que favorece la regeneración periodontal y que perdura a lo largo de más de un año. Se compone de las proteínas de la matriz del esmalte hidrofóbicas extraídas del esmalte de origen porcino embrionario en desarrollo en un portador de alginato de propilenglicol. El gel tiene la viscosidad adecuada para facilitar la aplicación directamente sobre las superficies radiculares expuestas durante la cirugía periodontal. Una vez aplicado sobre una superficie radicular expuesta la proteína se autoensambla en una matriz tridimensional insoluble y crea un entorno adecuado para la migración y fijación celular periodontal selectiva, de modo que restablece los tejidos de soporte del diente perdidos. Tras la formación de la nueva fijación, el hueso alveolar también puede regenerarse debido a la capacidad osteogénica del ligamento periodontal restaurado. Emdogain® se degrada por los procesos enzimáticos de la cicatrización normal de heridas.

Straumann® Emdogain® se suministra en jeringas estériles precargadas y listas para el uso. Está disponible en tres tamaños (0,15 ml, 0,3 ml y 0,7 ml de gel). Los diferentes tamaños de relleno permiten adaptar la cantidad al tamaño y al número de defectos en un solo paciente como parte de una sesión quirúrgica. Cada jeringa (precargada) es para un solo uso en un solo paciente.

Para mayor comodidad para el cliente se ofrecen los paquetes para procedimientos siguientes:

- Straumann® Emdogain® Multipack: combinación de 3 jeringas con Emdogain® (volumen de relleno de 0,3 ml o 0,7 ml) junto con 3 jeringas de Straumann® PrefGel®.

2. Uso previsto

Emdogain® está pensado para la aplicación tópica en combinación con la cirugía periodontal, para favorecer la regeneración del soporte dental perdido por enfermedad o traumatismo periodontal.

Straumann® Emdogain® se puede utilizar como apoyo a los procesos de cicatrización de los tejidos blandos como parte de procedimientos quirúrgicos orales.

3. Indicaciones

- Emdogain® ha demostrado su eficacia en lugares con bolsas periodontales de más de 6 mm asociadas con pérdida ósea vertical en la radiografía superior a 3 mm.
- Emdogain® también ha demostrado su eficacia en casos de furcación de más de 2 mm pero no en defectos completos.
- Emdogain® utilizado en defectos de recesión ha demostrado que ofrece el potencial de mejorar la cobertura radicular en comparación con el uso solo de un colgajo avanzado coronalmente, un buen resultado estético, una ganancia de tejido queratinizado y el potencial de regeneración de la fijación.
- Emdogain® está indicado como apoyo a la cicatrización de heridas limpias y no inflamadas de la encía y la mucosa oral como resultado de incisiones quirúrgicas (por ejemplo, colgajos mucoperiósticos).

4. Contraindicaciones

A partir de los resultados del análisis de riesgos, las siguientes poblaciones de pacientes están contraindicadas: pacientes con trastornos o enfermedades entre los que se incluyen, entre otros, los siguientes: diabetes no controlada o cualquier otra enfermedad sistémica no controlada, trastornos o tratamientos que puedan afectar a la cicatrización de las heridas, tratamiento crónico con esteroides a dosis altas, enfermedades metabólicas óseas, radiación u otra terapia inmunosupresora, e infecciones o deterioro vascular en el lugar de la cirugía.

5. Efectos secundarios, interacciones y precauciones; complicaciones con los productos Straumann

En raras ocasiones, en estudios clínicos se ha notificado el acaecimiento de acontecimientos adversos generales relacionados con el procedimiento, incluidos, entre otros, hemorragia gingival, hematoma, infección, (hiper)sensibilidad radicular, pequeña dehiscencia de la herida, irritación de la mucosa (dolor, dolor, inflamación) y lesiones similares a las aftas.

6. Advertencias

Estudios inmunológicos sugieren que un número reducido de pacientes puede sensibilizarse a Emdogain® como resultado de un uso reiterado. Tenga precaución en pacientes con predisposición a sufrir reacciones alérgicas y realice un estrecho seguimiento de los pacientes en los que se haga un uso reiterado. La experiencia después de la comercialización ha indicado que la tasa de reacciones adversas de sensibilización es baja. El tratamiento requerido ha variado desde no ser necesaria ninguna intervención hasta el uso de analgésicos y/o antihistamínicos. La seguridad y la eficacia de Emdogain® no se han establecido en pacientes sometidos a tratamiento con anticoagulantes. Estudie detenidamente estos pacientes antes de utilizar Emdogain®. Emdogain® está pensado únicamente para la aplicación alrededor de los dientes. La obtención de apoyo dental se produce únicamente a nivel de la superficie radicular cubierta por los tejidos blandos orales repuestos. Por consiguiente, Emdogain® debe utilizarse en áreas donde haya tejido adecuado para la cobertura radicular. Emdogain® solo debe utilizarse tras haber retirado la placa y el sarro de la zona enferma.

7. Atención/precauciones

- No lo utilice si el envase estéril está abierto o dañado. Para evitar una posible contaminación cruzada, deseche o devuelva el paquete dañado y el dispositivo adjunto.
- La jeringa y el dispositivo de aplicación son artículos de un solo uso. No vuelva a esterilizar ni reutilice la jeringa o el dispositivo de aplicación. Cada jeringa (precargada) es para el uso en un solo paciente. La reutilización de dispositivos de un solo uso entraña un riesgo potencial de infecciones del paciente o el usuario. La contaminación del dispositivo puede provocar lesiones o enfermedades graves al paciente.
- El producto debe almacenarse a 2-8 °C tras su entrega.
- La anatomía específica del sitio, el tratamiento quirúrgico, la estabilización de la herida durante la cicatrización y la higiene oral después de la cirugía son factores críticos para el éxito.
- Tenga en cuenta que la flexión de la cánula cuando está montada en la jeringa puede provocar la rotura de la misma.

8. Nota

Puede producirse la separación de Straumann® Emdogain®. La separación de Straumann® Emdogain® se identifica como un gel no homogéneo. La homogeneización del material separado puede lograrse sacudiendo el gel desde la parte superior hasta la parte inferior de la jeringa, girando la jeringa y repitiendo el procedimiento de diez a quince veces hasta que se produzca nuevamente la homogeneización.

9. Procedimiento

1. Retire Emdogain® de la conservación en frío aprox. 30 minutos antes del uso y deje que alcance la temperatura ambiente.
2. Conecte con cuidado la cánula de aplicación suministrada.
3. Utilice Emdogain® en un plazo de 2 horas y deseche el gel restante.

En combinación con cirugía periodontal convencional

1. Anestesie la zona elegida para la cirugía mediante anestesia en bloque y/o infiltración. Evite la inyección con un vasoconstrictor en la papila interdental o la encía marginal.

2. Efectúe incisiones intracrevicular es. A continuación, si se considera adecuado, realice una o dos incisiones verticales de liberación extendiéndose hacia la mucosa alveolar. Levante colgajos de espesor completo (mucoperiósticos) en las superficies bucales y palatales/linguales de los dientes. Preserve el mayor tejido conjuntivo gingival en el colgajo posible. Mantenga la viabilidad de las células periodontales mediante la hidratación de los tejidos blandos con solución salina.
3. Extraiga solo el tejido de granulación adherido al hueso alveolar y cualesquiera defectos óseos asociados que sean necesarios para ofrecer pleno acceso y visibilidad a las superficies radiculares. Elimine la placa y el sarro subgingivales. Retire la capa de barrillo restante con una limpieza superficial rápida con Straumann® PrefGel® (EDTA) durante 2 minutos o con ácido cítrico o ácido fosfórico durante 15 segundos. Enjuague bien con solución salina estéril. Evite la contaminación del área quirúrgica con saliva o sangre después del enjuague final.
4. Aplique inmediatamente Emdogain® en las superficies radiculares expuestas, comenzando por el nivel óseo más apical. Aplique Emdogain® hasta cubrir totalmente las superficies radiculares expuestas. (Debería producirse un desbordamiento del material sobrante durante la sutura)
5. Es esencial realizar una cobertura completa de la zona interproximal y una adaptación óptima de los tejidos blandos. Si se considera apropiado, puede utilizarse una fenestración perióstica en la base del colgajo para facilitar la reposición coronaria de los tejidos blandos. Es preferible utilizar materiales de sutura adecuados para una sutura estable extensa. La estabilidad de la herida es fundamental para el resultado de un procedimiento de regeneración con Emdogain®. Si la unión entre la superficie radicular y los tejidos conectivos de cicatrización se rompe, el defecto periodontal será fácilmente epitelializado, lo cual tendrá como resultando un fracaso clínico.
6. Hay que advertir a los pacientes de que se enjuaguen a diario con un enjuague bucal antiséptico (p. ej. solución de clorhexidina al 0,1-0,2%) hasta 3-6 semanas después de la cirugía. A criterio del médico también pueden utilizarse antibióticos si se considera apropiado.
7. Hay que advertir al paciente de que no se cepille en el área donde se ha realizado la cirugía hasta 3 semanas después de la intervención. Entonces solo se recomienda un cepillado suave sobre las superficies bucales y linguales utilizando el método de barrido. No debe realizarse una limpieza dental interproximal o sulcular hasta 6 semanas después de la intervención.
8. Las suturas pueden retirarse cuando los colgajos y la interfaz raíz/tejido blando sean estables, normalmente al cabo de 2-3 semanas. Igual que en la atención posoperatoria convencional, hay que reinstruir a todos los pacientes en medidas de higiene bucal adecuadas siempre que sea necesario. Se ha demostrado que la cicatrización de la fijación clínica y el hueso alveolar se prolongan durante más de un año, y hay que tener cuidado de no interferir con este proceso.

Juntamente con colgajo coronal avanzado para el tratamiento de defectos tipo recesión:

1. Anestesia la zona elegida para la cirugía mediante infiltración y, en caso necesario, anestesia en bloque. Evite la inyección de anestésico local con un vasoconstrictor en las papilas interdentales o la encía marginal.
2. Planifique y escale la superficie radicular expuesta para retirar la placa, el sarro, las irregularidades de la superficie radicular y, si se considera adecuado, para reducir la prominencia.
3. Efectúe una incisión sulcular en el lugar de la recesión. Extienda la incisión horizontalmente hacia la zona interdental adyacente en sentido ligeramente coronal a la CEJ.
4. Efectúe dos incisiones de liberación verticales divergentes en los ángulos de la línea mesial y distal conectadas con la incisión horizontal.
5. Levante un colgajo de espesor completo (mucoperióstico) hasta superar la unión mucogingival.
6. Realice un corte a través del periostio y continúe levantando un colgajo de espesor parcial mediante una disección roma. El objetivo es eliminar cualquier tensión muscular en los márgenes del colgajo y permitir una colocación coronal pasiva y sin tensiones del colgajo a nivel de la CEJ.
7. Desepitelialice la cara bucal de las papilas interdentales a fin de crear un lecho de tejido conjuntivo para suturar el colgajo avanzado coronariamente.
8. Acondicione la superficie radicular expuesta con Straumann® PrefGel® (EDTA) durante 2 minutos o con ácido cítrico o ácido fosfórico durante 15 segundos. Enjuague bien con solución salina estéril. Evite la contaminación de la superficie radicular condicionada con saliva o sangre después del enjuague final.
9. Aplique inmediatamente Emdogain® para cubrir totalmente la superficie radicular expuesta y acondicionada.
10. Coloque el colgajo coronalmente y fíjelo al nivel de la CEJ suturando el colgajo en el lecho receptor, es decir, las papilas desepitelializadas. Cierre también las incisiones verticales con suturas laterales. Utilice materiales de sutura para una sutura estable extensa. No debe aplicarse presión en el colgajo después de la sutura.
11. Hay que advertir al paciente de que no se cepille en el área, sino que se enjuague a diario con un enjuague bucal antiséptico (p. ej. solución de clorhexidina al 0,1-0,2%) hasta 3 semanas después de la cirugía. También hay que advertir a los pacientes de que eviten la tracción muscular u otros traumatismos en el área tratada durante el mismo período de tiempo.
12. Las suturas se retiran cuando la cicatrización clínica del colgajo es estable y las suturas ya no aportan estabilidad a la herida.
13. Tras el período de cicatrización inicial, se explica a los pacientes una técnica de limpieza dental que minimiza el traumatismo dirigido apicalmente sobre el margen gingival/los tejidos blandos del diente tratado. Al cabo de 4 a 6 semanas, los pacientes pueden retomar gradualmente sus medidas normales para la limpieza de los dientes.

Junto con procedimientos quirúrgicos orales para mejorar la cicatrización de los tejidos blandos:

- Junto con procedimientos quirúrgicos orales para mejorar la cicatrización de los tejidos blandos, Emdogain® se puede utilizar como apoyo a la cicatrización de heridas quirúrgicas en los tejidos blandos como parte de los procedimientos quirúrgicos orales habituales, como la cirugía de colgajo, los tratamientos con implantes, los procedimientos de injertos de tejidos blandos y los procedimientos de gingivectomía. En estos procedimientos Emdogain® se aplica en toda la zona de la herida y los márgenes de la herida quirúrgica antes del cierre del colgajo y la sutura definitiva. Los restos de Emdogain® se pueden utilizar para su aplicación en los márgenes de la herida tras su cierre. El Emdogain® que rebose de los márgenes de la herida se puede retirar si se considera necesario.
- En caso de procedimientos de gingivectomía, como son los procedimientos de injerto tisular o los procedimientos de gingivectomía periodontal que puede que no requieran sutura, Emdogain® se puede aplicar en los márgenes de la herida para facilitar la cicatrización de la herida como último paso del procedimiento.
- Deben utilizarse materiales de sutura para una sutura estable extensa. No debe aplicarse presión en el colgajo después de la sutura. Hay que advertir al paciente de que no se cepille la zona, sino que se enjuague a diario con un enjuague bucal antiséptico (p. ej. solución de clorhexidina al 0,1-0,2%) hasta 3 semanas después de la cirugía. También hay que advertir a los pacientes de que eviten la tracción muscular u otros traumatismos en el área tratada durante el mismo período de tiempo.

- Las suturas se retiran cuando la cicatrización clínica del colgajo es estable y las suturas ya no aportan estabilidad a la herida.

Junto con material de injerto óseo:
En caso de defectos extensos o cuando se desee soporte de los tejidos blandos, Straumann® Emdogain® se puede utilizar junto con un material de injerto óseo.

- Cuando se combina con materiales de injerto óseo, Straumann® Emdogain® se añade gota a gota al sustituto óseo y el producto resultante se mezcla con una espátula u otro instrumento adecuado para la mezcla hasta que se vuelve pastoso/de consistencia parecida a la de la arena gruesa húmeda, momento en que es adecuado para la aplicación.
- El defecto debe rellenarse completamente con la mezcla resultante. Debe evitarse un aumento excesivo. El injerto óseo debe compactarse ligeramente en el defecto para garantizar la estabilidad mecánica frente a la compresión. Debe evitarse una presión excesiva que pudiera provocar el aplastamiento de las partículas del injerto óseo.
- Para mejorar la cicatrización de la herida en el tejido blando, se aplica una capa de Straumann® Emdogain® en la parte superior del sustituto de injerto óseo inmediatamente antes de la sutura definitiva de la herida.
- En caso de tratamientos de la superficie radicular periodontal Straumann® Emdogain® debe aplicarse sobre la superficie radicular antes de la aplicación del injerto óseo o la mezcla de injerto óseo/Straumann® Emdogain® para garantizar una cobertura adecuada de la superficie radicular con Straumann® Emdogain®.

10. Fase de cicatrización
Consulte la parte concreta del procedimiento en la sección 9.

11. Información adicional
Consulte el sitio web de Straumann para obtener información adicional.

12. Advertencia
Los médicos deben tener conocimientos de periodoncia y experiencia en el manejo del producto Straumann aquí descrito ("Producto Straumann") para poder hacer uso del Producto Straumann de forma segura y adecuada de conformidad con estas instrucciones de uso.
El producto Straumann debe utilizarse según lo descrito en las instrucciones de uso facilitadas por el fabricante. Es responsabilidad del médico utilizar el dispositivo de acuerdo a estas instrucciones de uso y decidir si se ajusta a la situación particular del paciente.

El Producto Straumann forma parte de un concepto global y debe ser utilizado únicamente con los componentes e instrumentos originales correspondientes suministrados por Institut Straumann AG, su sociedad matriz y todas las filiales o sucursales de la misma (en adelante "Straumann"), salvo que se indique lo contrario para el Producto Straumann respectivo. Si Straumann no recomienda el uso de productos fabricados por terceros, dicho uso anulará toda garantía u otra obligación, explícita o implícita, de Straumann.

13. Validez
La publicación de estas instrucciones de uso supone la anulación de todas sus versiones anteriores.

14. Disponibilidad
Algunos artículos de la cartera Straumann® Regenerative no están disponibles en todos los países.

CE 0344	Los productos Straumann con la marca CE cumplen los requisitos de la Directiva relativa a productos sanitarios 93/42 CEE.
LOT	Código de lote
	Limitaciones de temperatura (2 °C a 8 °C)
REF	Número del catálogo
	Fecha de caducidad
	Precaución, consulte los documentos adjuntos
STERILE A	Esterilizado mediante técnicas de procesamiento asépticas
	No reutilizar
	Fabricante

straumann

Português Instruções de utilização: Straumann® Emdogain®

1. Descrição do produto

O Straumann® Emdogain® é um material implantável, reabsorvível que promove a regeneração periodontal que acontece ao longo de mais de um ano. É constituído por proteínas hidrófugas da matriz do esmalte extraídas do esmalte embrionário em desenvolvimento de origem suína numa base de alginato de propilenoglicol. O gel apresenta uma viscosidade adequada para facilitar a aplicação directamente nas superfícies da raiz expostas durante a cirurgia periodontal. Depois de aplicada sobre uma superfície de raiz exposta a própria proteína agrupa-se numa matriz tridimensional insolúvel e cria um ambiente adequado à migração e fixação selectiva de células periodontais, restabelecendo os tecidos perdidos de suporte do dente. Após a formação de uma nova fixação, o osso alveolar pode também ser regenerado devido à capacidade osteogénica do ligamento periodontal restaurado. O Emdogain® decompõe-se através dos processos enzimáticos normais de cicatrização da ferida.

O Straumann® Emdogain® apresenta-se em seringas pré-cheias estéreis e prontas a usar, estando disponível em três tamanhos (0,15 ml, 0,3 ml, 0,7 ml de gel). Os diferentes tamanhos de enchimento permitem a adaptação da quantidade ao tamanho e número de defeitos de um único doente, como parte de uma sessão cirúrgica. Cada seringa (pré-cheia) destina-se a uma única utilização num só doente.

Para comodidade do cliente, estão disponíveis as seguintes embalagens para procedimentos:

- embalagem múltipla de Straumann® Emdogain® combinação de 3 seringas de Emdogain® (com um volume de enchimento de 0,3 ml ou 0,7 ml) juntamente com 3 seringas de Straumann® PrefGel®.

2. Indicações de utilização

O Emdogain® destina-se a aplicação tópica em conjunção com cirurgia periodontal para proporcionar a regeneração do apoio ao dente perdido por doença ou trauma periodontal.

O Straumann® Emdogain® pode ser usado para promover os processos de cicatrização dos tecidos moles em procedimentos cirúrgicos orais.

3. Indicações

- O Emdogain® tem demonstrado ser eficaz em locais com bolsas periodontais com mais de 6 mm associadas a perda óssea vertical superior a 3 mm, em radiografia.
- O Emdogain® tem ainda demonstrado ser eficaz em envolvimentos de bifurcações que excedam os 2 mm mas não em defeitos totais.
- O Emdogain® usado em defeitos de recessão tem demonstrado um potencial para melhorar a cobertura da raiz, quando comparado com a utilização de uma única aba coronalmente avançada, além de ter bons resultados estéticos, de aumentar o tecido queratinizado, e de demonstrar potencial para a regeneração da união.
- O Emdogain® é indicado para promover a cicatrização de feridas limpas e não inflamadas da gengiva e mucosa oral resultantes de incisões cirúrgicas (por ex. abas do mucoperiósteo).

4. Contra-indicações

Com base nos resultados da análise de risco, a utilização deste produto está contra-indicada nas seguintes populações de pacientes: pacientes com doenças ou quadros clínicos que incluem, entre outros, os seguintes: diabetes não controlada ou outras doenças sistémicas não controladas, doenças ou tratamentos que comprometam a cicatrização de feridas, terapêutica crónica com doses elevadas de esteróides, doenças metabólicas ósseas, radiação ou outras terapêuticas imunossupressoras e infecções ou insuficiência vascular no local cirúrgico.

5. Efeitos secundários, interacções e precauções, complicações com os produtos Straumann

Em casos raros, foi relatada em estudos clínicos a ocorrência de eventos adversos gerais relacionados com o procedimento que incluíram, entre outros, hemorragia gengival, hematoma, infecção, (hiper)sensibilidade da raiz, pequena deiscência da ferida, irritação da mucosa (ulceração, dor, inchaço) e lesões semelhantes a aftas.

6. Advertências

Os estudos imunológicos sugerem que um pequeno número de pacientes pode tornar-se sensível ao Emdogain® em resultado da utilização repetida. Use de precaução em pacientes com predisposição para reacções alérgicas e acompanhe de perto os pacientes que estão a ser submetidos a uma utilização repetida do produto. A experiência pós-comercialização tem indicado que a taxa de reacções adversas de sensibilização é baixa. O tratamento necessário variou entre não ser necessária uma intervenção e analgésicos e/ou anti-histamínicos. A segurança e eficácia do Emdogain® não foram estabelecidas em pacientes submetidos a terapêutica anticoagulante. A utilização do Emdogain® nestes pacientes deve ser cuidadosamente ponderada. O Emdogain® destina-se a aplicação apenas em redor dos dentes. O ganho do suporte dentário acontece apenas ao nível da superfície da raiz coberta pelo tecido mole oral reposicionado. Por isso, o Emdogain® deve ser usado em áreas onde exista tecido adequado para a cobertura da raiz. O Emdogain® deve ser usado apenas após a remoção da placa bacteriana e tártaro do local doente.

7. Cuidados/Precauções

- Não utilize se a embalagem estéril se apresentar aberta ou danificada. Para impedir a possível contaminação cruzada, elimine ou devolva a embalagem danificada e o dispositivo incluso.
- A seringa e o dispositivo de aplicação destinam-se a uma única utilização. Não reesterilize nem reutilize a seringa nem o dispositivo de aplicação. Cada seringa (pré-cheia) destina-se a ser utilizada num só paciente. A reutilização de dispositivos de utilização única cria um risco potencial de infecção para o doente ou utilizador. A contaminação do dispositivo pode originar lesões ou doenças graves no paciente.
- Assim que for recebido, o produto deve ser guardado a 2–8 °C.
- A anatomia específica do local, a gestão cirúrgica, a estabilização da ferida durante a cicatrização, e a higiene oral pós-cirurgia são factores críticos para o sucesso.
- Lembre-se de que curvar a cânula após montagem na seringa pode provocar a quebra da seringa.

8. Nota

Pode ocorrer a separação do Straumann® Emdogain®. A separação do Straumann® Emdogain® é identificada como um gel não homogéneo. A homogeneização do material separado pode ser conseguida através da agitação do gel do topo até ao fundo da seringa, virando a seringa ao contrário e repetindo o procedimento dez a quinze vezes até recuperar a homogeneização.

9. Procedimento

1. Retire o Emdogain® do frio cerca de 30 minutos antes de usar e deixe que atinja a temperatura ambiente.
2. Fixe cuidadosamente a cânula de aplicação fornecida.
3. Use o Emdogain® no espaço de 2 horas e elimine qualquer gel restante.

Em conjunção com cirurgia periodontal convencional:

1. Anestesie a área seleccionada para a cirurgia por anestesia de bloqueio e/ou infiltração. Evite a injecção com um vasoconstritor na papila interdental ou gengiva marginal.
2. Faça incisões entre fissuras. Depois, se considerar adequado, faça uma ou duas incisões verticais de libertação, até à mucosa alveolar. Levante toda a espessura (do mucoperiósteo)

das abas nas superfícies bucal e palatal/lingual do dente. Preserve o máximo possível de tecido conjuntivo gengival da aba. Mantenha a viabilidade das células periodontais, hidratando o tecido mole com soro fisiológico.

3. Elimine apenas o tecido granuloso aderente ao osso alveolar e quaisquer defeitos ósseos associados de modo a conseguir total visibilidade e acesso às superfícies da raiz. Retire a placa bacteriana e o tártaro subgengivais. Retire a camada restante através de uma limpeza superficial rápida com Straumann® PrefGel® (EDTA) durante 2 minutos ou 15 segundos com ácido cítrico ou fosfórico. Enxagúe bem com soro fisiológico estéril. Após a lavagem final, evite a contaminação da área cirúrgica com saliva ou sangue.
4. Aplique imediatamente o Emdogain® sobre as superfícies expostas das raízes, começando pelo nível mais apical do osso. Aplique o Emdogain® até cobrir totalmente as áreas expostas da superfície das raízes. (Durante a sutura, é possível que ocorra o extravasamento do material excedente).
5. É essencial que a cobertura da área interproximal seja total e que a adaptação do tecido mole seja a melhor. Se considerar adequado, pode usar uma fenestragem do periósteo na base da aba, para facilitar a reposição coronal do tecido mole. Deve usar preferencialmente materiais de sutura adequados para maior estabilidade da oclusão. A estabilidade da incisão é essencial para o resultado do procedimento de regeneração quando se usa Emdogain®. Se a ligação entre a superfície da raiz e os tecidos conjuntivos da cicatrização se quebrar, o defeito periodontal passará rapidamente por uma epitelização, resultando em falha clínica.
6. O paciente deve ser aconselhado a bochechar diariamente com um elixir bucal antisséptico (por exemplo, solução de clorexidina a 0,1-0,2 %) até 3-6 semanas após a cirurgia. Podem ainda ser prescritos antibióticos quando considerado necessário com base na opinião clínica.
7. O paciente deve ser instruído para não escovar na área da cirurgia até 3 semanas após a cirurgia. Recomenda-se apenas a utilização do método "roll-stroke" para escovar a superfície bucal e lingual. Não deve ser realizada nenhuma limpeza dentária no sentido dos sulcos e na zona interproximal até 6 semanas após a cirurgia.
8. As suturas podem ser retiradas quando as abas e a interface entre a raiz/tecido mole se apresentar estável, habitualmente no prazo de 2 – 3 semanas. Relativamente aos cuidados pós-cirúrgicos convencionais, todos os doentes devem ser novamente instruídos sobre as medidas de higiene oral adequadas, conforme necessário. Tem sido demonstrado que a cicatrização do ligamento clínico e do osso alveolar continua por mais de um ano e que devem ser tidos todos os cuidados para não interferir neste processo.

Juntamente com a aba coronalmente avançada para o tratamento de defeitos sob a forma de recessão:

1. Anestesie a área seleccionada para a cirurgia por infiltração e, se necessário, por anestesia de bloqueio. Evite a injecção de anestesia local com um vasoconstritor nas papilas interdentais ou gengiva marginal.
2. Raspe e alise a superfície exposta da raiz para remover a placa bacteriana, o tártaro, irregularidades na superfície da raiz e, quando considerar adequado, para reduzir a proeminência.
3. Faça uma incisão subcular no local da recessão. Prolongue horizontalmente a incisão para a área interdental adjacente ligeiramente coronal à CEJ.
4. Faça duas incisões verticais divergentes de libertação nos ângulos da linha mesial e distal ligados à incisão horizontal.
5. Levante toda a espessura (do mucoperiósteo) da aba até passar a junção mucogingival.
6. Faça um corte através do periósteo e continue a levantar parte da espessura da aba por meio de uma dissecção cega. O objectivo é eliminar qualquer tensão muscular nas margens da aba e permitir um posicionamento coronal passivo e isento de tensão da aba ao nível da CEJ.
7. Despitelize o aspecto bucal das papilas interdentais, de modo a criar uma base de tecido conjuntivo para a sutura da aba coronalmente avançada.
8. Condicione a superfície exposta da raiz com o Straumann® PrefGel® (EDTA) durante 2 minutos ou 15 segundos com ácido cítrico ou fosfórico. Enxagúe bem com soro fisiológico estéril. Após a lavagem final, evite a contaminação da superfície da raiz com saliva ou sangue.
9. Aplique imediatamente o Emdogain® até cobrir totalmente a superfície exposta e condicionada da raiz.
10. Posicione coronalmente a aba e prenda-a ao nível da CEJ suturando-a na base receptora, ou seja, às papilas despitelizadas. Feche também as incisões verticais com suturas laterais. Use materiais de sutura para criar uma oclusão estável e alargada. Não deve ser aplicada pressão sobre a aba após a sutura.
11. O paciente deve ser aconselhado a não escovar na área da cirurgia, mas a bochechar diariamente com um elixir bucal antisséptico (por exemplo, solução de clorexidina a 0,1-0,2 %) até 3 semanas após a cirurgia. Os pacientes devem ainda ser instruídos para evitarem tracção muscular ou outros traumatismos na área tratada durante o mesmo período.
12. As suturas são removidas quando a cicatrização clínica da aba se apresentar estável e as suturas já não acrescentarem estabilidade à incisão.
13. Após o período inicial de cicatrização, os pacientes recebem instruções numa técnica de limpeza dentária, que minimiza o trauma dirigido apicalmente sobre a margem gengival/tecidos moles do dente tratado. Após 4–6 semanas, os pacientes podem retomar gradualmente as medidas normais de limpeza dentária.

Juntamente com procedimentos cirúrgicos orais para melhorar a cicatrização dos tecidos moles das incisões:

- Juntamente com procedimentos cirúrgicos orais para melhorar a cicatrização dos tecidos moles da incisão, o Emdogain® pode ser usado para promover a cicatrização dos tecidos moles da incisão como parte dos procedimentos cirúrgicos orais habituais como cirurgias de aba, procedimentos de implantação dentária, procedimentos de enxerto de tecidos moles e gengivectomias. Nestes procedimentos, o Emdogain® é aplicado em toda a área da incisão cirúrgica e nas margens da mesma antes da oclusão da aba e da sutura final. O Emdogain® residual pode ser usado para aplicar nas margens da incisão após o fecho da mesma. O gel Emdogain® que extravasa pelas margens da incisão pode ser removido se isso for considerado necessário.
- No caso de procedimentos de gengivectomia, por exemplo, procedimentos de enxerto de tecidos ou procedimentos de gengivectomia periodontal que podem não requerer sutura, pode aplicar o Emdogain® nas margens da incisão para facilitar a cicatrização da incisão, como etapa final do procedimento.
- Devem ser utilizados materiais de sutura para um fecho estável e alargado. Não deve ser aplicada pressão sobre a aba após a sutura. O paciente deve ser aconselhado a não escovar a área, mas a bochechar diariamente com um elixir bucal antisséptico (por ex. solução de clorexidina a 0,1–0,2 %) até 3 semanas após a cirurgia. Os pacientes devem ainda ser instruídos para evitar tracção muscular ou outros traumatismos na área tratada durante o mesmo período.
- As suturas são removidas quando a cicatrização clínica da aba se apresentar estável e as suturas já não acrescentarem estabilidade à incisão.

Em conjunção com material de enxerto ósseo:

Em caso de defeitos alargados ou quando se pretender um apoio aos tecidos moles, o Straumann® Emdogain® pode ser usado juntamente com o material do enxerto ósseo.

- Quando combinado com materiais de enxerto ósseo, o Straumann® Emdogain® é adicionado gota a gota ao substituto ósseo, misturando-se o produto com uma espátula ou outros instrumentos adequados para misturar, até se obter uma consistência pastosa/semelhante a areia molhada propícia à aplicação.
- O defeito deve ser preenchido o mais completamente possível com a mistura obtida. O aumento excessivo deve ser evitado. O enxerto ósseo deve ser suavemente compactado no defeito para assegurar estabilidade mecânica contra a compressão. Deve ser evitada uma pressão excessiva que resulte no esmagamento das partículas do enxerto ósseo.
- Para melhorar a cicatrização dos tecidos moles da incisão, é aplicada uma camada de Straumann® Emdogain® sobre o aumento do enxerto ósseo imediatamente antes do fecho final da incisão.
- No caso dos tratamentos da superfície periodontal da raiz, o Straumann® Emdogain® deve ser aplicado sobre a superfície da raiz antes da aplicação do enxerto ósseo ou da mistura de enxerto ósseo/Straumann® Emdogain®, de modo a assegurar uma cobertura adequada da superfície da raiz com Straumann® Emdogain®.

10. Fase de cicatrização

Consulte a parte respeitante ao procedimento específico da secção 9.

11. Outras informações

Consulte a página da Straumann na Internet para mais informações.

12. Atenção

Os médicos devem ter conhecimentos de Periodontologia e formação no manuseamento do produto Straumann aqui descrito ("Produto Straumann") para uma utilização segura e correcta do Produto Straumann, em conformidade com estas instruções de utilização.
O Produto Straumann deve ser utilizado de acordo com as instruções de utilização fornecidas pelo fabricante. É da responsabilidade do médico utilizar o dispositivo em conformidade com estas instruções de utilização e determinar se o mesmo se adapta à situação individual do paciente.

O Produto Straumann faz parte de um conceito geral e tem de ser usado apenas em conjunto com os componentes originais correspondentes e instrumentos distribuídos pelo Institut Straumann AG, pela respectiva empresa-mãe e todas as filiais ou subsidiárias desta empresa-mãe ("Straumann"), exceto em caso de declaração em contrário relativa ao Produto Straumann correspondente. Se a utilização de produtos fabricados por terceiros não for recomendada pela Straumann, tal utilização anulará qualquer garantia ou outra obrigação, expressa ou implícita, da Straumann.

13. Validade

Com a publicação das presentes instruções de utilização, todas as versões anteriores são revogadas.

14. Disponibilidade

Alguns artigos de portefólio regenerativo Straumann® não estão disponíveis em todos os países.

Os Produtos Straumann com a marca CE cumprem os requisitos da Directiva relativa a dispositivos médicos 93/42 CEE

LOT Código de lote

Limite de temperatura (2 °C – 8 °C/36 °F – 46 °F)

REF Número de catálogo

Prazo de validade

Cuidado, consulte a documentação anexa

STERILE A Esterilizado por técnicas de processamento assépticas

Não reutilizar

Fabricante

Appendix 3 – Instructions For Use IFU 700096 - Pref-Gel®

700096-6
P 01/13

Gebrauchsanweisung: Straumann® PrefGel 0,6 ml
Instructions for use: Straumann® PrefGel 0.6 ml
Mode d'emploi : Straumann® PrefGel 0,6 ml
Istruzioni per l'uso: Straumann® PrefGel 0,6 ml
Instrucciones de uso: Straumann® PrefGel 0,6 ml
Instruções de utilização: Straumann® PrefGel 0,6 ml
Bruksanvisning: Straumann® PrefGel 0,6 ml
Gebruiksaanwijzing: Straumann® PrefGel 0,6 ml
Brugsanvisning: Straumann® PrefGel 0,6 ml
Инструкции по применению. Straumann® PrefGel 0,6 мл

Hersteller / Manufacturer / Fabricant / Produttore / Fabricante / Fabricante / Fabricante / Tillverkare / Producent / Изготовитель

Institut Straumann AG, CH-4002 Basel/Switzerland, www.Straumann.com

English

Caution: U.S. Federal law restricts this device to sale by or on the order of a dental professional.

1. Product Description

Straumann® PrefGel is a neutral EDTA formulation intended for topical application onto exposed root surfaces during periodontal surgery in order to remove the smear-layer. Mechanical debridement of a root surface inevitably produces a smear-layer, which in turn may prevent or retard periodontal healing. Exposure of collagen fibers may be important for linking fibrin in the blood clot to the root surface. Clinical studies with PrefGel® have demonstrated the ability to remove the smear-layer and to expose the collagenous matrix of dentin surfaces.
The package contains 5 syringes Straumann® PrefGel 0.6 ml edetate disodium [EDTA] 2 H_2O 24% neutral in carboxymethyl cellulose (CMC) gel and 5 application needles.

2. Intended use

Straumann® PrefGel is intended for topical application onto exposed root surfaces during periodontal surgery in order to remove the smear layer.

3. Indications

- PrefGel® has been shown to effectively remove the smear-layer. PrefGel® has also been shown to produce a fibrillar collagenous meshwork on the exposed and conditioned root surface by selective removal of mineral.

4. Contraindications

No contraindications are currently identified for this medical product.

5. Side effects, interactions and precautions; complications with Straumann products

- PrefGel® does not induce any detectable necrosis in the surrounding periodontal tissues.
- PrefGel® has been well tolerated in clinical studies.
- Reversible and short duration procedure-related dentin hypersensitivity may occasionally occur.

6. Warnings

No warnings are currently identified for this medical product.

7. Caution/Precautions

- Do not use if sterile package is opened or damaged.
- To prevent possible cross contamination discard or return damaged package and the enclosed device.
- Syringe and application device are single use items. Do not re-sterilize or re-use. Re-use of single-use devices creates a potential risk of patient or user infection. Contamination of the device may lead to injury or serious illness of the patient.
- Each prefilled syringe is intended for use in one patient only.
- Straumann® PrefGel must be stored at 2–8 °C/ 36–46 °F upon receipt.
- Be aware that bending the needle may cause breakage.

8. Procedure

1. Remove PrefGel® from cold storage approx. 30 minutes before use and allow it to assume ambient temperature.
2. Remove the plastic top of the syringe.
3. Carefully attach the supplied application needle.
4. After application, discard any residual gel, the syringe and needle per local protocol.

Periodontal surgery:

1. Following reflection of mucoperiosteal flaps in the area selected for periodontal surgery, the exposed root surfaces are mechanically debrided in order to remove any remaining plaque and/or calculus.

2. PrefGel® is then topically applied onto the exposed and debrided root surfaces for 2 minutes. Only apply PrefGel® onto those parts of the root surfaces which will be covered by soft tissues once flaps are replaced and sutured. Active rubbing («burnishing») is not recommended.

3. After conditioning, the root surfaces must be rinsed thoroughly with sterile saline.

4. Care should be taken to avoid re-contamination of the conditioned root surfaces after the final rinse and prior to treatment with regenerative topical products (e.g. Straumann® Emdogain).

9. Further Information

Please refer to the Straumann website for additional information.

10. Please Note

Practitioners must have knowledge of periodontology and instruction in the handling of the Straumann product described herein ("Straumann Product") for using the Straumann Product safely and properly in accordance with these instructions for use.

The Straumann Product must be used in accordance with the instructions for use provided by the manufacturer. It is the practitioner's responsibility to use the device in accordance with these instructions for use and to determine if the device is suitable for the individual patient situation.

The Straumann Product is part of an overall concept and must be used only in conjunction with the corresponding original components and instruments distributed by Institut Straumann AG, its ultimate parent company and all affiliates or subsidiaries of such parent company ("Straumann"). Use of products made by third parties, which are not distributed by Straumann, will void any warranty or other obligation, express or implied, of Straumann.

11. Validity

Upon publication of these instructions for use, all previous versions are superseded.

12. Availability

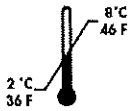
Some items of the Straumann® regenerative portfolio are not available in all countries.

CE 0123

Straumann-Produkte mit dem CE-Zeichen erfüllen die Anforderungen der Medizingeräte-Richtlinie 93/42 EWG /
Straumann Products with the CE mark fulfil the requirements of the Medical Devices Directive 93/42 EEC /
Les produits Straumann portant la marque CE sont conformes à la Directive 93/42 EEC relative au matériel médical /
I prodotti Straumann provvisti di marchio CE soddisfano i requisiti della Direttiva sui Prodotti Medicali 93/42 CEE /
Los productos Straumann con el símbolo CE cumplen los requisitos de la directiva sobre productos médicos 93/42 CEE /

LOT

Chargennummer / Batch code / Numéro de lot / Numero di lotto / Codigo de lote



Temperaturbeschränkung (2 °C-8 °C / 36 °F-46 °F)
Temperature limitation (2 °C-8 °C / 36 °F-46 °F)
Limite de température (2 °C-8 °C / 36 °F-46 °F)
Temperatura limite (2 °C-8 °C / 36 °F-46 °F)
Limitación de temperatura (2 °C-8 °C / 36 °F-46 °F)

REF

Katalognummer / Catalogue number / Référence du catalogue / Numero di catalogo / Número de catálogo

Verfallsdatum / Use by date / Date limite d›utilisation / Usare entro / Fecha de caducidad

Vorsicht, Begleitdokumente beachten / Caution, consult accompanying documents / Attention, lire les documents joints / Attenzione, consultare i documenti di accompagnamento / Atención, consultar la documentación adjunta

STERILE A

Sterilisiert anhand aseptischer Techniken / Sterilized using aseptic processing techniques / Stérilisé en utilisant des techniques aseptisées / Sterilizzato utilizzando tecniche asettiche / Esterilizado mediante técnicas de procesado asépticas

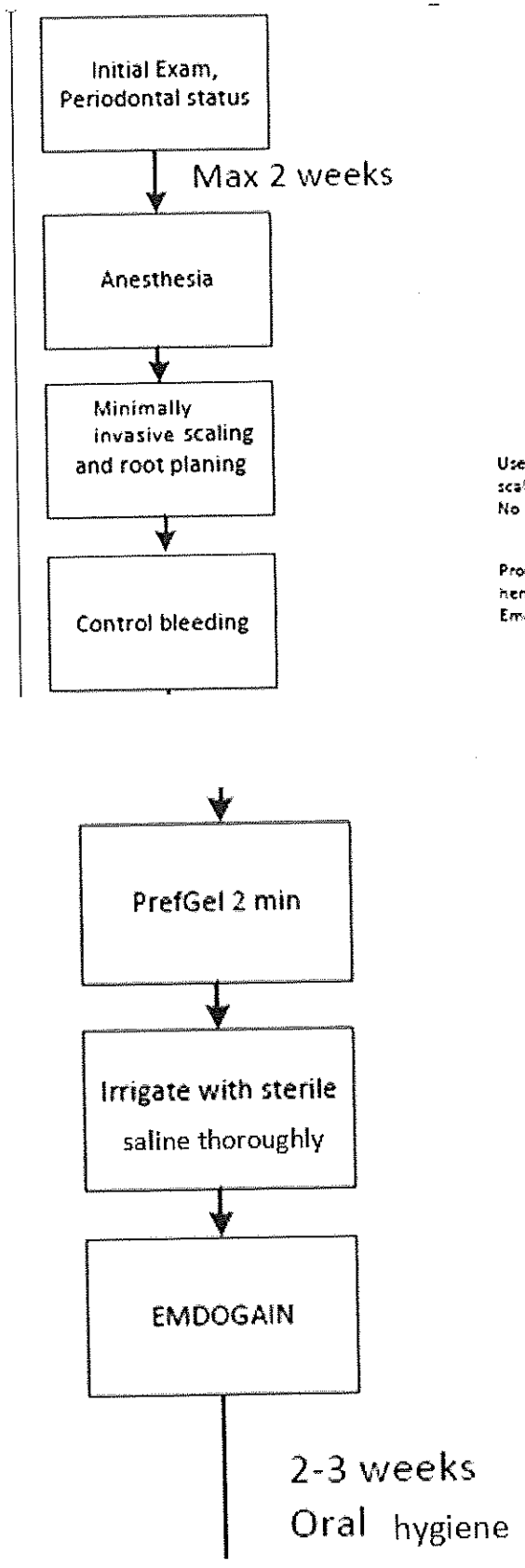
Nicht wiederverwenden / Do not re-use / Ne pas réutiliser / Non riutilizzare / No reutilizable

Rx only

Caution: U.S. Federal law restricts this device to sale by or on the order of a dental professional.

Hersteller / Manufacturer / Fabricant / Produttore / Fabricante

Appendix 3 – Treatment Workflow

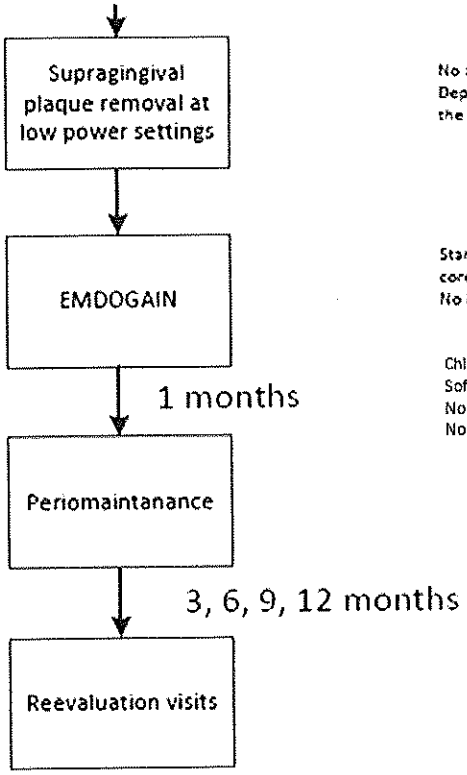


Use hand / diamond / ultrasonic scalers
No Lasers

Prohibit vasoconstrictors and hemostatic agents at the time of Emdogain application

Starting apically and advancing coronally

Chlorhexidine 1 week, with no brushing
Soft brush, 90° angle
No flossing or waterpik 1 month
No local or systemic antibiotics


Supragingival plaque removal at low power settings
No anesthesia
Deplaque to level curette enters the defect
EMDOGAIN
Starting apically and advancing coronally
No EDTA / PrefGel
1 months
Chlorhexidine 1 week, with no brushing
Soft brush, 90° angle
No flossing or waterpik 1 month
No local or systemic antibiotics
Periomaintanance
3, 6, 9, 12 months
Reevaluation visits

Appendix 4 – Visual Analog Scale (VAS)

straumann CR 01/15	Subject Initials:		1-2 Days after Treatment
	Subject ID:	-	
	Date:	/ /	

Instructions:

To be completed by the patient

Complete this page **1 to 2 days** after treatment.

Indicate the level of pain in the area of your mouth treated for the study.

Please mark the lines as instructed below.

RIGHT side of mouth

Please mark your pain level be drawing one vertical mark | through the line below.

No pain _____ Worst pain possible

LEFT side of mouth

Please mark your pain level be drawing one vertical mark | through the line below.

No pain _____ Worst pain possible

straumann CR 01/15	Subject Initials:		1 Week after Treatment
	Subject ID:	-	
	Date:	: :	

Instructions:

To be completed by the patient
Complete this page **1 week** after treatment.
Indicate the level of pain in the area of your mouth treated for the study.
Please mark the lines as instructed below.

RIGHT side of mouth

Please mark your pain level be drawing one vertical mark | through the line below.

No pain _____ Worst pain possible

LEFT side of mouth

Please mark your pain level be drawing one vertical mark | through the line below.

No pain _____ Worst pain possible

straumann CR 01/15	Subject Initials:		2 Weeks after Treatment
	Subject ID:	-	
	Date:	: :	

Instructions:

To be completed by the patient
Complete this page **2 weeks** after treatment.
Indicate the level of pain in the area of your mouth treated for the study.
Please mark the lines as instructed below.

RIGHT side of mouth

Please mark your pain level be drawing one vertical mark | through the line below.

No pain _____ Worst pain possible

LEFT side of mouth

Please mark your pain level be drawing one vertical mark | through the line below.

No pain _____ Worst pain possible

Appendix 5 – Declaration of Helsinki

Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964
and amended by the:
29th WMA General Assembly, Tokyo, Japan, October 1975
35th WMA General Assembly, Venice, Italy, October 1983
41st WMA General Assembly, Hong Kong, September 1989
48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996
52nd WMA General Assembly, Edinburgh, Scotland, October 2000
53rd WMA General Assembly, Washington DC, USA, October 2002 (Note of Clarification added)
55th WMA General Assembly, Tokyo, Japan, October 2004 (Note of Clarification added)
59th WMA General Assembly, Seoul, Republic of Korea, October 2008
64th WMA General Assembly, Fortaleza, Brazil, October 2013

Preamble

1. The World Medical Association (WMA) has developed the Declaration of Helsinki as a statement of ethical principles for medical research involving human subjects, including research on identifiable human material and data.

The Declaration is intended to be read as a whole and each of its constituent paragraphs should be applied with consideration of all other relevant paragraphs.

2. Consistent with the mandate of the WMA, the Declaration is addressed primarily to physicians. The WMA encourages others who are involved in medical research involving human subjects to adopt these principles.

General Principles

3. The Declaration of Geneva of the WMA binds the physician with the words, "The health of my patient will be my first consideration," and the International Code of Medical Ethics declares that, "A physician shall act in the patient's best interest when providing medical care."

4. It is the duty of the physician to promote and safeguard the health, well-being and rights of patients, including those who are involved in medical research. The physician's knowledge and conscience are dedicated to the fulfilment of this duty.

5. Medical progress is based on research that ultimately must include studies involving human subjects.

6. The primary purpose of medical research involving human subjects is to understand the causes, development and effects of diseases and improve preventive, diagnostic and therapeutic interventions (methods, procedures and treatments). Even the best proven interventions must be evaluated continually through research for their safety, effectiveness, efficiency, accessibility and quality.

7. Medical research is subject to ethical standards that promote and ensure respect for all human subjects and protect their health and rights.

8. While the primary purpose of medical research is to generate new knowledge, this goal can never take precedence over the rights and interests of individual research subjects.

9. It is the duty of physicians who are involved in medical research to protect the life, health, dignity, integrity, right to self-determination, privacy, and confidentiality of personal information of research subjects. The responsibility for the protection of research subjects must always rest with the physician or other health care professionals and never with the research subjects, even though they have given consent.

10. Physicians must consider the ethical, legal and regulatory norms and standards for research involving human subjects in their own countries as well as applicable international norms and standards. No national or international ethical, legal or regulatory requirement should reduce or eliminate any of the protections for research subjects set forth in this Declaration.

11. Medical research should be conducted in a manner that minimizes possible harm to the environment.

12. Medical research involving human subjects must be conducted only by individuals with the appropriate ethics and scientific education, training and qualifications. Research on patients or healthy volunteers requires the supervision of a competent and appropriately qualified physician or other health care professional.

13. Groups that are underrepresented in medical research should be provided appropriate access to participation in research.

14. Physicians who combine medical research with medical care should involve their patients in research only to the extent that this is justified by its potential preventive, diagnostic or therapeutic value and if the physician has good reason to believe that participation in the research study will not adversely affect the health of the patients who serve as research subjects.

15. Appropriate compensation and treatment for subjects who are harmed as a result of participating in research must be ensured.

Risks, Burdens and Benefits

16. In medical practice and in medical research, most interventions involve risks and burdens.

Medical research involving human subjects may only be conducted if the importance of the objective outweighs the risks and burdens to the research subjects.

17. All medical research involving human subjects must be preceded by careful assessment of predictable risks and burdens to the individuals and groups involved in the research in comparison with foreseeable benefits to them and to other individuals or groups affected by the condition under investigation.

Measures to minimize the risks must be implemented. The risks must be continuously monitored, assessed and documented by the researcher.

18. Physicians may not be involved in a research study involving human subjects unless they are confident that the risks have been adequately assessed and can be satisfactorily managed.

When the risks are found to outweigh the potential benefits or when there is conclusive proof of definitive outcomes, physicians must assess whether to continue, modify or immediately stop the study.

Vulnerable Groups and Individuals

19. Some groups and individuals are particularly vulnerable and may have an increased likelihood of being wronged or of incurring additional harm.

All vulnerable groups and individuals should receive specifically considered protection.

20. Medical research with a vulnerable group is only justified if the research is responsive to the health needs or priorities of this group and the research cannot be carried out in a non-vulnerable group. In addition, this group should stand to benefit from the knowledge, practices or interventions that result from the research.

Scientific Requirements and Research Protocols

21. Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and adequate laboratory and, as appropriate, animal experimentation. The welfare of animals used for research must be respected.

22. The design and performance of each research study involving human subjects must be clearly described and justified in a research protocol.

The protocol should contain a statement of the ethical considerations involved and should indicate how the principles in this Declaration have been addressed. The protocol should include information regarding funding, sponsors, institutional affiliations, potential conflicts of interest, incentives for subjects and information regarding provisions for treating and/or compensating subjects who are harmed as a consequence of participation in the research study.

In clinical trials, the protocol must also describe appropriate arrangements for post-trial provisions.

Research Ethics Committees

23. The research protocol must be submitted for consideration, comment, guidance and approval to the concerned research ethics committee before the study begins. This committee must be transparent in its functioning, must be independent of the researcher, the sponsor and any other undue influence and must be duly qualified. It must take into consideration the laws and regulations of the country or countries in which the research is to be performed as well as applicable international norms and standards but these must not be allowed to reduce or eliminate any of the protections for research subjects set forth in this Declaration.

The committee must have the right to monitor ongoing studies. The researcher must provide monitoring information to the committee, especially information about any serious adverse

events. No amendment to the protocol may be made without consideration and approval by the committee. After the end of the study, the researchers must submit a final report to the committee containing a summary of the study's findings and conclusions.

Privacy and Confidentiality

24. Every precaution must be taken to protect the privacy of research subjects and the confidentiality of their personal information.

Informed Consent

25. Participation by individuals capable of giving informed consent as subjects in medical research must be voluntary. Although it may be appropriate to consult family members or community leaders, no individual capable of giving informed consent may be enrolled in a research study unless he or she freely agrees.

26. In medical research involving human subjects capable of giving informed consent, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, post-study provisions and any other relevant aspects of the study. The potential subject must be informed of the right to refuse to participate in the study or to withdraw consent to participate at any time without reprisal. Special attention should be given to the specific information needs of individual potential subjects as well as to the methods used to deliver the information.

After ensuring that the potential subject has understood the information, the physician or another appropriately qualified individual must then seek the potential subject's freely-given informed consent, preferably in writing. If the consent cannot be expressed in writing, the non-written consent must be formally documented and witnessed.

All medical research subjects should be given the option of being informed about the general outcome and results of the study.

27. When seeking informed consent for participation in a research study the physician must be particularly cautious if the potential subject is in a dependent relationship with the physician or may consent under duress. In such situations the informed consent must be sought by an appropriately qualified individual who is completely independent of this relationship.

28. For a potential research subject who is incapable of giving informed consent, the physician must seek informed consent from the legally authorized representative. These individuals must not be included in a research study that has no likelihood of benefit for them unless it is intended to promote the health of the group represented by the potential subject, the research cannot instead be performed with persons capable of providing informed consent, and the research entails only minimal risk and minimal burden.

29. When a potential research subject who is deemed incapable of giving informed consent is able to give assent to decisions about participation in research, the physician must seek that assent in addition to the consent of the legally authorized representative. The potential subject's dissent should be respected.

30. Research involving subjects who are physically or mentally incapable of giving consent, for example, unconscious patients, may be done only if the physical or mental condition that prevents giving informed consent is a necessary characteristic of the research group. In such circumstances the physician must seek informed consent from the legally authorized representative. If no such representative is available and if the research cannot be delayed, the study may proceed without informed consent provided that the specific reasons for involving subjects with a condition that renders them unable to give informed consent have been stated in the research protocol and the study has been approved by a research ethics committee. Consent to remain in the research must be obtained as soon as possible from the subject or a legally authorized representative.

31. The physician must fully inform the patient which aspects of their care are related to the research. The refusal of a patient to participate in a study or the patient's decision to withdraw from the study must never adversely affect the patient-physician relationship.

32. For medical research using identifiable human material or data, such as research on material or data contained in biobanks or similar repositories, physicians must seek informed consent for its collection, storage and/or reuse. There may be exceptional situations where consent would be impossible or impracticable to obtain for such research. In such situations the research may be done only after consideration and approval of a research ethics committee.

Use of Placebo

33. The benefits, risks, burdens and effectiveness of a new intervention must be tested against those of the best proven intervention(s), except in the following circumstances:

Where no proven intervention exists, the use of placebo, or no intervention, is acceptable; or

Where for compelling and scientifically sound methodological reasons the use of any intervention less effective than the best proven one, the use of placebo, or no intervention is necessary to determine the efficacy or safety of an intervention

and the patients who receive any intervention less effective than the best proven one, placebo, or no intervention will not be subject to additional risks of serious or irreversible harm as a result of not receiving the best proven intervention.

Extreme care must be taken to avoid abuse of this option.

Post-Trial Provisions

34. In advance of a clinical trial, sponsors, researchers and host country governments should make provisions for post-trial access for all participants who still need an intervention identified as beneficial in the trial. This information must also be disclosed to participants during the informed consent process.

Research Registration and Publication and Dissemination of Results

35. Every research study involving human subjects must be registered in a publicly accessible database before recruitment of the first subject.

36. Researchers, authors, sponsors, editors and publishers all have ethical obligations with regard to the publication and dissemination of the results of research. Researchers have a duty to make publicly available the results of their research on human subjects and are accountable for the completeness and accuracy of their reports. All parties should adhere to accepted guidelines for ethical reporting. Negative and inconclusive as well as positive results must be published or otherwise made publicly available. Sources of funding, institutional affiliations and conflicts of interest must be declared in the publication. Reports of research not in accordance with the principles of this Declaration should not be accepted for publication.

Unproven Interventions in Clinical Practice

37. In the treatment of an individual patient, where proven interventions do not exist or other known interventions have been ineffective, the physician, after seeking expert advice, with informed consent from the patient or a legally authorised representative, may use an unproven intervention if in the physician's judgement it offers hope of saving life, re-establishing health or alleviating suffering. This intervention should subsequently be made the object of research, designed to evaluate its safety and efficacy. In all cases, new information must be recorded and, where appropriate, made publicly available.