Title Page

Title	Post-marketing observational study to e**valu**at**e** the effect of adalimumab treatment with AbbVie's patient support program on patient reported outcomes and health resource utilization in inflammatory arthritis, psoriasis and inflammatory bowel diseases in Hungary in a real-life setting: **VALUE**
Protocol Version Identifier	V1.0
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Marketing Authorization Holder(s)	AbbVie Hungary Ltd. Lechner Ödön Street 7. H-1095 Budapest
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Research Question and Objectives	This study aims to evaluate the effect of adalimumab with patient support program (PSP, referred here ABBVIE CARE 2.0) and clinical, health economic, patient-reported outcomes in patients with rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, psoriasis, Crohn's disease and ulcerative colitis in the routine clinical setting in Hungary. **Primary objective**: To evaluate the impact of adalimumab therapy with ABBVIE CARE 2.0 on patient functional health and wellbeing in patients with rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, psoriasis, Crohn's disease and ulcerative colitis. **Secondary objectives:** • To evaluate the impact of adalimumab therapy plus ABBVIE CARE 2. on general and disease specific quality of life (QoL), health resource utilization, treatment satisfaction, satisfaction with information provided by ABBVIE Care 2.0, medication adherence, disease activity and work productivity. • Define correlations between patient reported outcomes and the following factors: o patient socio-demographics, o disease characteristics, o patient types. • Evaluate the effect the exposure to PSP on patient reported outcomes.
Country(-ies) of Study	Hungary

Authors	[redacted]

This study will be conducted in compliance with this protocol.

Confidential Information

No use or disclosure outside AbbVie is permitted without prior written authorization from AbbVie.

Marketing Authorisation Holder(s)

Marketing Authorisation Holder(s)	AbbVie Ltd Maidenhead SL6 4XE Nagy-Britannia
MAH Contact Person	[redacted]

1.0 Table of Contents

2.0 Abbreviations

ACR	American College of Rheumatology
ADA	Adalimumab
AE	Adverse Event
AS	Ankylosing Spondylitis
ASDAS	Ankylosing Spondylitis Disease Activity Score
ASQoL	Ankylosing Spondylitis Quality of Life Index
CD	Crohn's Disease
CDAI	Clinical Disease Activity Index
CDMS	Clinical Data Management System
CRF	Case Report Form
CRO	Contract Research Organization
CRP	C-reactive Protein
DAS28	Disease Activity Score, 28 joints
DCF	Data Collection Form
DLQI	Dermatology Life Quality Index
DMARD	Disease-Modifying Anti-Rheumatic Drug
eCRF	Electronic Case Report Form
ESR	Erythrocyte Sedimentation Rate
EULAR	European League against Rheumatism
EQ-5D-5L	EuroQol five-dimension scale
GPV	Global Pharmacovigilance
HAQ-DI	Health Assessment Questionnaire Disability Index

HCP	Health Care Professional
HRQOL	Health Related Quality of Life
ICF	Informed Consent Form
Ig	Immunoglobulin
IMID	Immune-mediated Inflammatory Disease
INN	International Non-proprietary Name
IRB	Institutional Review Board
JIA	Juvenile Idiopathic Arthritis
MCID	Minimally Clinically Important Difference
MCS	Mental Component Score
MedDRA	Medical Dictionary for Regulatory Activities
mm	Millimeter
MMAS-4	Morisky Medication Adherence Scale, 4 questions
MPR	Medication Possess Rate
MTX	Methotrexate
NHIF	National Health Insurance Fund
NIS	Non-Interventional Study
PASI	Psoriasis Activity and Severity Index
PCS	Physical Component Score
pMayo	Partial Mayo Score
PMOS	Post-Marketing Observational Study
PRO	Patient Reported Outcome
Ps	Psoriasis
PSP	Patient Support Program

PsA	Psoriatic Arthritis
PT	Preferred Term
QoL	Quality of Life
RA	Rheumatoid arthritis
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SIBDQ	Short Quality of Life in Inflammatory Bowel Disease Questionnaire
SF-36v2	36-Item Short Form Health Survey, Version 2.0
SIF	Subject Information Form
SIMS	Satisfaction with Information About Medicines Scale
SJC	Swollen Joint Count
SmPC	Summary of Product Characteristics
SOC	System Organ Class
TA	Therapeutic Area
TAI	Total Activity Impairment
TJC	Tender Joint Count
TNF	Tumor Necrosis Factor
TSQM	Treatment Satisfaction Questionnaire for Medication
TWPI	Total Work Productivity Impairment
UC	Ulcerative Colitis
VAS	Visual Analogue Scale
WPAI	Work Productivity and Activity Impairment
WPAI-GH	Work Productivity and Activity Impairment, General Health
WPAI-SHP	Work Productivity and Activity Impairment, Specific Health Problem

3.0 Responsible Parties

Study Designated Physician (SDP):

[redacted]

AbbVie Ltd., Lechner Ödön fasor 7, 1095 Budapest, Hungary

Phone: [redacted]

Protocol Authors:

[redacted]

AbbVie Ltd. Lechner Ödön fasor 7, 1095 Budapest, Hungary, Phone: [redacted]

Bisotatistics and Data Management:

AdWare Research Ltd.

8230 Balatonfüred, Völgy str. 41., Hungary

4.0 Abstract

Title: Post-marketing observational study to e**valu**at**e** the effect of adalimumab treatment with AbbVie's patient support program on patient reported outcomes and health resource utilization in inflammatory arthritis, psoriasis and inflammatory bowel diseases in Hungary in a real-life setting: **VALUE.**

Rationale and Background: Biologic agents have revolutionized the therapy of patients with immune-mediated inflammatory diseases. Former affiliate non-interventional study (NIS) results in patients treated with adalimumab in RA and AS, Ps and PsA in real-life in Hungary proved favorable real life effectiveness of adalimumab in Hungary. Although several randomized, controlled studies conducted with adalimumab report the effect the drug on SF-36 PCS in various indications, very limited data are available on the effect of adalimumab with a PSP on functional health and wellbeing in patients with rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, psoriasis, Crohn's disease and ulcerative colitis in routine clinical setting in Hungary.
Treatment adherence is of particular importance in IMIDs as these are characterized by fluctuating and usually progressive disease courses and a need for lifetime management.
The goal of AbbVie patient support programs (PSPs) is to optimize treatment effectiveness through a suite of available services aiming at improving patient adherence. Existing evidence with adalimumab from PASSION and NURTURE studies has demonstrated that patient support programs for adalimumab are associated with improved adherence, clinical, health related quality of life and economic outcomes.
In Hungary, a PSP has been conducted since 2010 for patients with Rheumatology indications. AbbVie Hungary will be in the process of implementing a revised PSP (ABBVIE CARE 2.0) from Q1 2016. ABBVIE CARE 2.0 aims to build on the previous PSP to improve patient's experiences that have a positive impact on patient outcomes.

Research Question and Objectives:

This study aims to evaluate the effect of adalimumab with a patient support program (PSP, referred to here as ABBVIE CARE 2.0) on clinical, health economic, patient-reported outcomes in patients with rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, psoriasis, Crohn's disease and ulcerative colitis in the routine clinical setting in Hungary.

Primary objective: To evaluate the impact of adalimumab therapy with ABBVIE CARE 2.0 on patient functional health and wellbeing in patients with rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, psoriasis, Crohn's disease and ulcerative colitis.

Secondary objectives:

- To evaluate the impact of adalimumab therapy plus ABBVIE CARE 2. on general and disease specific quality of life (QoL), health resource utilization, treatment satisfaction, satisfaction with information provided by ABBVIE Care 2.0, medication adherence, disease activity and work productivity.
- Define correlations between patient reported outcomes and the following factors:
  - patient socio-demographics,
  - disease characteristics,
  - patient types.
- Evaluate the effect the exposure to PSP on patient reported outcomes.

Study Design: This multicenter study will be conducted in prospective, open label, multicenter, observational cohort setting in Hungary.

Population:

- Diagnosis of RA, AS, PsA, Ps, CD or UC by treating physician.
- Age ≥ 18 years at the time of the enrollment.
- RA, AS, PsA, Ps, UC or CD patients whom adalimumab treatment is indicated as per local SmPC and professional/reimbursement guidelines.
- Subjects assigned to adalimumab treatment not more than 1 month prior to inclusion.
- Patient to whom participation in AbbVie CARE 2.0 PSP program was offered and patient decided to join and have started the PSP.
- Patients willing to be involved in the study and to sign patient informed consent form (ICF) and subject information form (SIF) in order to allow use and disclosure of his/her personal health information.

Variables:

Primary endpoint: Change in general quality of life score SF-36v2 PCS from baseline to month 12 in each indication.

Secondary endpoints

1. Change in general SF-36v2 MCS scores, as well as EQ-5D-5L quality of life score from baseline to month 12 in each indication.
2. Change in disease specific quality of life scores from baseline to month 12
   b. SIBDQ in case of UC and CD
   c. DLQI in case of Ps
   d. ASQoL in case of AS and PsA patients with axial symptoms
3. Change in total TSQM-1.4 score from baseline to month 12 in each indication.
4. Change in total SIMS score from baseline to month 12 in each indication.
5. Change in total MMAS-4 score from baseline to month 12 in each indication.
6. Changes in WPAI-SHP score from baseline to month 12 in each indication.
7. Changes in health resource utilization during 12 months of adalimumab therapy and 12 months preceding the introduction of adalimumab therapy in each indication as follows:
   a. Difference in the number of hospital inpatient days.
   b. Difference in the number of hospitalizations.
   c. Difference in the number of sick leave days (in employed subjects only).
   d. Difference in the number of sick leaves (in employed subjects only).
   e. Difference in the number of outpatient visits to each kind of health care provider: general practitioner, rheumatologist, other specialists (ophthalmologist, gastroenterologist, dermatologist, physiatrist), physiotherapist, rheumatology nurse therapy.
8. Change in disease activities from baseline to month 12

a. Change in DAS28 score from baseline to month 12 in RA and peripheral PsA patients
b. Change in $ASDAS_{ESR}$ score from baseline to month 12 in AS and axial PsA patients
c. Change in CDAI score from baseline to month 12 in CD patients
d. Change in pMayo score from baseline to month 12 in UC patients
e. Change in PASI score from baseline to month 12 in Ps patients

9. Satisfaction with PSP in patients participating in AbbVie CARE 2.0 in each indication.
10. Correlation between patient outcomes and patient socio-demographics, patient type and indication.
11. Effect of continuous utilization of PSP on patient outcomes in each indication.

Data Sources: Patient charts and questionnaires.

Study Size: Enrollment of 387 patients is planned at approximately 25 sites in Hungary.

Analysis:

Primary analysis:

The primary endpoint is the change in general quality of life score SF-36v2 PCS from baseline to month 12 in each indication.

Secondary analysis:

Descriptive statistics of the change in general quality of life score SF-36v2 PCS from baseline to month 12 will be calculated in each therapeutic area (rheumatology: RA, AS and PsA; gastroenterology: UC and CD; dermatology: Ps).

Descriptive statistics of change in general quality of life score SF-36v2 PCS will be calculated by patient type.

Descriptive statistics of the secondary variables will be calculated by indication, by patient type and therapeutic area. Descriptive statistics will contain the number of cases, mean, standard deviation, 95% confidence interval, minimum, maximum and median for continuous variables and the number of cases and frequency for category variables.

A mixed linear model will also be performed on the primary variable (change in general quality of life score SF-36v2 PCS) using indication and patient type and the interaction between treatment, indication and patient type as fixed factors to investigate the effect of patient type on the outcome. To adjust for baseline imbalances, baseline SF-36v2 PCS scores will be included into the model. Resulting p-values of the mixed model will be interpreted in a descriptive manner, i.e. no formal hypothesis testing will be performed.

Descriptive statistics of patient outcomes will also be calculated by patient type, indication and socio-demographic parameters to investigate the possible correlations between patient outcomes and the above factors. Correlation between groups (by patient type, indication, socio-demographic parameters) will be calculated.

Effect the exposure to PSP on patient outcomes will be analyzed applying mixed linear models on the patient outcomes including length of PSP utilization, indication as fixed effects. Baseline patient outcome values will also be included in the model.

Descriptive statistics of patient outcomes will be calculated for the continuous and terminated patient groups by indication**.**

Safety analysis:

All recorded serious adverse events will be listed. SAEs will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) and will be tabulated by primary MedDRA system organ class (SOC)

and preferred term (PT). For treatments, surgical and medical procedures the international non-proprietary name (INN) Drug Terms and Procedures Dictionary will be used. **Interim analyses:** Interim analysis of 100 patient 12 months follow-up data is available is planned to be performed .
Milestones: FPFV: 09 March 2016 LPLV: 12 Oct 2017 CSR: 13 Aug 2018

5.0 Amendments

Number	Date	Section of Study Protocol	Amendment or Update	Reason
	dd Month YYYY	Text	Text	Text

6.0 Milestones

Major study milestones and their planned dates are as follows:

Start of Data Collection:	09 March 2016
End of Data Collection:	LPLV: 12 Oct 2017
Study Progress Report:	N/A
Interim Report:	Upon availability of 12 months follow-up data of first 100 enrolled patients (expected in Sept 2017)
Registration in the EU PAS register	N/A
Final Report of Study Results:	13 Aug 2018

7.0 Rationale and Background

7.1 Background

Biologic agents have revolutionized the therapy of patients suffering from immune-mediated inflammatory diseases (IMIDs). The achievement of low disease activity and remission has become a realistic goal for the patients. The complexities inherent to treatment acceptance, drug administration, and delivery of specialty injectable drugs have led to development of high-touch patient support programs intended to maximize treatment outcomes.

Short and long term effect of adalimumab on health-related function and well-being has been evaluated in several randomized, controlled studies in various therapeutic areas.

In psoriasis, Revicki DA et al. evaluated the efficacy based on PRO outcomes for adalimumab versus placebo in the first 16-week period of REVEAL study. Statistically significant difference was found in mean PCS score over 16 weeks between the adalimumab and placebo-treated patients. Baseline mean PCS was 48.9.There was a 3.7-point improvement on mean PCS scores in adalimumab-treated patients compared with a 0.4-point improvement in placebo-treated patients. Between-group difference in PCS change scores over the 16-week period was 3.3. These differences were considered clinically meaningful based on the MID of 2.5–3.0 points for the SF-36 PCS (44). No long term data are available in Ps for SF-36v2 PCS changes during real life setting.

With regards to IBD, the Crohn's Trial of the Fully Human Antibody Adalimumab for Remission Maintenance (CHARM) for adalimumab maintenance therapy incorporated several HRQOL instruments, including the SF-36 PCS and MCS (45). At Baseline SF-36 PCS scores were comparable among Induction only (n=106), 40 mg adalimumab EOW (n=140) and 40 mg Adalimumab weekly maintenance (n=128) arms (36.8 [SD: 8.0]; 37.1 [SD: 7.9] and 36.9 [6.9] respectively). At week 56 in the 40 mg adalimumab EOW arm the increase in the mean SF-36 PCS scores were 10.5 [SD: 8.5] and 10.2 [SD: 9.4] respectively while in the placebo arm the increase was 8.5 [SD: 8.6]. Limited data are available in UC for the long term effect of adalimumab on SF-36: in ULTA 1 study, anti-TNF-naive patients with moderate to severe UC who failed conventional therapy experienced significant improvements in IBDQ and SF-36 PCS scores through Week 8 with adalimumab 160-/80-mg induction therapy vs. placebo (46). In patients with sustained remission, significant improvements were seen in SF-36 PCS scores with mean improvement of 7.9 after 52 weeks of treatment in ULTRA 2 study (47).

Long-term improvements of SF-36 PCS score were seen is psoriatic arthritis (ADEPT trial, 29), ankylosing spondylitis (48, 49) and rheumatoid arthritis (50), with mean baseline values of 33.2, 32.5 and 37.3 and mean changes from baseline after 1 year of adalimumab treatment of 10.2, 7.6 and 10.0, respectively.

To achieve long-term optimal patient outcomes with regards to disease activity, health-related function and quality of life, the appropriate use of medication is central to the successful management of long term conditions. However, many patients do not take their medications as prescribed (1), and non-adherence is perceived a major problem in healthcare (2). Treatment adherence is of particular importance in IMIDs as these are characterized by fluctuating and usually progressive disease courses and a need for lifetime management. Still, non-adherence is a problem in these conditions, too (3-6).

Suboptimal adherence to therapy, as observed in patients with rheumatoid arthritis (RA) and other IMIDs such as psoriasis and inflammatory bowel diseases may contribute to the unsatisfactory therapeutic response or to treatment failure. Improvement of adherence might enhance the success of biological therapies in IMIDs.

According to the ALIGN study data (51), self-reported patient adherence to TNF-inhibitor therapy is different across therapeutic areas, with lowest adherence in AS (61.3% of patients are highly adherent) and highest in UC (80.7%). Treatment adherence is also influenced by the attitudes towards the therapy.

Poor adherence may result in worsening symptoms, progression of the disease, and the decline of function and loss of workability. Moreover, it could lead to unnecessary adjustments of the therapy and to the use of additional diagnostic procedures, accompanied by the delayed recovery of the patient as well as the escalation of treatment costs. For example, similar to other chronic disorders, adherence rates vary between 30 and 80 per cent in RA (7). The following are the components of adherence to medication ('therapeutic adherence', 8):

- *Compliance:* The extent to which the patient acts in accordance with the prescribed dosing interval, dose, and dosage regimen (i.e. conforms to the physician's instructions and to the dosage recommended in the SmPC). It is expressed as the percentage ratio of the total number of administered doses to that of the doses to be administered (as 'Compliance Rate' in prospective, and 'Medication Possession Rate [MPR]' in retrospective studies). The compliance rates (expressed as MPR) for adalimumab (ADA), infliximab, and etanercept were in the range between 63 and 90%. Owing to the small numbers of the studies and lack of statistical significance, however, no conclusions can be drawn regarding the differences between the individual agents (6).
- *Persistence:* The duration of time while the given patient in fact continues therapy. It is expressed as the duration of treatment (days, years); synonyms: drug survival/retention rate. As shown by the findings of clinical studies, persistence declines rapidly with time. That is, while 65 to 87% of the patients receive a given therapy in its initial year, this decreases to 41 to 56% by the second year (6).

Options for improving adherence to treatment (9):

1. Development of therapeutic tools and medicinal products.

2. Increasing the throughput and improving the operating rules of the health care delivery system.
3. Improving the means of interaction among health care professionals, along with the communication skills of health care professionals (HCPs).
4. Continuous patient-education, disease management and/or patient support programs. It is an established fact that well-informed patients are more likely to abide by therapeutic rules. Therefore, appropriate patient education itself greatly enhances therapeutic adherence. The main reason for this is that useful information allays unfounded fears and beliefs – about adverse effects, for example. Further, it makes the patient aware of the possible consequences of uncontrolled disease, and points out the beneficial effects of appropriate therapy.

Educational and disease management programs: above-mentioned components targeting the improvement of therapeutic adherence exert their influence mutually, as a complex intervention. Linking a medicinal product with favorable properties regarding adherence, the coordination of healthcare services, and patient education together may be considered a therapy-management program or a complex follow-up project. In the near future, the financing of such therapy-management programs will be borne by the pharmaceutical industry in the first place. On the longer term, however, it is to be hoped that – similar to prevention programs – the public health insurance sector might also contribute financial support. Moreover, even society as a whole could benefit from the increasing efficacy of drug therapy (9).

AbbVie offered an array of services as part of a patient support program (PSP) to individuals prescribed adalimumab in the past years. The goal of AbbVie PSP is to optimize treatment effectiveness through a suite of available services which include medication reminders, sharps disposal containers, travel kits, starter kits, nurse injection training, and in-home or telephonic nursing support/education.
As a new type of PSP, ABBVIE CARE 2.0 aims to improve the patient experiences and have a positive impact on patient outcomes.

Patients “cope” with a chronic illness either positively or negatively – and this difference plays a role in patient types (30-33). AbbVie has observed a consistent group of four patient types in immunology-related conditions: demanding, dependent, denying and

coping (56). The features used to describe each of the four archetypes below best describe the typical patient found in that type across therapeutic areas (TAs):

- TYPE I: They place great demands on themselves and their HCPs to find a solution.
- TYPE II: They deny and avoid the seriousness of their illness and resist adjusting their lives.
- TYPE III: Their stress, fear and anxiety seemingly increase as they learn more about their illness.
- TYPE IV: They trust and have faith that their doctor will do what's best for them.

These types can be determined by questionnaires developed by AbbVie (**Appendix 1**). The types differ from each other in the level of vigilance and emotional impact. Vigilance determines information-seeking behavior, self-management, patient –physician dynamics and adherence risk; whilst emotional impact refers to current state and future outlook, self-perception and social or family network. AbbVie would impact these elements via differentiated PSP experience.

.Existing evidence with adalimumab from PASSION (4, 23) and NURTURE (5) studies has demonstrated that patient support programs for adalimumab are associated with improved adherence, clinical, health related quality of life and economic outcomes.

PASSION was a multi-country post-marketing observational study sponsored by AbbVie to explore and describe the effectiveness of ADA on the course of RA treatment and patient satisfaction over time in the context of utilization of the PSP. The study enrolled patients with moderate to severe RA with an insufficient response to ≥ 1 disease-modifying anti rheumatic drug (DMARD) and initiated ADA at participating sites. Patients had to be ADA-naïve and treated with ≥ 1 prior biologic DMARD. Patients were prescribed ADA according to the local product label and had an option to utilize the PSP while participating in the study. Overall, 49.9% of enrolled patients utilized the PSP. Interim data showed that, in patients with moderate to severe RA who initiated ADA, better improvement in functional and clinical outcomes was achieved among the PSP users versus the non-PSP users.

The objective of PASSION post-hoc analysis (23) was to assess predictors of ADA PSP utilization among RA patients who initiate ADA treatment. In this multi-country, ex-US study, the PSP included "Core elements" (starter pack, call center/hotline, nursing services, educational material, and injection guide) offered in all participating countries

and "other elements" (e.g., refill reminders, email, newsletters, support groups, home delivery, and financial assistance) vary by country. PSP utilization (yes/no) was a dependent variable in a multivariate logistic regression model examining the potential predictors of using the ADA PSP. Results showed that in patients with moderate to severe RA treated per standard of care, white race, prior biologic use, and baseline disease parameters were positive predictors favoring PSP use.

The objective of NURTURE study was to quantify the relationship between participation in any component of the PSP and resource costs (medical and total). Longitudinal, patient-level data on the utilization of AbbVie's PSP were linked with Source Healthcare Analytics administrative claims data for patients initiating ADA treatment from January 2008 to June 2014. The sample included patients aged ≥ 18 years with a diagnosis of Crohn's disease, ulcerative colitis, rheumatoid arthritis, psoriasis, psoriatic arthritis, or ankylosing spondylitis that were anti-tumor necrosis factor (TNF) naïve prior to initiation of ADA. Patients who enrolled in the PSP (PSP cohort) were matched to those who did not enroll (non-PSP cohort) based on age, sex, year of ADA initiation, comorbidities, diagnosis, and initiation at a specialty pharmacy. AbbVie's free-to-patient PSP was associated with lowering medical costs (all-cause and disease-related) and total healthcare costs.
Former affiliate non-interventional study (NIS) results in patients treated with adalimumab in RA and AS, Ps and PsA in real-life in Hungary (16-19) proved favourable real life effectiveness of adalimumab in Hungary. The results also reflects the effectiveness of adalimumab in the local healthcare system with restrictive local reimbursement criteria (42) and situation, meaning that only dedicated biologic therapy centers can administer biologics in the country.

7.2 Rationale

Although several randomized, controlled studies conducted with adalimumab report the effect the drug on SF-36 PCS in various indications, very limited data are available on the effect of adalimumab on the patient functional health and wellbeing in patients with rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, psoriasis, Crohn's disease and ulcerative colitis in routine clinical setting in Hungary.
Moreover, we do not have local real-life data on the effect of adalimumab plus AbbVie patient support program on the above mentioned patient outcome since no prospective

study has yet examined the impact of adalimumab plus PSP outcomes among IMID patients in Hungary.

In Hungary, PSP has been conducted since 2010 in Rheumatology indications (RA and AS). No PSP has been conducted in Dermatology and IBD indications so far.
AbbVie Hungary will be in the process of implementing a revised PSP (ABBVIE CARE 2.0) from Q1 2016.. The frequency, content and quality of services in ABBVIE CARE 2.0 will be consistent across participating sites.

Elements of ABBVIE CARE 2.0 in Hungary will be:

- Reminder calls, emails, text messages – using new technologies.
- Nursing services, dietician and psychological support e.g. life coach.
- Starter pack, injection guide.
- Provision of educational materials (print, digital) regarding life with IMIDs and adalimumab.

Patient types will be differentiated by the investigator using patient types questionnaires and electronic tools in order to tailor the elements and communication channels to patients' needs and thus provide a highly personalized program.

8.0 Research Question and Objectives

This study aims to evaluate the effect of adalimumab with patient support program (PSP, referred here ABBVIE CARE 2.0) on clinical, health economic, patient-reported outcomes in patients with rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, psoriasis, Crohn's disease and ulcerative colitis in the routine clinical setting in Hungary.

Primary objective: To evaluate the impact of adalimumab therapy with ABBVIE CARE 2.0 on patient functional health and wellbeing in patients with rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, psoriasis, Crohn's disease and ulcerative colitis.

Secondary objectives:

• To evaluate the impact of adalimumab therapy plus ABBVIE CARE 2. on general and disease specific quality of life (QoL), health resource utilization, treatment satisfaction,

satisfaction with information provided by ABBVIE Care 2.0, medication adherence, disease activity and work productivity.

- To define correlations between patient reported outcomes and the following factors:
  - patient socio-demographics,
  - disease characteristics,
  - patient types.
- To evaluate the effect the exposure to PSP (length of participation in PSP) on patient reported outcomes.

9.0 Research Methods

9.1 Study Design

This multicenter study will be conducted in prospective, open label, multicenter, observational cohort setting in Hungary.

This study is a post-marketing observational study (PMOS) in which adalimumab is prescribed in the usual manner in accordance with the terms of the local marketing authorization and professional and reimbursement guidelines with regards to dose, population and indication.

As this is an observational, non-interventional study, patient's treatments are determined solely by the treating physician, which falls within the scope of the physician's/institution's general liability insurance coverage.

9.2 Setting

9.2.1 Study population

Study population will consist of adult (aged ≥18 years) patients with diagnosed rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA), psoriasis (Ps), Crohn's disease (CD) or ulcerative colitis (UC) that are being treated with adalimumab as per locally approved label and prescription guidelines. The assignment of a patient to adalimumab therapy must be done before patient enrolment in the study. The prescription of adalimumab and the involvement into PSP is clearly separated from the decision to include the patient in this study. PSP will be initiated together with the start of adalimumab therapy. No additional procedures (other than the standard of care) shall be applied to patients enrolled in this study.

Participation in AbbVie CARE 2.0 PSP will be offered for patients involved in biologic therapy centers where PSP is available prior to the enrollment to the study.

Study cohort population will consist of 6 treatment groups: rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA), psoriasis (Ps), Crohn's disease (CD) and ulcerative colitis (UC) group.

To ensure the appropriate size of the treatment groups as defined in 9.5, patients will be included in the groups only until the given group reaches its planned size. When a group reached its planned size only patients in the other treatment group will be included in this study. Patients with different indications will be allocated by sites by AbbVie based on the availability of patients at each sites.

9.2.1.1 Inclusion criteria

A patient will be enrolled in this PMOS if he/she fulfills ALL of the following criteria:

- Diagnosis of RA, AS, PsA, Ps, CD or UC by treating physician.
- Age ≥ 18 years at the time of the enrollment.

• RA, AS, PsA, Ps, UC or CD patients whom adalimumab treatment is indicated as per local SmPC and professional/reimbursement guidelines.

• Subjects assigned to adalimumab treatment not more than 1 month prior to inclusion.

• Patient to whom participation in AbbVie CARE 2.0 PSP program was offered and patient decided to join and has started the PSP.

• Patients willing to be involved in the study and to sign patient informed consent form (ICF) and subject information form (SIF) in order to allow use and disclosure of his/her personal health information.

9.2.1.2 Exclusion criteria

• Patients who cannot be treated with adalimumab according to the local adalimumab SmPC and local professional and reimbursement guidelines.

• Patients treated with > 1 prior biologic DMARD for RA, AS, PsA, Ps, UC or CD.

• Prior treatment with adalimumab for more than 1 months.

• Subjects currently participating in other clinical research.

• Patients who are unwilling or unable to complete the quality of life and other patient reported questionnaires.

• Patients who choose not to participate in ABBVIE Care 2.0.

9.2.2 Study duration and discontinuation

Each patient will be observed during his/her adalimumab treatment for a maximum period of 12 months.

If adalimumab is discontinued before the planned observational period of 12 months, the visit which the patient is attending is considered the termination visit. If discontinuation is between two visits, then the next scheduled visit should be considered the termination visit for the patient.

If treatment with adalimumab is discontinued, the standard practice is to review the patient after a period of 70 days (5 half-lives) following the administration of the last dose of physician prescribed treatment.

If the patient decides to discontinue participation in the PSP, he or she may continue the study and will be observed during his/her adalimumab treatment for a maximum period of 12 months.

9.3 Variables

9.3.1 Data collected

According to the requirements for non-interventional or observational studies, no additional diagnostic or monitoring procedures will be applied to the patients included in the study other than those which would ordinarily be applied in the course of the particular therapeutic strategy. Only data which are part of routine will be collected.

9.3.1.1 Patient reported outcome measures (PROs)

SF-36v2

Sort Form -36 version 2 (**Appendix 3**) is a multi-purpose, short-form health survey with only 36 questions (15). It yields an 8-scale profile of functional health and well-being scores as well as psychometrically-based physical and mental health summary measures and a preference-based health utility index. It is a generic measure, as opposed to one that targets a specific age, disease, or treatment group. Accordingly, the SF-36 has proven useful in surveys of general and specific populations, comparing the relative burden of diseases, and in differentiating the health benefits produced by a wide range of different

treatments. In 1996, Version 2.0 of the SF-36 (SF-36v2) was introduced, to correct deficiencies identified in the original version. Those improvements were implemented after study using both qualitative and quantitative methods. The SF-36v2 has 2 summary scores, the Physical Component Summary (PCS) and Mental Component Summary (MCS) scores, and 8 domain scores: physical function, bodily pain, role limitations–physical, general health, vitality, social function, role limitations–emotional, and mental health. Domain scores range from 0 to 100, with greater scores reflecting better health status. The minimal clinically important difference (MCID) estimates for the PCS are in the range of 0.51–3.91, with the best estimate at approximately 2.5 points (52) in Ps and between 2.5 and 5 in other therapeutic areas (53, 54). The SF-36v2 summary and domain scores have excellent reliability and good construct validity across the general population as well as chronic disease populations. SF-36v2 will be registered for all patients.

EQ-5D-5L score

EQ-5D-5L **(**14**, Appendix 2)** is a widely-used survey instrument for measuring economic preferences for health states, a standardized, self-administered, generic instrument to measure health outcome. It is one of several such instruments that can be used to determine the quality-adjusted life years associated with a health state. The name is derived from the survey methodology, which measures quality of life in five dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety /depression) each of which can take one of five responses. The responses record five levels of severity (no problems/slight problems/moderate problems/severe problems/extreme problems) within a particular EQ-5D-5L dimension. This descriptive system was developed by the EuroQoL Research foundation. It is composed of 5 questions measured by 5 levels of severity, as well as a visual analogue scale (VAS) to obtain a global assessment of health from the patient perspective. EQ-5D-5L will be registered for all patients.

Short Quality of Life in Inflammatory Bowel Disease Questionnaire

Short Quality of Life in Inflammatory Bowel Disease Questionnaire (**SIBDQ)** is a validated (20), self-administered IBD-specific quality of life instrument is designed to

assess patients' IBD symptoms during the 2 weeks prior to the assessment **(Appendix 4).** It has been validated in UC and CD as well (43**).** SIBDQ will be documented in case of UC and CD.

Dermatology Life Quality Index

Dermatology Life Quality Index (**DLQI**, 21) is a patient self-reported questionnaire for capturing psychosocial effects of chronic skin disease on different areas of life within the previous seven days. The ten questions cover six areas: symptoms/feelings, daily activities, leisure, work/school, personal relationship, effects of treatment on daily life. Total DLQI scores range from 0 to 30, with 0 corresponding to the best quality of life and 30 to the worst. The DLQI has well-established reliability and validity. The DLQI scoring is presented in **Appendix 5**, documented in case of Ps. DLQI will be registered for all dermatology and PsA patients.

Ankylosing Spondylitis Quality of Life

Developed from a needs-based model (22), the **ASQoL** is a disease-specific instrument designed to measure health related quality of life (HRQOL) in patients with AS. Patients answer yes/no to 18 items assessing the current impact of AS on their quality of life status. ASQoL has a total score ranging from 0 to 18, with lower scores representing better AS-specific quality of life. The ASQoL has demonstrated good reliability and construct validity across several different AS studies, validated translation is available in Hungarian (**Appendix 6**). It will be documented in in case of AS and PsA with axial symptoms.

Treatment Satisfaction Questionnaire for Medicine Version 1.4

Although numerous disease-specific measures of patients' treatment satisfaction for medication have been reported in the literature, less attention has been paid to developing a more general measure of TSQM one that would permit comparisons across medication types and patient conditions. To fill this gap, the TSQM was developed (10). TSQM is a

generic measure of treatment satisfaction for medication, was rigorously developed with sound psychometric properties. Multiple linguistically validated languages available. Three versions are available: **TSQM Ver 1.4** (14 items), TSQM Ver II (11 items), and TSQM Ver 9 (9 items). Domains include: Effectiveness, Side effects, Convenience, Global Satisfaction. This measure attempts to show that adherence is expected to be related with patients' satisfaction with therapy and such satisfaction can be a function of not only the effect of the treatment, but also the services offered. In VALUE, TSQM-1.4 will be employed, see in **Appendix 7**. TSQM-1.4 is administered and registered for all patients.

Satisfaction with Information about Medicines Scale

The Satisfaction with Information about Medicines Scale **(SIMS)** (11) assesses whether the individual has received enough information about a range of topics relating to prescribed medication. The psychometric properties of the SIMS were tested in patients from a variety of diagnostic categories in both inpatient and outpatient settings. The measure was well accepted by patients and showed satisfactory internal consistency, test-retest reliability, and criterion related validity. Patients will be asked to rate the amount of information they have received using the following response scale: “too much”, “about right”, “too little”, “none received”, “none needed”. Total satisfaction rating will be obtained by summing the scores for each item. If the patient is satisfied that he/she has received a particular aspect of medication information (with a rating of “about right” or “none needed”), this is given a score of 1. If the patient is dissatisfied with the amount of information received (with a rating of “too much”, “too little”, or “none received”), this is scored 0. Scores range from 0 to 17 with high scores indicating a high degree of overall satisfaction with the amount of medication information received. Two subscale scores, identifying patients’ satisfaction with information about the Action and usage of medication (items 1–9), and the Potential problems of medication (items 10–17) will also be calculated. The SIMS provides a valid and reliable tool for assessing how well the needs of individual patients for medicines information are being met (**Appendix 8**). SIMS will be registered and administered for all patients.

Morisky Medication Adherence Scale - 4 questions

The Morisky Medication Adherence Score (**MMAS-4**, **Appendix 9**) has been selected as [redacted]

Work Productivity and Activity Impairment - Specific Health Problem Questionnaire

The Work Productivity and Activity Impairment (WPAI) Questionnaire (13, **Appendix 10**) was created as a patient-reported quantitative assessment of the amount of absenteeism, presenteeism and daily activity impairment attributable to general health (WPAI-GH) or a specific health problem (**WPAI-SHP**). The WPAI-GH and the WPAI-SHP were created simultaneously and use the same template, but in the GH version the subject is instructed to respond with reference to the general health status while in the SHP version the subject responds with reference to a specified health problem, disease or condition. The following 4 outcomes will be expressed as a percentage from 0 to 100:

- % Presenteeism – percentage of impairment while working due to the respective IMID.
- % Absenteeism – percentage of work time missed due to the respective IMID.
- % Total work productivity impairment (TWPI) – percentage of overall work impairment due to the respective IMID
- % Total activity impairment (TAI) – percentage of general (non-work) activity impairment due to the respective IMID.

The percentage of work time missed (absenteeism) is calculated as Q2/(Q2 + Q4) x 100%. The percentage of impairment while working (i.e. presenteeism) is calculated as Q5/10 x 100%. The percentage of total work productivity impairment ((TPI) i.e., work productivity loss) is Q2/(Q2 + Q4) + (1–Q2/(Q2+Q4) x (Q5/10) x 100%. The percentage of total activity impairment (TAI) is calculated as Q6/10 x 100%.

WPAI-SHP is registered and administered for all patients.

9.3.1.2 Patient type

Patient type will be determined using Abbvie patient classification strata questionnaire **(Appendix 1)** by investigators.

9.3.1.3 Participation in AbbVie CARE 2.0

Participation in AbbVie CARE 2.0 (Yes or No) will be registered at each visit. Feedback on PSP program will be registered at the end of observation (V4 or the last visit of patients withdrawn from study or PSP) by patients. If a patient is leaving PSP, feedback shall be documented at the subsequent visit. For patients who decide to discontinue the PSP, the reason for discontinuation will be documented.

Feedback on ABBVIE CARE 2.0 Program is described in **Appendix 16.**

9.3.1.4 Health resource utilization

Health resource utilization during 12 months of adalimumab therapy and 12 months preceding the introduction of adalimumab therapy as follows:

- Number of hospital inpatient days.
- Number of hospitalizations.
- Number of sick leave days (in employed subjects only).
- Number of sick leaves (in employed subjects only).

- Number of outpatient visits to each kind of health care provider: general practitioner, rheumatologist, IMID specific and/or other specialists (ophthalmologist, gastroenterologist, dermatologist, physiatrist, physiotherapist, rheumatology nurse therapy.

9.3.1.5 Disease activity scores

DAS28 score

The Disease Activity Score measures a patient's level of disease activity at a given time using tender joint count (TJC), swollen joint count (SJC) across 44 joints, erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) and patient's health assessment along a VAS (0-100 mm). The modified Disease Activity Score, 28 joints (DAS28) score is a modified version that is scored across a reduced set of 28 joints, omitting the feet (24). In this study, DAS28 ESR will be calculated by the investigators (**Appendix 11**) and documented in patients with RA and PsA patients with peripheral symptoms.

$ASDAS_{ESR}$ score

ASDAS score (25) consists of five domains. Three of them will be collected during BASDAI score calculation: back pain, duration of morning stiffness and peripheral pain/swelling are all assessed on a VAS (0–100 mm) or on a NRS (0–10). Back pain is equivalent to BASDAI Question 2; duration of morning stiffness is same as in BASDAI Question 6; peripheral pain/swelling is equivalent to BASDAI Question 3. Patient's global assessment of disease activity (PGA) is measured on a VAS (0-100 mm) or on a NRS (0-10). Because missing in the BASDAI score calculation, PGA will be captured as a separate item on a NRS (0-10) in this study. The fifth domain is derived from inflammatory laboratory parameters: both CRP and ESR can be used, but ESR is preferred. The calculation of ASDAS score will be performed by the investigator (**Appendix 12**) for in AS and PsA patients with axial symptoms.

Clinical Disease Activity Index

Clinical Disease Activity Index (**CDAI**) (26, 34) was developed and validated before the beginning of the National Cooperative Crohn's Disease Study (35). CDAI variables are: 1. Number liquid stools (Sum of 7days), 2. Abdominal pain (Sum of 7 days ratings), 3. General wellbeing (Sum of 7 days ratings), 4. Extraintestinal complications (Number of listed complications), 5. Antidiarrhoeal drugs (Use in the previous 7 days), 6. Abdominal mass, 7. Hematocrit (Expected–observed Hct), 8. Body weight (Ideal / observed ratio). During calculation, individual severity scores of variables are adjusted by multiplier factors and these adjusted scores are summed. CDAI scores range from 0 to approximately 600. In order to identify the limit between remission and active disease, various cut-off values between 100 and 200 has been suggested: 150 points is a widely accepted and reasonable compromise in as much most patients rated by physicians as 'very well' would fall below and most others would fall above this value. The limit between active and very severe disease was defined as a cut-off value of 450 points. CDAI scores of 150–219 as mildly active disease and scores of 220– 450 as moderately active disease are also in use, although these are less firmly based distinctions. In spite it's several limitations [interobserver variability (36), general wellbeing' and 'intensity of abdominal pain' items are subjective and reflect patients' perceptions of their disease, CDAI is based on a diary that precludes the use of the CDAI in everyday practice, it is not accurate in patients with fistulizing and stenosing behavior and is not useful in patients with previous extensive ileo-colonic resections or stoma], currently CDAI is the most frequently used index for clinical trials and must be considered the gold standard for evaluation of disease activity. CDAI is detailed in **Appendix 13,** will be documented in CD patients.

Partial Mayo score

Partial Mayo (**pMayo**) score (**Appendix 14**) is the most accepted noninvasive ulcerative colitis activity index in clinical investigations with an additional potential for use in everyday practice (27).The Mayo score has been used in numerous UC clinical trials to measure disease severity. Although it has not been formally validated, it correlates well with IBDQ and SF-36 measures of quality of life (37). The Mayo score incorporates the

reported stool frequency, presence of rectal bleeding, endoscopic findings, and a physician's global assessment, which acknowledges the other three components of the score together with the patient's symptoms and their subjective assessment of wellbeing. Calculation of the Mayo score requires proctosigmoidoscopic examination to determine achievement of clinical remission, response, and mucosal healing. A noninvasive index that is a surrogate for mucosal healing was warranted to improve patient acceptability of clinical trials for UC and thus the partial Mayo (pMayo) score (38-41) was introduced later in which the endoscopic component was omitted. pMayo score has been shown to correlate well with Mayo score, as well as with an independently scored physician's global assessment, and had good discriminatory value between subjects in remission and those with active disease (Remission = 0-1, Mild Disease = 2-4, Moderate Disease = 5-6, Severe Disease =7-9). pMayo is being documented in UC patients.

Psoriasis Area and Severity Index score

Psoriasis Area and Severity Index (**PASI**) is the most widely used tool for the measurement of severity of psoriasis (28). PASI combines the assessment of the severity of lesions and the area affected into a single score in the range 0 (no disease) to 72 (maximal disease). PASI is widely used in clinical trials of therapies to treat psoriasis. Although absolute PASI score is often used to define entry into a trial, it is response to treatment that is important to measure efficacy and outcomes. This is usually presented as a percentage response rate e.g. PASI 50, PASI 75, PASI 90, PASI 100. PASI 75, for example, represents the percentage (or number) of patients who have achieved a 75% or more reduction in their PASI score from baseline. PASI 100 indicates patients who have achieved a complete resolution of all disease. By definition a patient who has achieved PASI 75 has also achieved PASI 50. There is a gradual tendency, as therapies become more effective to report higher efficacy rates in clinical trials - but aiming high may not be without risk of over-treating some patients. PASI described in **Appendix 15,** being documented in Ps patients.

9.4 Data Sources

According to the requirements for non-interventional or observational studies, no additional diagnostic or monitoring procedures will be applied to the patients included in the study other than those which would ordinarily be applied in the course of the particular therapeutic strategy.

Source documents are defined as original documents. The investigator will document patient data in his/her own patient files which will serve as source data for the study. Data are collected from the source documents for each patient in the study, consisting of medical records containing demographic data, medical, treatment and diagnostic documentation and laboratory assessments.

The investigator(s)/institution(s) will permit study-related monitoring, audits, independent ethics committee/- review board (IEC/IRB) review, and regulatory inspection(s), providing direct access to source data documents.

9.4.1 Study activities

As this study is observational in nature, the follow-up visits are not interventional and strictly scheduled, but rather left to the judgment of each investigator. The investigator should record visit data in the CRF from no more than five (5) visits, which are closest to the 3- month intervals within the 12-month study period for each patient.

Failure to observe these usual practice intervals of patient visits will not constitute a breach or violation of the protocol.

No more than five (5) patient's visits are indicated for CRF completion within the 12-month observational period:

- Visit 0 (V0): Baseline
- Visit 1 (V1): Follow-up at 3 months
- Visit 2 (V2): Follow-up at 6 months
- Visit 3 (V3): Follow-up at 9 months

- Visit 4 (V4): Follow-up at 12 months (Study End).

A patient may withdraw from this PMOS at any time without prejudice.

If the physician, for any reason, decides it is in the best interest of the patient to permanently discontinue adalimumab, the patient shall be withdrawn from the study. The reason for discontinuation should be documented in CRF.

9.4.1.1 Baseline visit (V0)

At baseline the patient will be checked for the Inclusion and Exclusion Criteria and, if enrolled, the following will be recorded, providing it is part of routine:

1. Date of visit and date of signing the Patient's Authorization to the investigator to use and/or disclose personal and/or health data, and of Informed Consent Form and SIF.

2. Patient socio-demographics: Gender; Year of birth; Work status: working for payment (working full-time, working part-time/hours per week), unemployed but seeking work, unemployed due to disability (early retirement because of IMID or other reasons), regularly retired, student; Occupation (to be classified as manual or non-manual job).

3. Patient type based on Abbvie's patient classification strata questionnaire (dependent, demanding, denying, non-coping).

4. Date of entering ABBVIE CARE 2.0.

3. IMID specific medical history:

Year of diagnosis; Past or present IMID- related comorbidities (e.g. uveitis; inflammatory bowel disease, psoriasis); Screening for tuberculosis (TB) (date and result of screening, prophylaxis if applicable).

4. IMID specific systemic medication: past and present use of classic DMARDs and biologic DMARDs (anti-TNF agents), current NSAIDs, including COX-2 inhibitors.

Date of first adalimumab administration and date of first adalimumab administration for this study.

5. Disease activity scores.

6. PROs: SF-36v2 and EQ-5D-5L, TA-specific QoL measures.

7. Workability: WPAI-SHP score.

8. Adherence: MMAS-4.

9. TSQM-1.4 and SIMS.

10. Selected IMID related health care resource utilization over the 12 months preceding first adalimumab administration in this study:

- Hospitalizations: Number of admissions to hospital and number of hospital inpatient days.

- Outpatient attendance: Number of visits to different health care providers: general practitioner, IMID specific and/or other specialists (e.g. ophthalmologist, gastroenterologist, dermatologist, psychiatrist), physiotherapist, nurse.

10. IMID related sick leaves over the 3 months preceding first adalimumab administration:

- Sick leave: Number of sick leaves and number of sick leave days.

11. Serious adverse events SAE, if any.

9.4.1.2 Follow-up visits (V1-V4)

1. Date of visit

2. Change in Work status

3. IMID specific systemic medication.

- Date of last adalimumab administration.
- If adalimumab therapy has been discontinued, the reason and date of the last dose shall be documented.
- At visit four (4), the date of the last adalimumab administration during the study shall be documented.
- Changes in IMID specific systemic medication (DMARDs, NSAIDs, including COX-2) since last visit.

4. Participation in ABBVIE CARE 2.0: yes or no (Y/N). If ABBVIE CARE 2.0 discontinued, the reason for it.

5. Disease activity scores.

6. PROs: SF-36 and EQ-5D-5L, TA-specific QoL measures

7. Workability: WPAI-SHP score

8. Adherence: MMAS-4

9. TSQM-1.4 and SIMS

10. Selected IMID related health care resource utilization since last visit:

- Hospitalizations: Number of admissions to hospital and number of hospital inpatient days.

- Outpatient attendance: Number of visits to different health care providers: general practitioner, IMID specific and/or other specialists (ophthalmologist, gastroenterologist, dermatologist and physiatrist), physiotherapist, nurse.

10. IMID related sick leaves since the last visit

- Sick leave: Number of sick leaves and number of sick leave days.

11. Feedback on ABBVIE CARE 2.0 for patients who attend PSP.

12. Serious adverse events SAE, if any.

Table 1. Activities and procedures per protocol

Activity/Procedure	Visits 0 (V0): Baseline						Visits 1-4 (V1-4): Follow up					
	RA	AS	PsA	Ps	CD	UC	RA	AS	PsA	Ps	CD	UC
Date of visit	X						X					
SIF / ICF	X											
Inclusion / Exclusion criteria	X											
Socio-demographic data, including Education, Occupation, Work or school status	X											
Patient type	X											
Medical history	X											
TB screening and prophylaxis	X											
Comorbidities	X											
ABBVIE CARE 2.0 participation	X						X					
Reason for dropping out of PSP							X					
Disease specific systemic medication	X											
Changes in disease specific systemic medication							X					
PROs												
SF-36v2	X						X					
EQ-5D-5L	X						X					
SIBDQ					X	X					X	X
DLQI			X	X					X	X		
ASQoL		X	X*					X	X*			
WPAI-SHP	X						X					
MMAS-4	X						X					

Activity/Procedure	Visits 0 (V0): Baseline						Visits 1-4 (V1-4): Follow up					
	RA	AS	PsA	Ps	CD	UC	RA	AS	PsA	Ps	CD	UC
SIMS	X						X					
TSQM-1.4	X						X					
Disease activity scores												
DAS28	X		X				X		X			
$ASDAS_{ESR}$		X	X					X	X			
PASI				X						X		
CDAI					X						X	
pMayo						X						X
Health resource utilization and sick leave	X						X					
Changes in work and occupational status							X					
Feedback on ABBVIE CARE 2.0 (V4)**							X					
SAE	X						X					

*In patients with axial symptoms. Definition of axial symptoms: BASDAI ≥ 4 (in Numerical Rating Scale)

**At V4. In case of early discontinuation of PSP or dropping out from PMOS, the questionnaire shall be registered .at the subsequent or closing visit, respectively

9.5 Study Size

The primary endpoint of the study is the change in general quality of life score SF-36v2 PCS from baseline to month 12

We would like to estimate the mean change in each treatment groups with a +/-3 points precision at a 95% confidence level. A 3 point difference was chosen due to the definition of MCID for SF-36 PCS in the literature (15).

Based on the literature (57, 58, 29, 45, 44) the standard deviation of the change in general quality of life score SF-36v2 PCS from baseline to month 12 is 8.3, 8.65, 10.2, 8.5, and 8.7 for RA, AS, PsA, UC and Ps indications, respectively. There is no available standard deviation data for CD therefore it is assumed that standard deviation in this indication is the same as in UC.

The required number of analyzed patients for obtaining a 95% confidence interval for the change not wider than 6 points (halfwidth of the 95% confidence interval is not wider than 3 points) is presented in **Table 2**. The number of patients that should be included in the study is calculated by assuming 25% dropout rate in each indication.

Table 2. Required number of enrolled and analyzed patients

Indication	SD	Analysed	Included
RA	8,3	44	59
AS	8,65	47	63
PsA	10,2	62	83
CD	8,5	45	60
UC	8,5	45	60
Ps	8,7	47	63
Total		290	387

Assuming 25% dropout rate, 387 **patients** in total should be included in the study.

9.6 Data Management

Each study center documents data in paper case report forms (CRFs). Examinations, diagnostic measures, findings and observations routinely performed in patients included in this PMOS will be entered by the investigator or staff into the CRFs provided by AbbVie, according to the protocol.

Disease activity and PRO scores will be calculated by investigators.

Only data specified in the protocol will be collected and submitted to the study data management center. Completed CRF visit modules will be sent immediately after completion to the contracted Contract Research Organization (CRO) defined by AbbVie.

The investigator must maintain source documents for each patient in the study, consisting of medical records containing demographic data, medical, treatment and diagnostic documentation and laboratory test data confirming psoriasis diagnosis.

Data collected on CRF's will be entered into Mythos 2.0 clinical data management system (CDMS), developed and maintained by AdWare Research Ltd. Automatic data check will be performed.

By the time of the study closure the electronic database will be closed as well. The closed database will be exported into SAS or SPSS format; data analysis will be carried out by SAS or SPSS software. After the analysis phase was finished the electronic database will be archived at AdWare Research Ltd.

9.6.1 Endpoints

1. Primary endpoint: Change in general quality of life score SF-36v2 PCS from baseline to month 12 in each indication.

2. Secondary endpoints

1. Change in general SF-36v2 MCS scores, as well as EQ-5D-5L quality of life score from baseline to month 12 in each indication.

2. Change in disease specific quality of life scores from baseline to month 12

   b. SIBDQ in case of UC and CD

   c. DLQI in case of Ps

   d. ASQoL in case of AS and PsA patients with axial symptoms

   3. Change in total TSQM-1.4 score from baseline to month 12 in each indication

   4. Change in total SIMS score from baseline to month 12 in each indication.

   5. Change in total MMAS-4 score from baseline to month 12 in each indication.

   6. Changes in WPAI-SHP score from baseline to month 12 in each indication.

7. Changes in health resource utilization during 12 months of adalimumab therapy and 12 months preceding the introduction of adalimumab therapy in each indication as follows:

    a. Difference in the number of hospital inpatient days.

    b. Difference in the number of hospitalizations.

    c. Difference in the number of sick leave days (in employed subjects only).

    d. Difference in the number of sick leaves (in employed subjects only).

    e. Difference in the number of outpatient visits to each kind of health care provider: general practitioner, rheumatologist, other specialists (ophthalmologist, gastroenterologist, dermatologist, physiatrist), physiotherapist, rheumatology nurse therapy.

8. Change in disease activities from baseline to month 12

    a. Change in DAS28 score from baseline to month 12 in RA and peripheral PsA patients

    b. Change in $ASDAS_{ESR}$ score from baseline to month 12 in AS and axial PsA patients

    c. Change in CDAI score from baseline to month 12 in CD patients

    d. Change in pMayo score from baseline to month 12 in UC patients

    e. Change in PASI score from baseline to month 12 in Ps patients

8. Satisfaction with PSP in patients participating in AbbVie CARE 2.0 in each indication

9. Correlation between patient outcomes and patient socio-demographics, patient type and indication.

10. Effect of exposure to PSP on patient outcomes in each indication.

9.6.2 Statistical analysis

9.6.2.1 Primary analysis

The primary endpoint is the change in general quality of life score SF-36v2 PCS from baseline to month 12 in each indication.

Descriptive statistics of change in general quality of life score SF-36v2 PCS will be calculated in each indication. Descriptive statistics will contain the number of cases, mean, and standard deviation, 95% confidence interval, minimum, maximum and median.

9.6.2.2 Secondary analysis

Descriptive statistics of the change in general quality of life score SF-36v2 PCS from baseline to month 12 will be calculated in each therapeutic area (rheumatology: RA, AS and PsA; gastroenterology: UC and CD; dermatology: Ps).

Descriptive statistics of change in general quality of life score SF-36v2 PCS will be calculated by patient type.

Descriptive statistics of the secondary variables will be calculated by indication, by patient type and therapeutic area. Descriptive statistics will contain the number of cases, mean, standard deviation, 95% confidence interval, minimum, maximum and median for continuous variables and the number of cases and frequency for category variables.

A mixed linear model will also be performed on the primary variable (change in general quality of life score SF-36v2 PCS) using indication and patient type and the interaction between treatment, indication and patient type as fixed factors to investigate the effect of patient type on the outcome. To adjust for baseline imbalances, baseline SF-36v2 PCS

scores will be included into the model. Resulting p-values of the mixed model will be interpreted in a descriptive manner, i.e. no formal hypothesis testing will be performed.

Descriptive statistics of patient outcomes will also be calculated by patient type, indication and socio-demographic parameters to investigate the possible correlations between patient outcomes and the above factors. Correlation between groups (by patient type, indication, socio-demographic parameters) will be calculated.

Effect of the length of PSP utilization (i.e. PSP exposure) on patient outcomes will be analyzed applying mixed linear models on the patient outcomes including PSP utilization (continuous vs terminated), indication as fixed effects. Baseline patient outcome values will also be included in the model.

Descriptive statistics of patient outcomes will be calculated for the continuous and terminated patient groups by indication.

9.6.2.3 Safety analysis

All recorded serious adverse events will be listed.

SAEs will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) and will be tabulated by primary MedDRA system organ class (SOC) and preferred term (PT).

For treatments, surgical and medical procedures the international non-proprietary name (INN) Drug Terms and Procedures Dictionary will be used.

9.6.2.4 Interim analyses

Interim analysis of 100 patient 12 months follow-up data is available is planned to be performed in order to have preliminary data for local market access strategy. The primary secondary and safety analysis described in 9.7.2.1-9.7.2.3 will be performed in the interim analysis.

9.7 Quality Control

The sites will be instructed in the protocol regarding the use of the questionnaires, the functionality and handling of the CRF, and the requirements to maintain source documents for each patient in the study (see Section 9.4) in order to ensure that all patient questionnaires will be completed by patients.

Different quality assurance methods will be implemented to ensure integrity of the information reported over the course of the project. These activities include but are not limited to monthly enrolment reporting and CRF validation before data submission to Data Management System.

All data will be entered via paper CRF. The CRFs will be submitted to be entered into the electronic database maintained by external vendor AdWare.

Mythos 2.0 CDMS system will be used for data entry and all data management activities. The electronic database will be validated with sample-data before data entry by AdWare Research Ltd.

After data entry, computer logic checks will be run to check for inconsistent data. Any necessary corrections will be made to the database and documented via queries, source data clarification forms and an audit trail regarding all changes will be available. A manual review of selected line listings will also be performed at the end of the study.

9.8 Limitations of the Research Methods

Factors unobservable in the data could be related to both ABBVIE CARE 2.0 enrollment and patient outcomes.

In sites where ABBVIE CARE 2.0 is available, patients can decide whether they want to continue the PSP or not throughout the observation period. The number of patients discontinuing participation in ABBVIE CARE 2.0 may be limited based on our experience so far: the majority (over 90%) of patients maintained their participation in the PSP in Hungary (55).

As a very low number of patients is expected to discontinue participation in the PSP comparisons between continuous and terminated patients may have low power. Results must be carefully interpreted.

Furthermore, those patients who observe less treatment effect may tend to discontinue more frequently from PSP participation therefore the estimation of the effect of continuous PSP may be biased.

No hypothesis testing will be performed in the primary analysis. All other statistical tests performed in secondary analysis will be performed without formal hypothesis testing and resulting p-values will be interpreted in a descriptive manner.

9.9 Other Aspects

9.9.1 Investigator selection criteria

The investigational sites will be academic and community based biologic therapy centers experienced in biologic therapy of respective IMIDs where ABBVIE Care 2.0 is available. Investigators must have the available patient population, representative of the target patient population in their center, and the ability to appropriately conduct the PMOS in accordance with applicable legal and regulatory requirements.

It is planned to involve 25 sites (12 rheumatology, 6 dermatology and 7 gastroenterology centers) into the study.

9.9.2 Product supply

As this is a PMOS, AbbVie is NOT involved in the product supply since the drug is being used according to the approved marketing label and is to be prescribed by the physician under usual and customary practice of physician prescription.

10.0 Protection of Human Subjects

The patients must provide written authorization to the investigator to use and disclose personal and/or health data before entry into the study. Separate Informed Consent is also required by the Local Law. These documents will be signed and dated by patients prior to patients' inclusion.

To maintain subject confidentiality, no demographic data that can identify the patient will be collected. Instead, only the patient's year of birth and gender will be documented in the CRF.

The PMOS will be conducted in accordance with the protocol and applicable local guidelines and regulations. It is the physician's/investigator's responsibility to comply with all local laws and regulations.

Approvals from Central Ethics Committee and Competent Authority will be obtained by AbbVie.

All patients' data entered in the patient's paper CRF will be forwarded - without naming the patient - for evaluation to CRO.

11.0 Management and Reporting of Complaints

A Complaint is any written, electronic, or oral communication that alleges deficiencies related to the physical characteristics, identity, quality, purity, potency, durability, reliability, safety, effectiveness, or performance of a product/device after it is released for distribution.

The investigational product in this trial contains both:

- Biologic compound(s) and
- Device component(s) (pre-filled syringe, pen).

Complaints associated with any component of this investigational product must be reported to the Sponsor (Section 11.2.2). For adverse events, please refer to Sections 11.1.1 through 11.1.6. For product complaints, please refer to Section 11.2.

11.1 Medical Complaints

11.1.1 Adverse Event Definition and Serious Adverse Event Categories

An adverse event (AE) is defined as any untoward medical occurrence in a patient, which does not necessarily have a causal relationship with their treatment. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not the event is considered causally related to the use of the product.

Such an event can result from use of the drug as stipulated in the labeling, as well as from accidental or intentional overdose, drug abuse, or drug withdrawal. Any worsening of a pre-existing condition or illness is considered an adverse event.

If an adverse event meets any of the following criteria, it is considered a serious adverse event (SAE):

Death of Patient:	An event that results in the death of a patient.
Life-Threatening:	An event that, in the opinion of the investigator, would have resulted in immediate fatality if medical intervention had not been taken. This does not include an event that would have been fatal if it had occurred in a more severe form.
Hospitalization:	An event that results in an admission to the hospital for any length of time. This does not include an emergency room visit or admission to an outpatient facility.
Prolongation of Hospitalization:	An event that occurs while the study patient is hospitalized and prolongs the patient's hospital stay.
Congenital Anomaly:	An anomaly detected at or after birth, or any anomaly

	that results in fetal loss.
Persistent or Significant Disability/Incapacity:	An event that results in a condition that substantially interferes with the activities of daily living of a study patient. Disability is not intended to include experiences of relatively minor medical significance such as headache, nausea, vomiting, diarrhea, influenza, and accidental trauma (e.g., sprained ankle).
Important Medical Event Requiring Medical or Surgical Intervention to Prevent Serious Outcome:	An important medical event that may not be immediately life-threatening or result in death or hospitalization, but based on medical judgment may jeopardize the patient and may require medical or surgical intervention to prevent any of the outcomes listed above (i.e., death of patient, life threatening, hospitalization, prolongation of hospitalization, congenital anomaly, or persistent or significant disability/incapacity). Additionally, any elective or spontaneous abortion or stillbirth is considered an important medical event. Examples of such events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.

11.1.2 Severity

The following definitions will be used to rate the severity for any adverse event being collected as an endpoint/data point in the study and for all serious adverse events.

Mild:	The adverse event is transient and easily tolerated by the patient.
Moderate:	The adverse event causes the patient discomfort and interrupts the patient's usual activities.
Severe:	The adverse event causes considerable interference with the patient's usual activities and may be incapacitating or life threatening.

11.1.3 Relationship to Pharmaceutical Product

The following definitions will be used to assess the relationship of the adverse event to the use of product:

Reasonable Possibility	An adverse event where there is evidence to suggest a causal relationship between the product and the adverse event.
No Reasonable Possibility	An adverse event where there is no evidence to suggest a causal relationship between the product and the adverse event.

If no reasonable possibility of being related to product is given, an alternate etiology must be provided for the adverse event.

11.1.4 Serious Adverse Event Collection Period

Serious adverse events will be reported to AbbVie from the time the physician obtains the patient's authorization to use and disclose information (or the patient's informed consent) until 30 days or 5 half-lives following the intake of the last dose of physician-prescribed treatment.

All adverse events reported from the time of study drug administration until 70 days following discontinuation of study drug administration have elapsed will be collected, whether solicited or spontaneously reported by the subject. In addition, serious adverse events will be collected from the time the subject signed the study-specific informed consent. Adverse event information will be collected and recorded on the appropriate paper CRFs.

Subjects will be contacted approximately 70 days following study drug discontinuation for an assessment of any new or ongoing AEs.

11.1.5 Serious Adverse Event Reporting

This protocol requires all SAEs and AESIs as outlined in protocol.

The safety profile of adalimumab which has over 3.5 million patient years of post-marketing exposure is stable and well established; non-serious events will not be actively solicited as these events are not likely to contribute to the further understanding of the safety profile of the product. Any non-serious AEs will be collected as spontaneous reports if AbbVie is notified.

Adalimumab therapy has a well-established and well described safety profile based on extensive postmarketing experience and continued clinical trial patient exposure since the first approved indication in 2002 for rheumatoid arthritis. AbbVie is committed to continue to collect safety information including those events that may occur in this study in order to confirm this established safety profile and to identify any unknown potential adverse reactions, rare events and those events with a long latency. AbbVie is participating in an FDA-requested, TNF inhibitor class wide exploration of the rare appearance of malignancy in subjects/patients who are 30 years of age or younger at the time of diagnosis. The risk of malignancy in this age group has not been established and is difficult to study due to its rarity. AbbVie appreciates your attention to the additional reporting requirements needed in this unlikely event, outlined in this section under Adverse Event Reporting.

In the event of a serious adverse event, and additionally, any non-serious event of malignancy in patients 30 years of age and younger, whether related to study drug or not, the physician will notify the AbbVie contact person identified below within 24 hours of the physician becoming aware of the event by completing the paper CRF and sending it to the following AbbVie Hungary pharmacovigilance mailbox address:

[redacted]

or

to the following Fax number : [redacted]

within 24 hours of the physician becoming aware of the event.

11.1.6 Pregnancy Reporting

In the event of a pregnancy occurrence in the patient, the physician will notify AbbVie according the Section 0 within 24 hours of the physician becoming aware of the pregnancy. Subjects who become pregnant during the study must be discontinued. Pregnancies will be collected from the date of the first dose through 150 days following the last dose of study drug.
Information regarding a pregnancy occurrence in a study subject and the outcome of the pregnancy will be collected.

Pregnancy in a study subject is not considered an AE. However the medical outcome of an elective or spontaneous abortion, stillbirth or congenital anomaly is considered a SAE and must be reported to AbbVie within 24 hours of the site becoming aware of the event.
Information regarding pregnancy outcome will be requested from the Investigator 4 and 12 weeks postpartum, as applicable.

11.2 Product Complaint

11.2.1 Definition

A Product Complaint is any Complaint (see Section 11.0 for the definition) related to the biologic or drug component of the product or to the medical device component(s).

For a product this may include, but is not limited to, damaged/broken product or packaging, product appearance whose color/markings do not match the labeling, labeling discrepancies/inadequacies in the labeling/instructions (example: printing illegible), missing components/product, device not working properly, or packaging issues.

For medical devices, a product complaint also includes all deaths of a patient using the device, any illness, injury, or adverse event in the proximity of the device, an adverse event that could be a result of using the device, any event needing medical or surgical intervention including hospitalization while using the device and use errors.

Any information available to help in the determination of causality by the device to the events outlined directly above should be captured.

11.2.2 Reporting

Product Complaints concerning the investigational product and/or device must be reported to AbbVie Ltd. within 24 hours of the study site's knowledge of the event via [redacted] AND [redacted] or to the following Fax number : [redacted].

Product Complaints occurring during the study will be followed-up to a satisfactory conclusion. All follow-up information is to be reported to the Sponsor (or an authorized representative) and documented in source as required by the Sponsor. Product Complaints associated with adverse events will be reported in the study summary. All other complaints will be monitored on an ongoing basis.

Product complaints involving a non-Sponsor investigational product and/or device should be reported to the identified contact or manufacturer, as necessary per local regulations.

Product Complaints may require return of the product with the alleged complaint condition (syringe, pen, etc.). In instances where a return is requested, every effort should be made by the investigator to return the product within 30 days. If returns cannot be accommodated within 30 days, the site will need to provide justification and an estimated date of return.

The description of the complaint is important for AbbVie in order to enable AbbVie to investigate and determine if any corrective actions are required.

12.0 Plans for Disseminating and Communicating Study Results

At the end of the study, a study report will be written in collaboration with the principal investigator who will also sign the report. The required standard study report template must be followed. Final study report will be written as per the ICH E3 Study Results-Synopsis guideline/template. The completed CRFs and the study report must be treated as

the confidential property of AbbVie and may not be released to unauthorized people in any form (publications or presentations) without express written approval from AbbVie. The results of this PMOS will be published by AbbVie or any of the participating investigators after agreement with AbbVie.

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Annex 1. Additional Information

Appendices: patient questionnaires

Appendix 1. Types of patients

1.1 IBD patient classification questionnaire

Q1	When thinking about your condition now, to what extent do you feel …	
	Q1a	Anxious?
	Q1b	Dependent / helpless?
		Responses
		Not at all = 1
		2
		3
		4
		Extremely = 5
Q2	How often do you do each of the following to look for information on your condition?	
	Read scientific or medical websites / journals	
		Responses
		Only when first diagnosed / given treatment - not since
		At least once per week

		At least once per month
		At least once every couple of months
		Almost never
		Never
Q3.	To what extent do you agree with the statement	
	I am optimistic I will be able to lead a normal life	
		Responses
		Strongly disagree
		Disagree
		Neither agree nor disagree
		Agree
		Strongly agree

1.2 RA patient classification questionnaire

Q1	In general, how much has your RA had an impact on your day to day life for each of the following:	
	Q1a	Ability to engage in leisure / hobbies activities
	Q1b	Taking part in family activities
	Q1c	Completing everyday basic activities
		Responses
		No impact
		Small impact
		Moderate impact
		Large impact
		Not applicable
Q2	How would you describe your relationship with the doctor you normally see for your RA?	
	Q2a	I feel I inconvenience my doctor if I ask him questions
	Q2b	I would like my doctor to spend more time with me

		Responses
		Strongly disagree
		Disagree
		Neither agree nor disagree
		Agree
		Strongly agree
		Not stated

1.3 SpA patient classification questionnaire

Q1	When thinking about your condition now, to what extent do you feel any of the following?	
	Q1a	Trapped
	Q1b	Angry
	Q1c	Confused
		Responses
		1 Not at all
		2
		3
		4
		5 Extremely
		Cannot remember
Q2	How often do you do each of the following to look for information on your condition?	
	Q2a	Scientific or medical websites / journals
	Q2b	Internet chat room, forum or patient blog site
		Responses

		Never
		Only when first dxed or txed
		Almost never
		Every couple of months
		Once per month
		Once a week

1.4 Ps patient classification questionnaire

E5r6 How has psoriasis has affected how you interact with other people – Psoriasis has negatively impacted my ability to work

	Strongly Disagree						Strongly Agree	
	☐	☐	☐	☐	☐	☐	☐	

E4r5 How does your psoriasis make you feel – I miss out on most social activities because of my psoriasis

	Strongly Disagree						Strongly Agree	
	☐	☐	☐	☐	☐	☐	☐	

V1r6 Please rate the impact that your psoriasis has had on the following day to day activities: Desire to interact with people

	No Negative Impact						Very High Negative Impact	
	☐	☐	☐	☐	☐	☐	☐	

V8 Do you sometimes find it difficult planning or organizing to take your medication? (For example, when the medication changes or when or going on holiday)?

	☐ No	
	☐ Yes	

V10 Do you feel sad, low or anxious a lot of the time?

	☐ No	
	☐ Yes	

C12r4 What symptoms do you typically experience due to your psoriasis?

	☐ Burning	
	☐ Flaking	
	☐ Itching	
	☐ Pain	
	☐ Pain/stiffness in joints	
	☐ Reduced mobility	
	☐ Nail pitting/ deformation	
	☐ None of the above	

Predicted type:

Probability to belong to type
Depend
Demand Denying
Coping

Appendix 2. EQ-5D-5L

By placing a tick in one box each group below, please indicate which statements describe your own health state today.

Mobility

I have no problems in walking about	☐
I have slight problems in walking about	☐
I have moderate problems in walking about	☐
I have severe problems in walking about	☐
I am confined to bed	☐

Self-Care

I have no problems with self-care	☐
I have slight problems washing or dressing myself	☐
I have moderate problems washing or dressing myself	☐
I have severe problems washing or dressing myself	☐
I am unable to wash or dress myself	☐

Usual Activities ***(e.g., work, study, housework, family or leisure activities)***

I have no problems with performing my usual activities	☐
I have slight problems with performing my usual activities	☐
I have moderate problems with performing my usual activities	☐
I have severe problems with performing my usual activities	☐
I am unable to perform my usual activities	☐

Pain/Discomfort

I have no pain or discomfort	☐
I have slight pain or discomfort	☐
I have moderate pain or discomfort	☐

I have severe pain or discomfort ☐

I have extreme pain or discomfort ☐

Anxiety/Depression

I am not anxious or depressed ☐

I am slightly anxious or depressed ☐

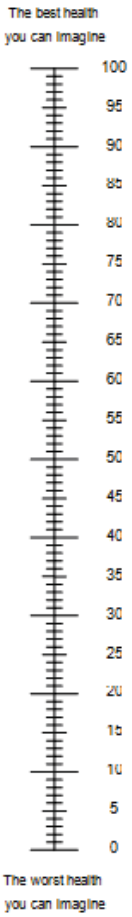
I am moderately anxious or depressed ☐

I am very anxious or depressed ☐

I am extremely anxious or depressed ☐

- We would like to know how good or bad your health is TODAY.
- This scale is numbered from 0 to 100.
- 100 means the best health you can imagine.
  0 means the worst health you can imagine.
- Mark an X on the scale to indicate how your health is TODAY.
- Now, please write the number you marked on the scale in the box below.

YOUR HEALTH TODAY = ☐



Appendix 3. **SF-36v2 questionnaire**

INSTRUCTIONS: This survey asks your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activites.
Please answer every question by marking the answer as indicated. If you are unsure about how to answer a question, please give the best answer you can.
When complete, please return the questionnaire in the envelope provided.

1. In general, would you say your health is:

(circle one)

Excellent 1
Very good 2
Good 3
Fair 4
Poor 5

2. Compared to one year ago, how would you rate your health in general now?

(circle one)

Much better now than one year ago 1
Somewhat better than one year ago 2
About the same as one year ago 3
Somewhat worse than one year ago 4
Much worse now than one year ago 5

3. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

(Circle one number on each line)

Activities	Yes, limited a lot	Yes, limited a little	No, not limited at all
Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports.	1	2	3
Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling or playing golf	1	2	3
Lifting or carrying groceries	1	2	3

Climbing several flights of stairs	1	2	3
Climbing one flight of stairs	1	2	3
Bending, kneeling or stooping	1	2	3
Walking more than a mile	1	2	3
Walking half a mile	1	2	3
Walking one hundred yards	1	2	3
Bathing or dressing yourself	1	2	3

4. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

(Circle one number on each line)

	Yes	No
Cut down on the amount of time you spent on work or other activities	1	2
Accomplished less than you would like	1	2
Were limited in the kind of work or other activities	1	2
Had difficulty performing the work or other activities (for example, it took extra effort)	1	2

5. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

(Circle one number on each line)

	Yes	No
Cut down on the amount of time you spent on work or other activities	1	2
Accomplished less than you would like	1	2
Didn't do work or other activities as carefully as usual	1	2

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours or groups?

(circle one)

Not at all..... 1
Slightly..... 2

Moderately 3
Quite a bit 4
Extremely 5

7. How much bodily pain have you had during the past 4 weeks?

(circle one)

None 1
Very mild 2
Moderate 3
Severe 4
Very severe 5

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

(circle one)

Not at all 1
A little bit 2
Moderately 3
Quite a bit 4
Extremely 5

9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks…

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
Did you feel full of life?	1	2	3	4	5	6
Have you been a very nervous person?	1	2	3	4	5	6
Have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5	6

Have you felt calm and peaceful?	1	2	3	4	5	6
Did you have a lot of energy?	1	2	3	4	5	6
Have you felt downhearted and low?	1	2	3	4	5	6
Did you feel worn out?	1	2	3	4	5	6
Have you been a happy person?	1	2	3	4	5	6
Did you feel tired?	1	2	3	4	5	6

10. During the past 4 weeks, how much of the time has your physical health or emotional problems interferes with your social activities (like visiting friends, relatives, etc.)?

(circle one)

All of the time 1
Most of the time 2
Some of the time 3
A little of the time 4
None of the time 5

11. How TRUE or FALSE is each of the following statements to you?

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
I seem to get ill more easily than other people	1	2	3	4	5
I am as healthy as anybody I know	1	2	3	4	5
I expect my health to get worse	1	2	3	4	5
My health is excellent	1	2	3	4	5

Calculation: http://www.sf-36.org/nbscalc/index.shtml

Physical Component Score (PCS, 0-400):……..

Mental Component Score (MCS, 0-400):……

Appendix 4. SIBDQ

Short Quality of Life in Inflammatory Bowel Disease Questionnaire (SIBDQ)

This questionnaire is designed to find out how you have been feeling during the last 2 weeks. You will be asked about symptoms you have been having as a result of your inflammatory bowel disease the way you have been feeling in general, and how your mood has been.

1. How often has the feeling of fatigue or of being tired and worn out been a problem for you during the last 2 weeks? Please indicate how often the feeling of fatigue or tiredness has been a problem for you during the last 2 weeks by picking one of the options from
(Systemic)
1 All of the time
2 Most of the time
3 A good bit of the time
4 Some of the time
5 A little of the time
6 Hardly any of the time
7 None of the time

2. How often during the last 2 weeks have you had a delay or cancel a social engagement because of your bowel problem? Please choose an option from
(Social)
1 All of the time
2 Most of the time
3 A good bit of the time
4 Some of the time
5 A little of the time
6 Hardly any of the time
7 None of the time

3. How much difficulty have you had, as a result of your bowel problems, doing leisure or sports activities you would have liked to have during the last 2 weeks? Please choose an option from
(Social)
1 A great deal of difficulty, activities made impossible
2 A lot of difficulty
3 A fair bit of difficulty
4 Some difficulty
5 A little difficulty
6 Hardly any difficulty

7 No difficulty, the bowel problems did not limit sports or leisure activities

4. How often during the last 2 weeks have you been troubled by pain in the abdomen? Please choose an option from
(Bowel)
1 All of the time
2 Most of the time
3 A good bit of the time
4 Some of the time
5 A little of the time
6 Hardly any
of the time
7 None of the time

5. How often during the last 2 weeks have you felt depressed or discouraged? Please choose an option from
(Emotional)
1 All of the time
2 Most of the time
3 A good bit of the time
4 Some of the time
5 A little of the time
6 Hardly any of the time
7 None of the time

6. Overall in the last 2 weeks, how much of a problem have you had with the passing large amount of gas? Please choose an option from
(Bowel)
1 A major problem
2 A big problem
3 A significant problem
4 Some trouble
5 A little trouble
6 Hardly any trouble
7 No trouble

7. Overall, in the last 2 weeks, how much of a problem have you had maintaining or getting to, the weight you would like to be at? Please choose an option from
(Systemic)
1 A major problem
2 A big problem
3 A significant problem
4 Some trouble
5 A little trouble
6 Hardly any trouble
7 No trouble

8. How often during the last 2 weeks have you felt relaxed and free of tension? Please choose an option from
(Emotional)
1 None of the time
2 A little of the time
3 Some of the time
4 A good bit of the time
5 Most of the time
6 Almost all of the time
7 All of the time

9. How much of the time during the last 2 weeks have you been troubled by a feeling of having to go to the bathroom even though your bowels were empty? Please choose an option from
(Bowel)
1 All of the time
2 Most of the time
3 A good bit of the time
4 Some of the time
5 A little of the time
6 Hardly any of the time
7 None of the time

10. How much of the time during the last 2 weeks have you felt angry as a result of your bowel problem? Please choose an option from
(Emotional)
1 All of the time
2 Most of the time
3 A good bit of the time
4 Some of the time
5 A little of the time
6 Hardly any of the time
7 None of the time

Scoring: http://tools farmacologiaclinica.info/index.php?sid=10014&lang=en&loadsecurity=67

SCORE:……

Appendix 5. DLQI

Dermatology Life Quality Index (DLQI)

The aim of this questionnaire is to measure how much your skin problem has affected your life OVER THE LAST WEEK. Please check one box for each question.

1.	Over the last week, how **itchy**, **sore**, **painful** or **stinging** has your skin been?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	
2.	Over the last week, how **embarrassed** or **self conscious** have you been of your skin?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	
3.	Over the last week, how much has your skin interfered with you going **shopping** or looking after your **home** or **yard**?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
4.	Over the last week, how much has your skin influenced the **clothes** you wear?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
5.	Over the last week, how much has your skin affected any **social** or **leisure** activities?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
6.	Over the last week, how much has your skin made it difficult for you to do any **sport?**	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
7.	Over the last week, has your skin prevented you from **working** or **studying**?	Yes No	☐ ☐	Not relevant ☐
	If »No«, over the last week how much has your skin been a problem at **work** or **studying**?			
8.	Over the last week, how much has your skin created problems with your partner or any of your **close friends** or **relatives**?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
9.	Over the last week, how much has your skin caused any **sexual difficulties**?	Very much A lot	☐ ☐	Not relevant ☐

		A little Not at all	□ □	
10.	Over the last week, how much of a problem has the **treatment** for your skin been, for example by making your home messy, or by taking up time?	Very much A lot A little Not at all	□ □ □ □	Not relevant □

Total DLQI score:

Instructions for use

Dermatology Life Quality Index (DLQI)

The Dermatology Life Quality Index questionnaire is designed for use in adults, i.e. patients over the age of 16. It is self explanatory and can be simply handed to the patient who is asked to fill it in without the need for detailed explanation. It is usually completed in one to two minutes.

Scoring

The scoring of each question is as follows:

Response	Score
Very much	scored 3
A lot	scored 2
A little	scored 1
Not at all	scored 0
Not relevant	scored 0
Question unanswered	scored 0
Question 7: “prevented work or studying”	scored 3

The DLQI is calculated by summing the score of each question resulting in a maximum of 30 and a minimum of 0. The higher the score, the more quality of life is impaired. The DLQI can also be expressed as a percentage of the maximum possible score of 30.

****Please Note:** That the scores associated with the different answers should not be printed on the DLQI itself, as this might cause bias****

Meaning of DLQI Scores
0-1 = no effect at all on patient's life
2-5 = small effect on patient's life
6-10 = moderate effect on patient's life
11-20 = very large effect on patient's life
21-30 = extremely large effect on patient's life

Detailed analysis of the DLQI
The DLQI can be analysed under six headings as follows:

Section	Questions	Score
Symptoms and feelings	Questions 1 and 2	Score maximum 6
Daily activities	Questions 3 and 4	Score maximum 6
Leisure	Questions 5 and 6	Score maximum 6
Work and School	Question 7	Score maximum 3
Personal relationships	Questions 8 and 9	Score maximum 6

Treatment	Question 10	Score maximum 3

The scores for each of these sections can also be expressed as a percentage of either 6 or 3.

Interpretation of incorrectly completed questionnaires
There is a very high success rate of accurate completion of the DLQI. However, sometimes subjects do make mistakes.

1. If one question is left unanswered this is scored 0 and the scores are summed and expressed as usual out of a maximum of 30.
2. If two or more questions are left unanswered the questionnaire is not scored.
3. If question 7 is answered 'yes' this is scored 3. If question 7 is answered 'no' or 'not relevant' but then either 'a lot' or 'a little' is ticked this is then scored 2 or 1. If it is answered 'no', but the second half is left incomplete, the score will remain 0.
4. If two or more response options are ticked, the response option with the highest score should be recorded.
5. If there is a response between two tick boxes, the lower of the two score options should be recorded.
6. The DLQI can be analysed by calculating the score for each of its six sub-scales (see above). When using sub-scales, if the answer to one question in a sub-scale is missing, that sub-scale should not be scored.

Minimal Clinically Important Difference of the DLQI
In order to help the clinical interpretation of the DLQI scores a banding system (consisting of 5 bands) has been validated. According to this system, a DLQI score 0-1 = no effect at all on patient's life DLQI score of 2-5 = small effect on patient's life, DLQI score of 6-10 = moderate effect on patient's life, DLQI score of 11-20 = very large effect on patient's life, DLQI score of 21-30 = extremely large effect on patient's life.

The Minimal Clinically Important Difference (MCID) of the DLQI in **inflammatory skin diseases** (range=2.2-6.9) has been estimated in 5 studies. For details please refer to the following article:

Basra MKA, Fenech R, Gatt RM, Salek MS, Finlay AY. The Dermatology Life Quality Index 1994-2007: a comprehensive review of validation data and clinical results. Br J Dermatol. 2008; 159:997-1035.

For **general inflammatory skin conditions** a change in DLQI score of at least 4 points is considered clinically important (based on our latest published data). This means that a patient's DLQI score has to either increase or decrease by at least 4 points in order to suggest that there has actually been a meaningful change in that patient's quality of life since the previous measurement of his/her DLQI scores.

Appendix 6. ASQoL

Please read each statement carefully. We would like you to tick 'Yes' if you feel the statement applies to you And tick 'No' if it does not. Please choose the response that applies best to you at the moment.

1. My condition limits the places I can go.

Yes No

2. I sometimes feel like crying.

Yes No

3. I have difficulty dressing.

Yes No

4. I struggle to do jobs around the house

Yes No

5. It's impossible to sleep

Yes No

6. I am unable to join in activities with my friends/family

Yes No

7. I am tired all the time

Yes No

8. I have to keep stopping what I am doing to rest

Yes No

9. I have unbearable pain

Yes No

10. It takes a long time to get going in the morning

Yes No

11. I am unable to do jobs around the house

Yes No

12. I get tired easily

Yes No

13. I often get frustrated

Yes No

14. The pain is always there

Yes No

15. I feel I miss out on a lot

Yes No

16. I find it difficult to wash my hair

Yes
No

17. My condition gets me down

Yes No

18. I worry about letting people down

Yes No

Thank you for taking the trouble to fill in this questionnaire.

Scoring:
Yes=1, No=0

Appendix 7. TSQM-1.4

TSQM (Version 1.4)
Treatment Satisfaction Questionnaire for Medication

Instructions: Please take some time to think about your level of satisfaction or dissatisfaction with the medication you are taking in this clinical trial- We are interested in your evaluation of the effectiveness, side effects, and convenience of the medication over the last two to three weeks, or since you last used it. For each question, please place a single check mark next to the response that most closely corresponds to your own experiences.

1. How satisfied or dissatisfied are you with the ability of the medication to prevent or treat your condition?

   ☐1 Extremely Dissatisfied
   ☐2 Very Dissatisfied
   ☐3 Dissatisfied
   ☐4 Somewhat Satisfied
   ☐5 Satisfied
   ☐6 Very Satisfied
   ☐7 Extremely Satisfied

2. How satisfied or dissatisfied are you with the way the medication relieves your symptoms?

   ☐1 Extremely Dissatisfied
   ☐2 Very Dissatisfied
   ☐3 Dissatisfied
   ☐4 Somewhat Satisfied
   ☐5 Satisfied
   ☐6 Very Satisfied
   ☐7 Extremely Satisfied

3. How satisfied or dissatisfied are you with the amount of time it takes the medication to start working?

☐1 Extremely Dissatisfied
☐2 Very Dissatisfied
☐3 Dissatisfied
☐4 Somewhat Satisfied
☐5 Satisfied
☐6 Very Satisfied
☐7 Extremely Satisfied

4. As a result of taking this medication, do you experience any side effects at all?

☐0 Yes
☐1 No (if No, then please skip to Question 9)

5. How bothersome are the side effects of the medication you take to treat your condition?

☐1 Extremely Bothersome
☐2 Very Bothersome
☐3 Somewhat Bothersome
☐4 A Little Bothersome
☐5 Not at All Bothersome

6. To what extent do the side effects interfere with your physical health and ability to function (i.e., strength, energy levels, etc.)?

☐1 A Great Deal
☐2 Quite a Bit
☐3 Somewhat
☐4 Minimally
☐5 Not at All

7. To what extent do the side effects interfere with your mental function (i.e., ability to think clearly, stay awake, etc.)?

☐1 A Great Deal
☐2 Quite a Bit
☐3 Somewhat
☐4 Minimally
☐5 Not at All

8. To what degree have medication side effects affected your overall satisfaction with the medication?

☐1 A Great Deal
☐2 Quite a Bit
☐3 Somewhat
☐4 Minimally
☐5 Not at All

9. How easy or difficult is it to use the medication in its current form?

☐1 Extremely Difficult
☐2 Very Difficult
☐3 Difficult
☐4 Somewhat Easy
☐5 Easy
☐6 Very Easy
☐7 Extremely Easy

10. How easy or difficult is it to plan when you will use the medication each time?

☐1 Extremely Difficult
☐2 Very Difficult
☐3 Difficult
☐4 Somewhat Easy
☐5 Easy
☐6 Very Easy
☐7 Extremely Easy

11. How convenient or inconvenient is it to take the medication as instructed?

☐1 Extremely Inconvenient
☐2 Very Inconvenient
☐3 Inconvenient
☐4 Somewhat Convenient
☐5 Convenient
☐6 Very Convenient
☐7 Extremely Convenient

12. Overall, how confident are you that taking this medication is a good thing for you?

☐1 Not at All Confident
☐2 A Little Confident
☐3 Somewhat Confident
☐4 Very Confident
☐5 Extremely confident

13. How certain are you that the good things about your medication outweigh the bad things?

☐1 Not at All Certain
☐2 A Little Certain
☐3 Somewhat Certain
☐4 Very Certain
☐5 Extremely Certain

14. Taking all things into account, how satisfied or dissatisfied are you with this medication?

☐1 Extremely Dissatisfied
☐2 Very Dissatisfied
☐3 Dissatisfied
☐4 Somewhat Satisfied
☐5 Satisfied
☐6 Very Satisfied
☐7 Extremely Satisfied

Appendix 8. Satisfaction with Information About Medicines Scale (SIMS)

Information About Medicines

We would like to ask you about **the information you have received about your medicines**. Please rate the information you have received about each of the following aspects of your medicines. If you use more than one medicine, please give your overall feeling about information you have received **about all your medicines.**

Rated:

too much / too little / none received (score 0);

about right / none needed (score 1).

1. What your medicine is called.
2. What your medicine is for.
3. What it does.
4. How it works.
5. How long it will take to act.
6. How you can tell if it is working.
7. How long you will need to be on your medicine.
8. How to use your medicine.
9. How to get a further supply.
10. Whether the medicine has any unwanted effects (side effects).
11. What are the risks of you getting side effects.
12. What you should do if you experience unwanted side effects.
13. Whether you can drink alcohol whilst taking this medicine.
14. Whether the medicine interferes with other medicines.
15. Whether the medication will make you feel drowsy.
16. Whether the medication will affect your sex life.
17. What you should do if you forget to take a dose.

Other information (please specify below):

……
……
……
……
……
……

Total score (items 1-17):……..
Action and usage subscale (items 1-9):…….
Potential problems of medication subscale (items 10-17):……..

Scores range from 0 to 17 with high scores indicating a high degree of overall satisfaction with the amount of medication information received.

Appendix 9. Morisky Medication Adherence Scale – 4 questions (MMAS-4)

Appendix 10. Work Productivity and Activity Impairment - Specific Health Problem Questionnaire (WPAI-SHP)

The following questions ask about the effect of your PROBLEM (Rheumatoid arthritis = RA, Ankylosing Spondylitis = AS, Psoriatic Arthritis = PsA, Psoriasis =Ps, Inflammatory Bowel Disease = IBD) on your ability to work and perform regular activities. Please fill in the blanks or circle a number, as indicated.

1. **Are you currently employed (working for pay)?** _____ NO ___ YES

   If NO, check "NO" and skip to question 6.

The next questions are about the past seven days, not including today:

2. **During the past seven days, how many hours did you miss from work because of problems associated with your RA, AS, PsA, Ps or IBD? Include hours you missed on sick days, times you went in late, left early, etc., because of your RA, AS, PsA, Ps or IBD:**_____ HOURS

3. **During the past seven days, how many hours did you miss from work because of any other reason, such as vacation, or holidays?**_____HOURS

4. **During the past seven days, how many hours did you actually work?**
_____HOURS (If "0", skip to question 6.)

5. **During the past seven days, how much did your RA, AS, PsA, Ps or IBD affect your productivity while you were working?** Think about days you were limited in the amount or kind of work you could do, days you accomplished less than you would like, or days you could not do your work as carefully as usual. If **RA, AS, PsA, Ps or IBD** affected your work only a little, choose a low number. Choose a high number if **RA, AS, PsA, Ps or IBD** affected your work a great deal. Consider only how much **RA, AS, PsA, Ps or IBD** affected productivity while you were working.

Consider only how much PROBLEM affected productivity while you were working.

PROBLEM had no effect on my work	0	1	2	3	4	5	6	7	8	9	10	PROBLEM completely prevented me from working

CIRCLE A NUMBER

6. **During the past seven days, how much did your RA, AS, PsA, Ps or IBD affect your ability to do your regular daily activities, other than work at a job?** By regular activities, we mean the usual activities you do, such as work around the house, shopping, childcare, exercising, studying, etc. Think about times you were limited in the amount or kind of activities you could do and times you accomplished less than you would like. If RA, AS, PsA, Ps or IBD affected your activities only a little, choose a low number. Choose a high number if RA, AS, PsA, Ps or IBD affected your activities a great deal.

Consider only how much **RA, AS, PsA, Ps or IBD** affected your ability to do your regular daily activities, other than work at a job.

Consider only how much P[redacted]ur ability to do your regular daily activities, other than work at a job.

PROBLEM had no effect on my daily activities	0	1	2	3	4	5	6	7	8	9	10	PROBLEM completely prevented me from doing my daily activities

CIRCLE A NUMBER

WPAI Scoring

WPAI:SHP

WPAI outcomes are expressed as impairment percentages, with higher numbers indicating greater impairment and less productivity, i.e., worse outcomes, as follows:

Questions:

1 = currently employed

2 = hours missed due to specified problem

3 = hours missed due to other reasons

4 = hours actually worked

5 = degree problem affected productivity while working

6 = degree problem affected regular activities

Scores:

Multiply scores by 100 to express in percentages.

Percent impairment while working due to problem: Q5/10x100.

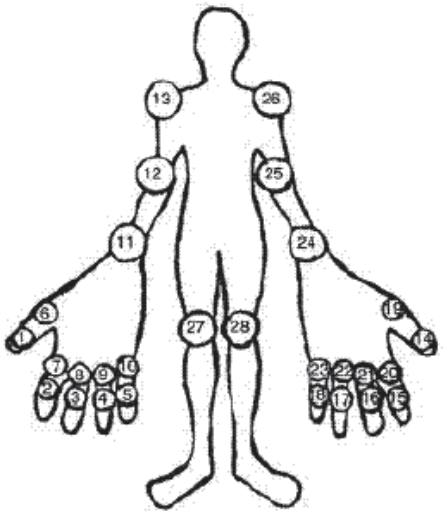
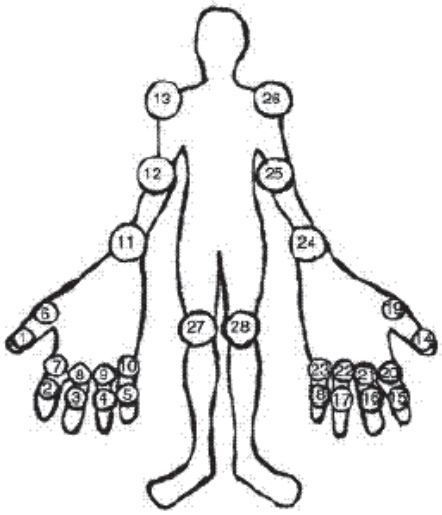
Presenteeism %: Percent work time missed due to problem: Q2/(Q2+Q4)x100.

Total Work Productivity Impairment (TWP) %: Percent overall work impairment due to problem: Q2/(Q2+Q4)+[(1-Q2/(Q2+Q4))x(Q5/10)].

Total Activity Impairment (TAI) %: Percent activity impairment due to problem: Q6/10 (x100%).

Appendix 11. DAS28 score

Disease Activity Index/ 28 joints (DAS 28)

1. Tender joints	2. Swollen joints
☐ No ☐ Yes	☐ No ☐ Yes
If yes, the TOTAL number of tender joints: ☐	If yes, the TOTAL number of swollen joints: ☐
	

3. ESR (mm/1rst hr): ☐☐☐)

4. Patient's global assessment of disease activity (0-100 mm VAS):

Considering all the ways in which the arthritis may affect your patient at this time, please ask him/her the following question:

How active is the disease at the moment?

0 — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10

INACTIVE (0) HIGHLY ACTIVE (10)

Formula for calculation of DAS28 $_{ESR}$:

$DAS_{28\ ESR} = 0.56 \times \sqrt{TJ} + 0.28 \times \sqrt{SJ} + 0.70 \times \ln (ESR\ 1^{st}\ hour) + 0.014 \times$ Patients global assessment of disease

DAS 28 score: .....

Appendix 12. $ASDAS_{ESR}$ score

Calculation of ASDAS:

$ASDAS_{ESR}$= 0.079*total back pain (BASDAI question 2) + 0.113*patient global + 0.0736*peripheral pain/swelling (BASDAI question 3) + 0.069*duration of morning stiffness BASDAI question 6) + 0.293* $\sqrt{}$ ESR

Back pain, patient global, duration of morning stiffness, and peripheral pain/swelling are all assessed on a numerical rating scale (NRS) (0–10).

ESR in mm/h; all patient assessments on a 0 to 10 Numerical rating scale

Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)

Please tick the box which represents your answer to each question. All questions refer to last week.

1. How would you describe the overall level of fatigue/tiredness you have experienced?

NONE 0 1 2 3 4 5 6 7 8 9 10 VERY SEVERE

2. How would you describe the overall level of AS neck, back or hip pain you have had?

NONE 0 1 2 3 4 5 6 7 8 9 10 VERY SEVERE

3. How would you describe the overall level of pain/swelling in joints other than neck, back, hips you have had?

NONE 0 1 2 3 4 5 6 7 8 9 10 VERY SEVERE

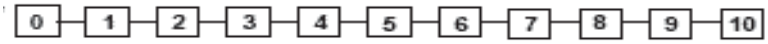
4. How would you describe the overall level of discomfort you have had from any areas tender to touch or pressure?

NONE 0 1 2 3 4 5 6 7 8 9 10 VERY SEVERE

5. How would you describe the overall level of morning stiffness you have had from the time you wake up?

NONE  VERY SEVERE

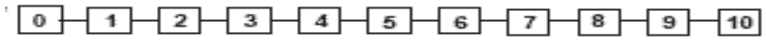
6. How long does your morning stiffness last from the time you wake up?



0 h 1 h 2 or more h

Patient global assessment (0-10 NRS):

How active was your spondylitis on average during the last week?



Not active Very active

ASDAS score: …….

Appendix 13. CDAI score

			Factor	Subtotal
1. Number of liquid or very soft stools (Record the frequency per day)	__+__+__+__+__+__+__=__ Days: 1 2 3 4 5 6 7 Sum	×	2	
2. Abdominal pain rating: 0 = none, 1 = mild, 2 = moderate, 3 = severe	__+__+__+__+__+__+__=__ Days: 1 2 3 4 5 6 7 Sum	×	5	
3. General well-being: 0 = generally well, 1 = slightly underpar, 2 = poor, 3 = very poor, 4 = terrible	__+__+__+__+__+__+__=__ Days: 1 2 3 4 5 6 7 Sum	×	7	
4. Number of 6 listed categories the subject now has **Check all items that apply:** ☐ Arthritis/arthralgia ☐ Iritis/uveitis ☐ Erythema nodosum/pyoderma gangrenosum/aphthous stomatitis ☐ Fissure, abscess and/or anal fistula (draining/non-draining) ☐ Other cutaneous fistula (draining/non-draining) Fistula ☐ Fever over 100°F (37.8°C) during past week	_____ Record "0" if no categories checked	×	20	
5. Taking Lomotil/Imodium/ Loperamide/opiates for diarrhea 0 = no, 1 = yes	_____	×	30	
6. Abdominal mass 0 = none, 2 = questionable, 5 = defined		×	10	
7. Hematocrit: ___.__	Male: (47 – hematocrit) = Female: (42 – hematocrit) = Subtotal If hematocrit > normal, enter "0"	×	6	
8. Body weight: ___.__(kg) Standard weight: ___.__(kg)	100 × [1 – (Body wt/Standard wt)] = Percent below standard weight: _____ If body wt > std. wt, enter "0"	×	1	
			Total	

Appendix 14. pMayo score

pMAYO SCORE	
1. Stool Frequency Subscore	*(Check only one)* ☐$_0$ Normal number of stools for this subject ☐$_1$ 1-2 stools more than normal ☐$_2$ 3-4 stools more than normal ☐$_3$ 5 or more stools than normal
2. Rectal Bleeding Subscore	*(Check only one)* ☐$_0$ No blood seen ☐$_1$ Streaks of blood with stool less than half the time ☐$_2$ Obvious blood with stool most of the time ☐$_3$ Blood alone passed
3. Physician's Global Assessment Subscore	*(Check only one)* ☐$_0$ Normal (Subscores are 0) ☐$_1$ Mild disease (Subscores are mostly 1's) ☐$_2$ Moderate disease (Subscores are 1 to 2) ☐$_3$ Severe disease (Subscores are 2 to 3)
Partial Mayo Score (Subscore 1 + Subscore 2 + Subscore 3)	☐

Appendix 15. PASI score

Psoriasis Area and Severity Index (PASI)

PASI Scoring

Four anatomic sites - head, upper extremities, trunk, and lower extremities - are assessed for erythema, induration (plaque thickness) and desquamation (scaling), as seen on the day of the examination. The severity of each sign is assessed using a 5-point scale:

- 0 = No symptoms
- 1 = Slight
- 2 = Moderate
- 3 = Marked
- 4 = Very marked

The below table outlines the characteristics of each category.

	Erythema[a]	Desquamation	Induration
0 = none	No redness	No scaling	No elevation over normal skin
1 = slight	Faint redness	Fine scale, partially covering lesions	Slight but definite elevation, typically edges indinstinct or sloped
2 = moderate	Red coloration	Fine to coarse scale, covering most or all of the lesions	Moderate elevation with rough or sloped edges
3 = marked	Very or bright red coloration	Coarse, non-tenacious scale predominates, covering most or all of the lesions	Marked elevation typically with hard or sharp edges
4 = very marked	Extreme red coloration; dusky to deep red coloration	Coarse, thick, tenacious scale over most or all lesions; rough surface	Very marked elevation typically with hard sharp edges

a. Do not include residual hyperpigmentation or hypopigmentation as erythema.

The area affected by psoriasis within a given anatomic site is estimated as a percentage of the total area of that anatomic site and assigned a numerical value according to the degree of psoriatic involvement as follows:

- 0 = no involvement
- 1 = <10%
- 2 = 10 to <30%
- 3 = 30 to <50%
- 4 = 50 to <70%
- 5 = 70 to <90%
- 6 = 90 to 100%

Assignments for the following body regions are as follows:

- Neck: include with the head
- Buttocks: include with the lower extremities
- Axillae: include with the trunk
- Genitals: include with the trunk
- The inguinal canal separates the trunk and legs anteriorly

The PASI score for each body region is obtained by multiplying the sum of the severity scores by the area score, then multiplying the result by the constant weighted value assigned to that body region. Since the head, upper extremities, trunk, and lower extremities correspond to approximately 10, 20, 30, and 40% of body surface area, respectively, the PASI score is calculated using the formula:

$$PASI = 0.1 (E_h + I_h + D_h)A_h + 0.2 (E_u + I_u + D_u)A_u + 0.3 (E_t + I_t + D_t)A_t + O.4 (E_l + I_l + D_l)A_l$$

where *E, I, D,* and A denote erythema, induration, desquamation, and area, respectively, and *h, u, t,* and l denote head, upper extremities, trunk, and lower extremities,

respectively. PASI scores range from 0.0 to 72.0 with the highest score representing complete erythroderma of the severest degree.

Appendix 16. Feedback on ABBVIE CARE 2.0

(Patient Support Program (PSP) Satisfaction Form)

How would you evaluate the performance of the AbbVie CARE 2.0 Program?

Please help us with deliberate and honest answers so we could improve our program.

Please tick as applies

AbbVie CARE 2.0 Program in total:

☐1 very good
☐2 good
☐3 less satisfying
☐4 I do not use the services

Call center/Hotline:

☐1 very good
☐2 good
☐3 less satisfying
☐4 I do not use the services

Educational materials provided to you by your physician about your life with ____:

☐1 very good
☐2 good
☐3 less satisfying
☐4 I do not use the services

Educational materials provided to you by your physician about adalimumab:

☐1 very good
☐2 good
☐3 less satisfying

☐4 I do not use the services

Injection guide:

☐1 very good

☐2 good

☐3 less satisfying

☐4 I do not use the services

Nursing services:

☐1 very good

☐2 good

☐3 less satisfying

☐4 I do not use the services

Starter pack:

☐1 very good

☐2 good

☐3 less satisfying

☐4 I do not use the service

Any other service relating to the Patient Support Program

Email contact:

☐1 very good

☐2 good

☐3 less satisfying

☐4 I do not use the services

Medication/Appointment Reminders:

☐1 very good

☐2 good

☐3 less satisfying

☐4 I do not use the services

Other educational materials:

☐1 very good

☐2 good

☐3 less satisfying

☐4 I do not use the services

How would you evaluate the effectiveness of the AbbVie CARE2.0 Program?
Please tick as applies

Relieves my daily burden

☐1 fully applies

☐2 applies

☐3 applies less

☐4 not applicable at all

Is always there for me

☐1 fully applies

☐2 applies

☐3 applies less

☐4 not applicable at all

Offers real added value service

☐1 fully applies

☐2 applies

☐3 applies less

☐4 not applicable at all

Is exceptional

☐1 fully applies

☐2 applies

☐3 applies less

☐4 not applicable at all

What was the best element/moment/most useful part of the program for You?

(Short free text)

What was the less useful element of the program?

(short free text)

Would You recommend the program for other patients?

Yes

No

AbbVie Inc. (AbbVie)

Post Marketing Observational Study

AbbVie Ltd. Hungary (AbbVie)

Post Marketing Observational Study

Protocol P15-673

Post-marketing observational study to evaluate the incremental impact of AbbVie's patient support program on patient reported outcomes and health resource utilization in inflammatory arthritis, psoriasis and inflammatory bowel diseases in Hungary: **VALUE**

Approved by:

[redacted]

21 Oct 2015
Date

21 Oct 2015
Date

21 Oct 2015
Date

Oct 21, 2015
Date