Protocol: J2T-MC-KGBY

Study to Assess Lebrikizumab Pen Ease of Use in Patients with Atopic Dermatitis

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Study to Assess Lebrikizumab Pen Ease of Use in Patients with Atopic Dermatitis

Protocol #23037
Study J2T-MC-KGBY

ELI LILLY & COMPANY

Lilly Corporate Center
893 Delaware Street
Indianapolis, IN 46285

Protocol Date:

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Protocol Amendments

Number	Date of Issue	Section(s) and Page(s) Amended

SUMMARY INFORMATION

TITLE:	Study to Assess Lebrikizumab Pen Ease of Use in Patients with Atopic Dermatitis
PROTOCOL NUMBER:	#23037/J2T-MC-KGBY
SPONSOR:	Eli Lilly & Company 893 Delaware Street Indianapolis, IN 46285
CRO:	Concentrics Research, an IQVIA Company 9335 Delegates Row Indianapolis, IN 46240
CRO CONTACT:	PPD Director, Operations Phone : PPD PPD
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PROTOCOL AGREEMENT

Study to Assess Lebrikizumab Pen Ease of Use in Patients with Atopic Dermatitis

PROTOCOL #23037/J2T-MC-KGBY
Date: 12 April 2024

The signatures below of the Concentrics Research representative and the representative of the Sponsor constitute their respective approvals of this protocol and provide the necessary assurances that this study will be conducted as stated in the protocol, including all statements as to confidentiality. It is agreed that the conduct and results of this study will be kept confidential and that survey data and other pertinent data will become the property of Eli Lilly & Company (Lilly).

PPD _____ *Electronically signed by:* PPD
Reason: Approved
Date: Apr 15, 2024 09:28 EDT

15-Apr-2024

Concentrics Research Representative Signature — Date

PPD _____ *Electronically signed by:* PPD
Reason: Approved
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Lilly Representative Signature — Date

PPD _____ *Electronically signed by:* PPD
Reason: Approved
Date: Apr 15, 2024 10:35 EDT

15-Apr-2024

Lilly Representative Signature — Date

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2 STUDY SYNOPSIS

Name of Company: Eli Lilly & Company (Lilly)
Protocol Number: #23037 (J2T-MC-KGBY)
Name of Investigational Product/Active Ingredients: Lebrikizumab Pen
Title of Study: Study to Assess Lebrikizumab Pen Ease of Use in Patients with Atopic Dermatitis
Name of Contract Research Organization (CRO): Concentrics Research, an IQVIA Business
Participant Environment: The participant environment will be non-clinical and emulate the noise, lighting, and surroundings of a home environment. Study rooms are equipped with 1-way mirrors, cameras, and remote monitoring equipment for participant observation. There will be 1 research site used in this study.
Study Type: Ease of use with a simulated injection
Objective: To evaluate the ease of use and confidence of lebrikizumab administrations via a prefilled pen using the modified Subcutaneous Administration Assessment Questionnaire (mSQAAQ)[9,10] following training on the pen.
Design This study is an open-label, single site ease of use study of the lebrikizumab pen and consists of a single study visit for approximately 51 adult participants. All participants will receive training and perform simulated injections on an injection pad using the pen. Participants will be under the supervision of study site staff when handling the pen and will complete the mSQAAQ[9,10] following the simulated injection. No treatment will be administered to the participants.
Study Population The study population will be comprised of adults, ages 18 and older, who have been diagnosed with Atopic Dermatitis (AD). These participants will be pen and autoinjector (AI) naïve (i.e., not previously used a pen or AI); however, they will be permitted to participate if they have other injection experience (e.g., pre-filled syringe [PFS]).
Recruitment One research site will be used for this study, the Concentrics Center for Research in Indianapolis, IN. Participants will be recruited from the site's database. Approximately 56 participants will be enrolled with 51 participants planned to complete the study. Recruitment will include telephone prescreening based on the inclusion and exclusion criteria and collection of demographics. A broad range of participants will be recruited to assure racial and ethnic diversity that approximates the U.S. Census.[1]

Inclusion Criteria

1. Are at least ≥18 years of age at the time of screening
2. Self-report being diagnosed with AD by a physician (GP, dermatologist, or other physician) and able to provide approximate diagnosis date.
3. Autoinjector or Pen naïve (have not used an autoinjector or pen previously; permissible to have used a PFS or vial and syringe).
4. Willing and able to attend an in-person interview session.
5. Able to read, speak, write, and understand the English language.
6. Able and willing to give signed informed consent prior to study entry.
7. Able to complete the protocol requirements.

Exclusion Criteria

1. Cognitive or physical difficulties that could interfere with ability to understand the training, perform the injection tasks, or complete the study questionnaires as judged by the investigator.
2. Are currently enrolled or have participated in the last 3 months, in a clinical study involving an investigational product or any other type of medical research judged not to be scientifically or medically compatible with this study.
3. Is a health care practitioner who is trained in giving injections.
4. Investigator, site personnel, or immediate family member of investigator or site personnel at Concentrics Center for Research. Immediate family is defined as a spouse, parent, child, or sibling, whether biological or legally adopted.
5. Is an employee of any of the following companies: Eli Lilly and Company, Concentrics Research, IQVIA, or any of its affiliates.
6. Currently pregnant.
7. Known hypersensitivity to any component of lebrikizumab or its excipients.
8. Treatment with a live (or live attenuated) vaccine within the past 12 weeks.
9. Current or chronic infection with hepatitis B, hepatitis C, or human immunodeficiency virus (HIV) per participant self-report.

Methodology:

Following recruitment and pre-screening, qualified participants will be scheduled for an on-site visit at the research site. This is a one-visit study.

Once at the site, the site staff will:

1. Confirm the participant's identity by checking a government-issued ID such as a Driver's License.
2. Provide the Informed Consent document for the participant to review and sign.
3. Assign a participant ID number.
4. Reconfirm inclusion/exclusion criteria and demographics.
5. Administer urine pregnancy test for participants assigned female at birth (AFAB) unless considered individual not of childbearing potential (INOCBP)
6. Obtain medical history including approximate date of the participant's AD diagnosis, any previous or current AD treatments.
7. Administer the REALM Test.[2]

8. Provide a study overview.
9. Provide training to the participant on the use of the device.
10. Site staff will observe participant injection experience using the injection pad.
11. Administer the modified Subcutaneous Administration Assessment Questionnaire (mSQAAQ)
12. End participant's study visit.

Adverse events (AEs) and product complaints will be gathered from the point that the informed consent is signed until participant leaves site on date of visit. Participants with adverse events will be followed for 7-days post AE, via phone call.

Participant Materials

The participant materials will be comprised of the following:

1. Lebrikizumab pen
2. Instructions for Use
3. Injection pad
4. Instructional video
5. mSQAAQ

Test product(s): Lebrikizumab is provided as a sterile liquid and contains no preservatives. Each lebrikizumab pen is designed to deliver 250 mg lebrikizumab and for single-dose subcutaneous administration only. The lebrikizumab drug product is formulated as 125 mg/mL in 20 mM histidine acetate buffer, 175 mM sucrose, and 0.03% (w/v) polysorbate 20 at pH 5.7.

Duration of Study – This study will require one visit. Participants will be enrolled and completed at Visit 1.

Sample Size

The planned analysis population for this descriptive study is 51 participants. Sample size was calculated based on the following assumptions: [redacted]% of the participants will respond "agreed" or "strongly agreed" to each individual mSQAAQ[9,10] question. with associated 95% confidence intervals. No comparative analyses are planned for this study.

Data Analysis:

A descriptive analysis will be performed on results of each individual question from the mSQAAQ.[9,10] All participants having given an informed consent will be included in the analysis population.

The main endpoint of the study will be assessed via mSQAAQ, which is a patient reported outcome (PRO) instrument consisting of 10 individual questions answered on a Likert scale from 1 (Strongly Disagree) to 7 (Strongly Agree). Each question will be analysed and presented individually.

The results of each question will be reported by descriptive statistical analyses on the analysis population. Collected demographic information on study participants will be presented for the total analysis population

as well as any selected sub-populations. A descriptive analysis of any AEs and/or product complaints reported during the study will be included for the total analysis population.

3 ABBREVIATIONS

AD	Atopic Dermatitis
ADE	Adverse Device Effect
AE	Adverse Event
AFAB	Assigned Female at Birth
AI	Autoinjector
CA	Competent Authority
CI	Confidence Interval
COPD	Chronic Obstructive Pulmonary Disease
CRA	Clinical Research Associate (clinical monitor)
CRF	Case Report Form
CRO	Clinical Research Organization
CRSwNP	Chronic Rhinosinusitis with Nasal Polyps
EDC	Electronic Data Capture
e-CRF	Electronic Case Report Form
GCP	Good Clinical Practice
GP	General Practitioner
HIV	Human immunodeficiency virus
IB	Investigator's Brochure
ICH	International Conference on Harmonization
IEC	Independent Ethics Committee
IFU	Instructions for Use
INOCBP	Individuals Not of Childbearing Potential
IP	Investigational Product
IPF	Idiopathic Pulmonary Fibrosis
IRB	Institutional Review Board
mSQAAQ	Modified Subcutaneous Administration Assessment Questionnaire

NA	Not applicable
PAR	Perennial Allergic Rhinitis
PHI	Personal Health Information
PRO	Patient Reported Outcome
PFS	Pre-filled Syringe
REALM	Rapid Estimation of Adult Literacy in Medicine
RHL	Refractory Hodgkin's Lymphoma
RMP	Research Management Platform (IQVIA EDC system)
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SC	Subcutaneous
UADE	Unanticipated Adverse Device Effect

4 INTRODUCTION

This descriptive study is intended to provide feedback from participants about their experience using the lebrikizumab pen when delivering a simulated injection into an injection pad. The participant's experience will be evaluated based on their responses to the modified Subcutaneous Administration Assessment Questionnaire (mSQAAQ), a PRO questionnaire for evaluating one's experience (e.g., ease of use and confidence in using) with a device to administer a SC injection.[9,10]

Participants will perform a simulated injection and provide their feedback on the experience. The participants will perform the tasks independently after training by the study team. Since there is active drug in the pen, the site staff will remain in the room with the participant during their simulated injection into the injection pad. After the simulated injection, a trained study site staff will distribute the mSQAAQ for the participant to complete independently onsite.

5 BACKGROUND

5.1 Description of the Drug Product

Lebrikizumab (LY3650150) is an IgG4 mAb that binds with high affinity and slow off-rate to IL-13 and selectively inhibits IL-13 signaling through the IL-4Rα/IL-13Rα1 pathway, thereby blocking the downstream effects of IL-13 with high potency. Lebrikizumab-bound IL-13 can still bind IL-13Rα2, allowing subsequent internalization and natural clearance of IL-13. Blockade of IL-13 signaling is expected to be of benefit in diseases in which IL-13 is a central cytokine to the disease pathogenesis, such as atopic dermatitis (AD).

Lebrikizumab has been investigated for the treatment of AD, asthma, COPD, IPF, and RHL. Currently, lebrikizumab is being actively developed for the treatment of AD. Lebrikizumab is also being investigated for the treatment of perennial allergic rhinitis (PAR) and chronic rhinosinusitis with nasal polyps (CRSwNP).

An Investigator's Brochure for the drug provides a summary of the clinical studies conducted for lebrikizumab and the associated findings.

5.2 Description of the Investigational Device

The lebrikizumab pen has a drug product container assembled inside the pen (Figure 1). The combined container and pen form a prefilled, single-use, injection device that delivers a fixed dose of drug product subcutaneously. The drug will remain in the container until the drug is injected. The pen uses a fixed needle injection depth that is inserted perpendicular to the skin without the need to raise a skinfold (i.e., a flat-surface injection) to deliver an SC injection.

To facilitate understanding of the operation of the pen, refer to Figure 1 and the J2T-MC-KGBY instructions for use (IFU). Further guidance and information for the final disposition of unused study interventions are provided in the Pharmacy Manual[7] and Dose Preparation Instructions[8].

The solution in the pen requires storage under refrigerated conditions (2ºC to 8ºC). Prior to use, the pen is removed from the refrigerator and allowed to warm to room temperature for 45 minutes. The pen can remain at room temperature for up to 8 hours. If the pen is not used within the allowed timeframe, it should be returned to refrigerated conditions and the temperature excursion process should be followed. Further guidance on the excursion process is provided in the Pharmacy Manual[7].

The pen is prepared by removing the Twist-off Cap that pulls the syringe needle shield off. The pen base is placed flat and firmly onto the patient's skin at the injection site. The base of the device helps to orient the needle perpendicular to the skin. After placement on the skin,

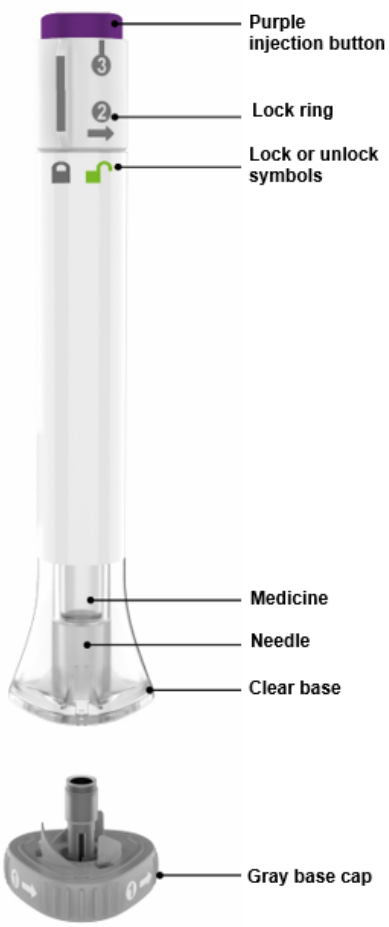
the device is unlocked by turning the Lock Ring to align the raised plastic feature (lock indicator) to the Unlock Symbol. The device can be activated only when the lock indicator is aligned with the Unlock Symbol. The user activates the device by pressing the Injection Button. This generates an audible and tactile click and the device automatically performs the following steps:

1. Inserts needle into the skin
2. Injects the solution
3. Delays needle retraction to ensure complete delivery
4. Retracts the needle.

The user must hold the device firmly against the skin during the injection cycle but is not required to maintain pressure on the Injection Button. The device generates an audible and tactile click at the end of the needle retraction process. The device locks the retracted needle in place for disposal of the used pen into a sharp container.

The pen was developed according to the requirements established by the ISO and standards for needle-based injection systems for medical use (ISO 11608-1 and ISO 11608-5). An Investigator's Brochure for the device outlines the testing and associated findings for the device.

Figure 1: Lebrikizumab Pen



5.3 Intended Participant Environment

The participant environment will be non-clinical and emulate the noise, lighting, and surroundings of a home environment. In order to observe the participants, the rooms are equipped with 1-way mirrors, cameras, and remote monitoring equipment.

5.4 Rationale for Study Design

Autoinjectors (AI) and prefilled syringes (PFS) are commonly accepted as safe and effective for their intended use. Thus, the development of the AI to deliver lebrikizumab is based on the evidence of benefit, as observed in similar approved AIs. Whereas other commercially available AIs are designed to deliver 1 mL of the drug product, the lebrikizumab AI is designed to deliver 2 mL of the study drug. The 2-mL AI has been used in the lebrikizumab clinical development program in Studies J2T-DM-KGAA (KGAA) and J2T-MC-KGBG (KGBG).[4] The results of these studies demonstrate that the 2-mL AI is a viable device for the SC administration of lebrikizumab. The 2-mL AI for delivering lebrikizumab will be referred to as the lebrikizumab pen for the purposes of this study.

The study design for the current ease of use study is descriptive in nature (51 participants) and intended to provide relevant information about the participant experience with the lebrikizumab pen. The population will be comprised of individuals with AD with no prior AI or pen experience, although those with experience with other injectables will be permitted.

Evaluation of the participant's experience will be based on the mSQAAQ[9,10], an instrument for assessing ease of use and confidence in use of a subcutaneous device.

5.5 Study Benefit and Risk Assessment

While there are no direct therapeutic benefits to participants participating in this study, the results from this study will offer valuable insights into the participant's experience with the lebrikizumab pen as related to ease of use and confidence in injection. The risks associated with participation in this study will be minimized because the simulated injections will be performed into injection pads and participants will be under the direct supervision of study staff when handling the injection devices. Participants are not injecting themselves in this study.

5.6 Risks and Foreseeable Adverse Events/Device Effects

The following is a list of potential risks associated with participation in this study:

- Accidental needle stick injury
- Accidental exposure to drug product (accidental self-injection)

- Injection site reaction or hypersensitivity event associated with exposure to drug product via accidental injection

The following is a list of potential risks associated with the study devices:

- Improper functioning and/or mechanical failure of the device or its components (for example, no injection, slow injection into injection pad, partial injection into injection pad, cracked syringes, high force to operate device, damaged needle)
- Skin reaction due to exposure of drug product on skin

5.7 Methods to Minimize Risks

Training on the study device will be provided by study staff prior to the participant performing the simulated injection. Training for correct sharps handling/disposal is part of the study training, and no cross contamination is expected due to each participant receiving their own device, as well as injecting drug into an injection pad. Participants will be instructed to place the base cap in the sharps container once it is removed from the device, so they do not have the temptation to recap. Study staff will monitor the participants at all times in the room and intervene should a dangerous situation occur.

Participants will be under direct supervision of the study staff when handling the device.

The following controls will be in place to prevent an accidental dose of drug product:

1. The participants will only handle the devices under direct supervision of study staff after receiving training.
2. Participants will be told that they should not inject themselves, and these devices will only be used for simulated injections into an injection pad.
3. If a participant appears to begin injecting themselves rather than the injection pad, the site staff will immediately interrupt the process and stop the participant from completing this self-injection.
4. In the unlikely circumstance that a participant does have an accidental needle stick or accidental injection, it is not likely the participant would receive a full dose since a full dose takes up to 15 seconds for delivery.

If a needlestick injury occurs or if a patient is exposed to drug, medical personnel will be available to address any potential medical issues or concerns. Clinical staff members will follow (monitor) the participant as per clinical judgment for a potential adverse event (AE) and follow the appropriate device-reporting procedures for 7 days following the visit.

More detailed information about the known and expected benefits and risks of lebrikizumab may be found in the lebrikizumab investigator's brochure (IB)[3].

6 DESCRIPTION OF DESIGN AND TRIAL POPULATION

6.1 Overall Trial and Design and Plan

This study is an open-label, single site, ease of use study of the lebrikizumab pen and consists of a single study visit for approximately 56 adult participants. All participants will receive training and perform simulated injections on a practice pad using the pen. Participants will be under the supervision of a study interviewer when handling the pen and will complete the mSQAAQ[9,10] following the simulated injection.

No treatment will be administered to the participants.

6.2 Administrative Structure of the Trial

This is an ease-of-use study (with a simulated injection) with a planned analysis population of 51 participants. The participant will be taken to a non-clinical observation room equipped with a 1-way mirror and cameras. The setting is a non-clinical setting arranged similar to a home environment with similar lighting and sound.

The participant will be given training on the use of the pen and then given an opportunity to simulate administration of a dose into an injection pad. Following the injection experience, the participant will self-administer the mSQAAQ[9,10].

6.3 Selection of Participant Population

The participants will be recruited from the site database. A log of all participants enrolled into the study (i.e. having signed the Informed Consent Form) will be maintained by the research site. Minimal personal health information (PHI) will be gathered which will include the approximate date of their AD diagnosis, any previous or current treatments, any known experience with administering drugs by injection to self or others, and if the individual is of child-bearing potential (see Section 9.2.1) , they will be tested to rule out pregnancy given the risk of accidental exposure to drug.

Individuals who self-report having been diagnosed with AD will be pre-screened by phone based on the inclusion and exclusion criteria. Those who qualify (i.e. inclusion criteria apply, and exclusion criteria do not apply) will be scheduled for a 1-visit study at the research site.

The enrolled study population of approximately N=56 will be comprised of adults, ages 18 and older.

While there will be no other assigned quota groups, additional characteristics of the study population will be diverse and may include age, gender, education, literacy, or other patient characteristics.

6.3.1 REALM Test for Literacy

The REALM test[2] will be given to all enrolled individuals to identify participant health literacy levels. The REALM is based on a list of 66 words, which participants are asked to read out loud. The number of correctly pronounced words is noted on a scoring sheet. Those scoring 61 and above are categorized as having normal literacy and those scoring 60 or below as having limited literacy. Scores of 60 or lower correspond to a 7-8th grade reading level or lower (See Table 1).

Table 1 REALM Test Interpretation

Literacy Level	Raw Score	Grade Equivalent
Limited Literacy	0-60	7th/8th Grade and Below
Normal Literacy	61-66	High School and Above

6.3.2 Main Requirement for Study Entry

Participants for this study will be recruited from the research site's database. Phone screening will be conducted to assess inclusion/exclusion and population characteristics. Interested and qualified consumers will be invited to participate in the study at the research site.

6.3.3 Inclusion Criteria

Participants will be included in the study if the following inclusion criteria are met:

1. Are at least ≥18 years of age at the time of screening
2. Self-report being diagnosed with AD by a physician (GP, dermatologist, or other physician) and able to provide approximate diagnosis date.
3. Autoinjector or Pen naïve (have not used an autoinjector or pen previously; permissible to have used a PFS, or vial and syringe).
4. Willing and able to attend an in-person interview session.
5. Able to read, speak, write, and understand the English language.
6. Able and willing to give signed informed consent prior to study entry.
7. Able to complete the protocol requirements.

6.3.4 Exclusion Criteria

Participants will be excluded from the study if:

1. Cognitive or physical difficulties that could interfere with ability to understand the training, perform the injection tasks, or complete the study questionnaires as judged by the investigator.
2. Are currently enrolled or have participated in the last 3 months, in a clinical study involving an investigational product (IP) or any other type of medical research judged not to be scientifically or medically compatible with this study.
3. Is a health care practitioner who is trained in giving injections.
5. Investigator, site personnel, or immediate family member of investigator or site personnel at Concentrics Research. Immediate family is defined as a spouse, parent, child, or sibling, whether biological or legally adopted.
6. Is an employee of any of the following companies: Eli Lilly and Company or Concentrics Research, IQVIA, or any of its affiliates.
7. Currently pregnant.
8. Known hypersensitivity to any component of lebrikizumab or its excipients.
9. Treatment with a live (or live attenuated) vaccine within the past 12 weeks.
10. Current or chronic infection with hepatitis B, hepatitis C, or human immunodeficiency virus (HIV) per participant self-report.

6.3.5 Removal of Individual Participants from Therapy or Assessments

The following may result in a participant being removed prematurely from study participation:

- A participant withdraws consent to participate in the study.
- A participant was erroneously included in the study.
- The study is terminated by the Sponsor.
- A participant is unable to comply with study procedures (e.g., under the influence of drugs or alcohol or participant is combative)

6.4 Objective

To evaluate the ease of use and confidence with using the lebrikizumab pen to administer an injection using the Modified Subcutaneous Administration Assessment Questionnaire (mSQAAQ) following training on the pen.

7 TREATMENTS

No treatment will be administered; this will be a simulated test to evaluate the ease of use of the lebrikizumab pen.

Study Device Storage and Accountability

The investigator or designee must confirm appropriate storage conditions have been maintained during transit for all study devices received and any discrepancies are reported and resolved before use of the study device.

Only participants enrolled in the study may receive study device. Only authorized study personnel may supply, prepare, or administer study device.

All study devices must be stored in a secure, environmentally controlled, and monitored (manual or automated) area in accordance with the labeled storage conditions with access limited to the investigator and authorized study personnel.

The investigator or authorized study personnel are responsible for study device accountability, reconciliation, and record maintenance, that is, receipt, reconciliation, and final disposition records.

Further guidance and information for the final disposition of unused study devices are provided in the Pharmacy Manual.

8 MATERIALS

The following materials will be used in the study:

8.1 Training Video

Participants will be provided with training in the use of the device prior to their simulated injection experience. This training will include an instructional video specific to describing parts of the lebrikizumab pen, pen operation instructions, and a demonstration of dose delivery into an injection pad.

8.2 Instructions for Use

Instructions for Use document will be provided together with the pen. The participant training will include a review of the IFU and the participant will be permitted to refer to these instructions during their simulated injection experience.

8.3 Lebrikizumab Pen and Injection Pad

Participants will be provided with a lebrikizumab pen that has been brought to room temperature for at least 45 minutes prior to the simulation. An injection pad will be provided for the simulated injection and participants will be instructed in the placement of the injection pads for the simulation.

8.4 mSQAAQ Questionnaire

After the simulated injection, the participant will be provided with a self-administered questionnaire, the mSQAAQ[9,10]. This modified, short questionnaire, is an instrument that includes 10 questions about the ease of use and confidence in using the pen. The instructions for completion are embedded within the questionnaire. Participants will read the instructions before responding to the items in the mSQAAQ.

This tool is comprised of 10 questions. Responses are scored on a 7-point Likert scale ranging from ‘strongly disagree’ to ‘strongly agree:’

(1) Strongly disagree; (2) Disagree; (3) Slightly Disagree; (4) Neither agree nor disagree; (5) Slightly agree; (6) Agree; (7) Strongly agree

9 INVESTIGATIONAL PLAN

9.1 Visit Schedule

This study will require one visit. Participants will be enrolled and completed at Visit 1. A Study Flowchart can be found in Figure 2 and a Schedule of Events is located in Table 2.

9.2 Details of Study Procedures

9.2.1 Recruitment and Pre-Screening

Participants will be recruited by the research site who will access their site database comprised individuals who have participated in previous studies and/or expressed interest in participating in future studies. Potential participants will be pre-screened by phone with the inclusion and exclusion criteria including any previous pen experience. Participants who qualify (i.e. inclusion criteria apply, and exclusion criteria do not apply) will be referred to the research site.

9.2.2 Visit 1

This is a single center, single visit simulated use study. All participants will be completed at the end of Visit 1. There is no treatment period; this study involves a simulated injection with a pen device into an injection pad followed by a self-administered questionnaire (mSQAAQ)[9,10] about the participant's experience.

9.2.3 Enrollment and Visit 1 Activities

Participants arriving at the research site will be given an informed consent document to read and sign. The participant will be given an opportunity to ask any questions and will be reminded that participation is voluntary and that the option exists to withdraw at any time. Inclusion and exclusion criteria will be re-confirmed as well as demographic information and previous pen experience; for this study, all participants are required to be pen and AI naïve (i.e., no prior experience with a pen or AI).

Participants who were assigned female at birth (AFAB) will be asked to take a urine pregnancy test to confirm they are not pregnant. Individuals not of childbearing potential (INOCBP) will be exempt from a urine pregnancy test. Individuals AFAB are considered INOCBP if they are not capable of producing ova or embryo, and/or are not capable of potentially gestating a fetus. Such individuals include those who have a congenital anomaly such as Müllerian agenesis resulting in confirmed infertility, are infertile due to surgical sterilization, or are menopausal. Acceptable surgical sterilization methods are hysterectomy, bilateral salpingo-oophorectomy, bilateral salpingectomy, or bilateral oophorectomy.

The Rapid Estimate of Adult Literacy in Medicine (REALM)[2] test will be administered to assess health literacy. A brief medical history will be conducted to gather information about the approximate date of participants' AD diagnosis and any previous or current AD treatments. No laboratory assessments will be required, and no samples will be taken from study participants. Participants will then be given a brief study overview about the nature of the study in which they will simulate use of the pen into an injection pad.

9.2.4 Device Training

Training will be provided to participants in advance of the simulated injection. This training will be in the form of a clinical study training video describing parts of the lebrikizumab pen, pen operation instructions, and a demonstration of dose delivery into an injection pad. Study staff will also provide additional training and guidance such as introducing study materials to the participant, directing participant to review the IFU, assisting with attachment of the injection pad, and providing the mSQAAQ[9,10] following injection simulation. Participants will be allowed to ask questions on training instructions to site staff during training.

9.2.5 Simulated Injection

Participants will be provided with IFU (Appendix 14.1), an injection pad and a pen device. The pen device will be taken out of the refrigerator at least 45 minutes prior to the simulation. The injection pad will be placed on the participant's thigh or abdomen, based on their preference. Participants will be directed to simulate an injection using the pen device by injecting directly into the injection pad.

The pen device contains active drug. Should a participant inadvertently stick themselves with the needle, follow-up care will be provided and an Adverse Event CRF and Product Complaint Form (if applicable) will be completed. Devices involved in product complaints or adverse events will need to be labeled and stored by site for future investigation by the Sponsor. Adverse events will be gathered from the point that the informed consent is signed until participant leaves site on date of visit. Participants with adverse events during the Visit will be followed for 7-days post visit (See Section 12).

9.2.6 mSQAAQ

After the simulated injection, participants will be provided with a self-administered questionnaire, the mSQAAQ to complete.[9,10] After the mSQAAQ is completed, the visit will be completed.

Figure 2: Study Flowchart

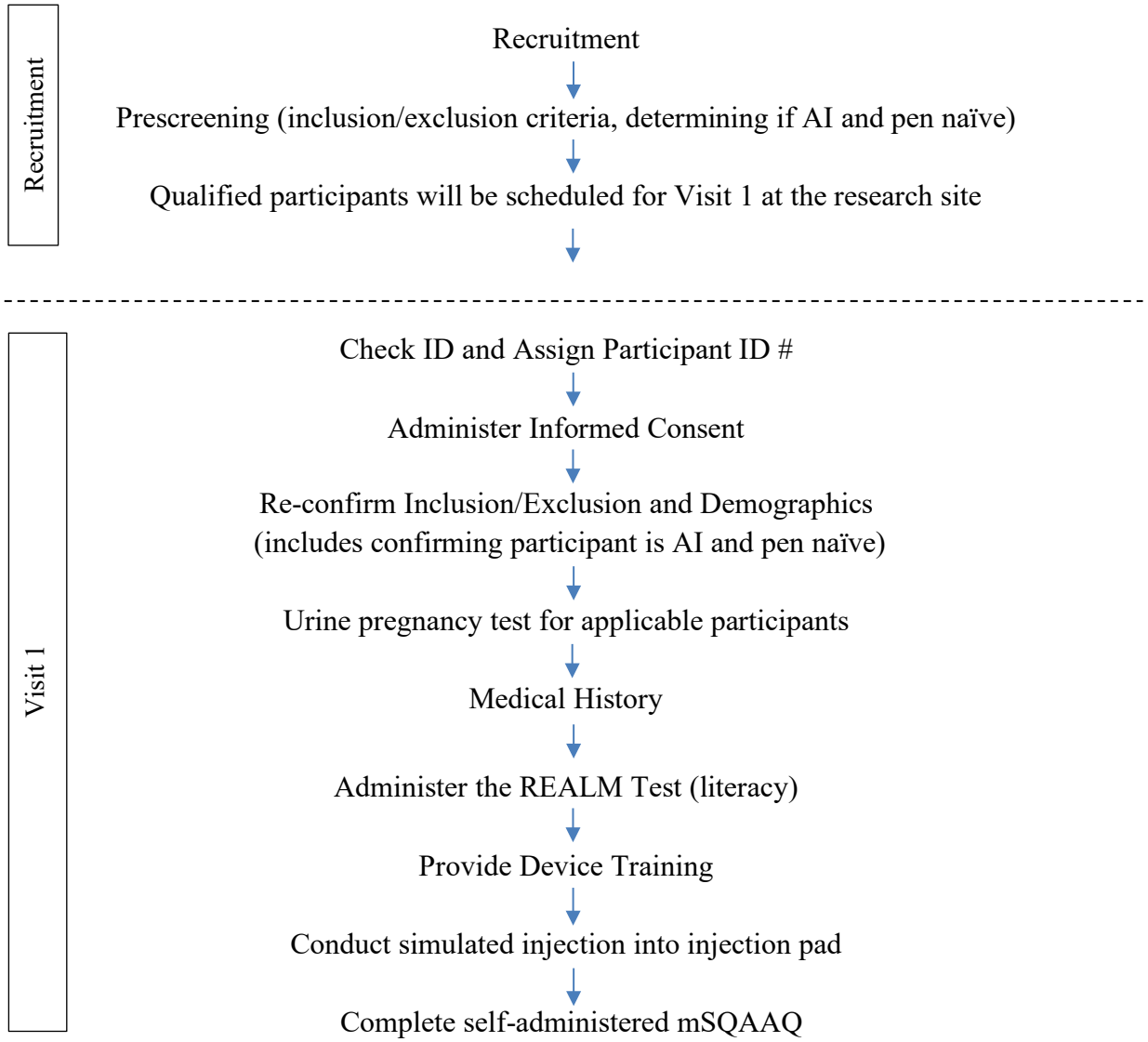


Table 2 Schedule of Events

Activity	Prescreening	Visit 1	Post-Visit 1(If needed)
Prescreening (inclusion/exclusion, demographics, confirm date of diagnosis)	X		
Check ID		X	
Assign a participant ID number		X	
Administer Informed Consent		X	
Reconfirm Inclusion/Exclusion Criteria and demographics		X	
Confirm AI and pen naïve (PFS permitted)		X	
Pregnancy test for participants AFAB unless considered INOCBP		X	
Medical history including approximate date of the participant's AD diagnosis, any previous or current AD treatments		X	
Administer the REALM Test		X	
Provide a study overview		X	
Provide training on the device, including training video		X	
Participant performs simulated injection (into injection pad)		X	
Self-administered mSQAAQ		X	
Product complaints and adverse events management		X	X
End-of-Visit		X	

10 DATA COLLECTION, MANAGEMENT, AND ANALYSIS

10.1 Data Collection

Case Report Form (CRF) data will be collected using a 21 CFR Part 11 compliant electronic data capture system (EDC), the IQVIA Research Management Platform (RMP) v2.6. Data from recruitment and pre-screening will be captured separately and not entered into the RMP EDC system. Since the study is being conducted in person, a paper informed consent and a paper 24-hour SAE report form will be used.

CRF data will include:

- Confirmation of inclusion and exclusion criteria
- Participant demographics
- REALM[2] score
- Confirmation of pen/AI experience (i.e., pen/AI naïve, any other experience with injectables)
- Pregnancy test results for participants AFAB unless considered INOCBP
- Brief medical history (approximate date of AD diagnosis and previous or current treatments)
- Responses to the 10 questions in the mSQAAQ[9,10]
- Adverse events (AE)
- Serious adverse events (SAE)

10.2 Sample Size

The planned final sample size of 51 is sufficient to provide descriptive insights about the study population. Given the nature of the study it is expected that [redacted]%+ of participants enrolled will complete the study and provide full analyzable data.

Under the assumption that [redacted]% of the participants will respond “agreed” or “strongly agreed” to the device being “easy to use” and “they are confident they can use the device” we will have 95% confidence that the response rate is located in this range of proportions: [[redacted]% - [redacted]%]. Table 3 shows a variety of possible sample sizes. For the purpose of the intended claims the 95% CI lower bound should remain above [redacted]%, preferably above [redacted]%, and the parameters for the calculation of sample size have been selected for that.

Table 3 Sample Size Calculation

Proportion	Margin	Lower CI	Upper CI	Sample Size
95.0%	CCI			
95.0%				
90.0%				
85.0%				
80.0%				

Table 4 shows the possible 95% confidence intervals (CI) if the response rate does not reach the assumed 95%. All sample sizes have been calculated with the shown assumptions for proportion of response, margin of error, and a 95% confidence interval.

Table 4 Confidence Interval for Selected Sample Sizes by Response Proportion

Proportion	CCI
95.0%	
90.0%	
85.0%	
80.0%	

10.3 Data Management & Statistical Analysis

10.3.1 Data Analysis

A descriptive analysis will be conducted to assess the ease of use and confidence of use of the lebrikizumab pen. All participants having given an informed consent will be included in the analysis population.

The main endpoint of the study will be assessed via the mSQAAQ[9,10]. The primary outcome reported from each individual question will be the proportion of participants responding "agreed" or "strongly agreed" to the question. Participants who do not complete an individual item in the mSQAAQ will have their remaining questions analyzed per instrument instructions.

Collected demographic information and health literacy level of study participants will be presented for the total analysis population as well as any selected sub-populations. A descriptive analysis of any AEs and/or product complaints reported during the study will be included for the total analysis population.

10.3.2 Data Quality Assurance

Concentrics will act as the contract research organization (CRO) for the study and will conduct the study in a manner consistent with the general principles of Good Clinical Practices (GCP). Study site supervisory staff will be trained regarding all study procedures, including, quality control, CRFs, mSQAAQ,[9,10] documentation and communication with the CRO.

Quality checks will be performed by the data management team at Concentrics Research on all data collected to ensure completeness, accuracy and consistency of the data captured (e.g. all required fields are completed, follow-up questions were asked where appropriate). Any discrepancies or questions with respect to the data will be handled via queries sent to the research site for clarification and/or resolution.

10.4 Interim Analysis

There is no plan to perform interim analyses for this study.

10.5 Handling of Missing Data

Any participants who attend a study visit but do not complete the simulated injection and mSQAAQ[9,10] will be excluded from the analysis. Partial completion of the mSQAAQ will be analyzed per the instrument instructions.

11 Monitoring

Risk-based monitoring will be conducted for this study. The pre-study visit has been waived by the CRO.

The Site Initiation Visit will be combined with a virtual Investigator's Meeting. During this meeting the study protocol, objectives, methods, data collection and data entry procedures and adverse event procedures will be reviewed.

During the course of the study there will be 3 interim monitoring visits. Some visits will be on-site, and some will be remote. The CRA will review the eCRFs and source documents and review Study Device accountability.

One close-out visit is planned. At this visit, a final review of all documentation and data entry will be completed. Study Device accountability will be reviewed and the plan for Study Device return or destruction will be discussed.

12 Safety

12.1 Adverse Event Definition

An AE is defined as any untoward medical occurrence in a participant or clinical investigation (vital signs, physical change, etc.) that does not necessarily have a causal relationship with the treatment. An AE can be any unfavorable or unintended sign (including an abnormal finding on vital signs, physical change, etc.), symptom, or disease temporally associated with the use of an IP, whether or not related to the IP.

This includes any adverse occurrence that is new in onset or aggravated in severity, duration, or frequency from the baseline condition (including the physical examination), or abnormal results of diagnostic procedures (including vital sign abnormalities).

Examples of untoward medical events that should be considered AEs are those that:

- resulted in discontinuation from the study,
- required treatment or any other therapeutic intervention,
- required further diagnostic evaluation (excluding a repetition of the same procedure to confirm the abnormality),
- are associated with clinical signs or symptoms judged by the Investigator to have a significant clinical impact.

Examples of what an AE is not:

- A surgical procedure
- A situation where an untoward event did not occur, (e.g. a social hospitalization)
- The disease being studied, unless progression is more severe than anticipated
- Baseline conditions that have not worsened in severity or frequency
- Abnormal findings or test results (unless considered clinically significant in the opinion of the investigator or specifically defined elsewhere in the protocol) related to the disease being studied (unless more severe than expected).

12.2 Adverse Device Effect Definition

An adverse device effect (ADE) is any adverse event related to the use of an investigational medical device (This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device. Includes any event resulting from use error or from intentional misuse of the investigational medical device. Also includes ‘comparator’ if the comparator is a medical device.).

12.3 Procedures

Adverse events will be gathered from the point that the informed consent is signed until participant leaves site on date of visit. Participants with unrelated adverse events will be followed for 7-days post AE. All SAEs, and related AEs will be followed until the event has resolved. This is a 1-visit study.

A description of the event or diagnosis including dates, severity, relationship to the device and/or IP, action taken and outcome, and whether or not the event was also serious, must be reported on the AE Case Report Form (CRF) for each adverse event.

12.4 Severity

Adverse events are graded according to seriousness and severity. The seriousness of an event is determined by the regulatory criteria in Section 13.7.

The Investigator will evaluate the severity of each AE. Adverse event severity will be graded as follows:

Mild: Awareness of symptoms but easily tolerated

Moderate: Discomfort enough to interfere with but not prevent daily activity

Severe: Unable to perform usual activity

12.5 Relationship

The Investigator will judge the likelihood that the AE was related to the device or IP according to the following criteria:

- Not related: There is no possible temporal and/or causal relationship to the device or IP
- Related: There is a possible temporal and/or causal relationship to the device or IP

12.6 Action Taken and Outcome

Action Taken with IP or device will not be collected given the nature of this study. The Outcome of each AE will be entered as either: Recovered/Resolved, Recovered/Resolved with Sequelae, Not Recovered/Not Resolved, Fatal, or Unknown.

12.7 Adverse Event Follow-up

Investigators will follow unrelated AEs until 7-days after the study visit. All SAEs, and related AEs will be followed until the event has resolved.

12.8 Serious Adverse Events

An AE or ADE that results in any of the following outcomes is serious:

- Death (note that death is the outcome of an SAE, and the cause of death should be listed as the AE)
- Life-threatening event. An event, in the view of either the investigator or sponsor, which places the patient or participant at immediate risk of death. (It does not include an adverse event or suspected adverse reaction that, had it occurred in a more severe form, might have caused death)
- In-patient hospitalization or prolongation of existing hospitalization
- A persistent or significant incapacity, permanent damage or disability or substantial disruption of the ability to conduct normal life functions
- Congenital anomaly or birth defect
- Other important medical event that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, it may jeopardize the participant or may require medical or surgical intervention to prevent one of the outcomes listed in this definition.
- Hospitalization for elective surgery for a prior condition that did not worsen or for social reasons will not be treated as serious.

A serious adverse device effect (SADE) is a serious event that has resulted in any of the consequences characteristic of a serious adverse event. For the purpose of this study, the term SAE will include SADEs.

12.8.1 Serious Adverse Event Reporting

Any SAE which occurs after the Informed Consent document is signed until participant leaves site on date of visit must be reported to Lilly. Lilly must be notified within 24 hours after the site/investigator becomes aware of the SAE.

If the Principal Investigator determines that the event is serious, the following procedures will be implemented:

- The Investigator will report the SAE directly to Lilly. Contacts for SAE reporting can be found in site training materials.
- Investigator will provide, at a minimum, the protocol number, participant's initials, participant number, date of the SAE, SAE term and relationship to IP and/or device. The SAE report form should be submitted with any supporting data available or copies of CRF pages.
- Advarra IRB will be notified of the SAE by the site within the timeframes described below:

1. Unanticipated problems that are serious adverse events should be reported to the IRB within 10 business days of the investigator becoming aware of the event.
2. Any other unanticipated problem should be reported to the IRB within 10 business days of the investigator becoming aware of the problem.

An initial report followed promptly by a complete report will be forwarded to Advarra IRB.

12.8.2 Serious Adverse Event Follow-up

Investigators will follow all SAEs until the SAE has resolved.

The Investigator and Medical Monitor will determine if additional follow-up is required. Follow-up information relating to an SAE must be submitted to Lilly as soon as additional data related to the event are available. All efforts must be taken to obtain follow-up information promptly.

Follow-up information may consist of:

- A hospital discharge summary for participants who are hospitalized or hospitalized over a prolonged period due to the SAE. If possible, the discharge summary should be obtained when it becomes available.
- A copy of the autopsy report, if a death occurs and an autopsy is performed, should be obtained if possible when it becomes available.

Any SAE that is ongoing at the end of visit 1 should be followed as described above. Data after visit 1 should be recorded on the source documents and submitted to Lilly on an SAE report form. For ongoing SAEs, the Principal Investigator must submit follow-up reports to Lilly regarding the participant's subsequent course until the case is closed.

12.9 Unexpected Adverse Event

As defined by 21 CFR 312.32 (a), an unexpected adverse drug experience is:

"An adverse event or suspected adverse reaction is considered "unexpected" if it is not listed in the investigator brochure or is not listed at the specificity or severity that has been observed; or, if an investigator brochure is not required or available, is not consistent with the risk information described in the general investigational plan or elsewhere in the current application, as amended. For example, under this definition, hepatic necrosis would be unexpected (by virtue of greater severity) if the investigator brochure referred only to elevated hepatic enzymes or hepatitis. Similarly, cerebral thromboembolism and cerebral vasculitis would be unexpected (by virtue of greater specificity) if the investigator brochure listed only cerebral vascular accidents. "Unexpected," as used in this definition, also refers to adverse events or suspected adverse reactions that are mentioned in the

investigator brochure as occurring with a class of drugs or as anticipated from the pharmacological properties of the drug but are not specifically mentioned as occurring with the particular drug under investigation."

The study sponsor will expedite reporting all serious unexpected suspected adverse reactions (SUSARs): initial reporting by the sponsor for nonfatal or non-life threatening SUSARs must be submitted as soon as possible but no later than within 15 calendar days following the sponsor's initial receipt of the information, and for fatal or life-threatening SUSARs, initial reports must be submitted no later than 7 calendar days following the sponsor's initial receipt of the information. Any relevant additional information obtained by the sponsor that pertains to a previously submitted IND safety report must be submitted as a Follow-up IND Safety Report without delay as soon as the information is available but no later than 15 calendar days after the sponsor receives the information.

Such expedited reports will comply with the applicable regulatory requirements and with the FDA's Guidance for Industry and Investigators Safety Reporting Requirements for INDs and BA/BE Studies (21 CFR 312.32).

12.9.1 Unanticipated Adverse Device Effect

As defined by 21 CFR 812.3 (s), an unanticipated adverse device effect (UADE) is:

"any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of participants."

The PI will report evaluation results for any unanticipated adverse device effect per 21 CFR 812.150 (b)(1) within 10 days working days to the reviewing IRB(s).

All unanticipated adverse device effects will be evaluated and reported as warranted within 10 working days after sponsor first receives notice of the effect per 21 CFR 812.46 (b) and 21 CFR 812.150 (b)(1).

12.9.2 Definition of Product Complaints

A product complaint is any written, electronic, or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a study intervention. When the ability to use the study intervention safely is impacted, the following are also product complaints:

- deficiencies in labeling information

- use errors for device or drug-device combination products due to ergonomic design elements of the product.

Product complaints related to study interventions used in clinical trials are collected to ensure the safety of participants, monitor quality, and to facilitate process and product improvements.

If the participant identifies a product complaint or a problem with the study intervention, investigators will instruct participants to contact the site as soon as possible so that the situation can be assessed.

An event may meet the definition of both a product complaint and an AE/SAE. In such cases, it should be reported as both a product complaint and as an AE/SAE.

Device deficiencies are product complaints.

12.9.3 Recording and Follow-Up of AE and/or SAE and Product Complaints

When an AE/SAE/product complaint occurs, it is the responsibility of the investigator to review all documentation (for example, hospital progress notes, laboratory reports, and diagnostics reports) related to the event.

The investigator will then record all relevant AE/SAE/product complaint information in the participant's medical records, in accordance with the investigator's normal clinical practice. AE/SAE information is reported on the appropriate CRF page and product complaint information is reported on the Product Complaint Form.

Note: An event may meet the definition of both a product complaint and an AE/SAE. In such cases, it should be reported as both a product complaint and as an AE/SAE.

It is **not** acceptable for the investigator to send photocopies of the participant's medical records to the sponsor or designee in lieu of completion of the CRF page for AE/SAE and the Product Complaint Form for product complaints.

There may be instances when copies of medical records for certain cases are requested by the sponsor or designee. In this case, all participant identifiers, with the exception of the participant number, will be redacted on the copies of the medical records before submission to the sponsor or designee.

The investigator will attempt to establish a diagnosis of the event based on signs, symptoms, and/or other clinical information. Whenever possible, the diagnosis (not the individual signs/symptoms) will be documented as the AE/SAE.

13 INVESTIGATOR OBLIGATIONS

13.1 Ethical and Regulatory Considerations

This study will be conducted in accordance with Good Clinical Practice (GCP) Guidelines E6 (2)[5] and the Code of Federal Regulations (Title 21 CFR Parts 11, 50, 54, and 56).[6]

13.2 Institutional Review Board

The Concentrics Research will ensure that an appropriately constituted Institutional Review Board (IRB), in compliance with the requirements of 21 CFR 56, reviews and approves the clinical study before the study is initiated. IRB approval must refer to the study by exact protocol title, number, and amendment number (if applicable), identify the documents reviewed, and state the date of review.

Concentrics Research will ensure that Lilly approves any changes to the Informed Consent template prior to submission to the IRB.

Should changes to the Informed Consent document become necessary during the study, Concentrics Research will ensure that the changes are approved by Lilly prior to submission to the IRB. Should changes to the study protocol become necessary, the protocol amendment will be approved by the IRB prior to implementation. Protocol administrative changes will be reviewed by the IRB.

13.3 Informed Consent

A properly executed, written Informed Consent, in compliance with 21 CFR Part 50 and HIPAA authorization, will be obtained from each participant prior to enrollment and the initiation of screening evaluations required by this protocol. A copy of the Informed Consent document will be reviewed and approved by Lilly for acceptability and submitted by or on behalf of the Investigator, together with the protocol, to the IRB for review and approval prior to the start of the study. The Informed Consent will be written in language fully comprehensible to the prospective participant.

13.4 Participant Confidentiality

All communications, reports, and participant samples will be identified only by a coded number and/or initials to maintain participant confidentiality. All records will be kept confidential to the extent permitted by law. If a waiver or authorization separate from the statement in the Informed Consent is required for permitting access to a participant's medical records (e.g. HIPAA), the investigator will obtain such authorization prior to enrolling a participant in the study. The Principal Investigator will keep a separate log of participants,

codes, names, and addresses. Documents which identify the participant by name (for example, the Informed Consent document) will be kept in strict confidence.

Lilly and its business associates agree to keep all participant information confidential. Only coded data will be released identifying participants by participant number only. Data resulting from analyses will be entered into a database that is not accessible to the public.

Lilly and its business associates will take every possible step to reduce the risk of releasing information to the public that would enable participants to be personally identified.

REFERENCES

1. U.S. Census Bureau, Quick Facts, as of July 2023. https://www.census.gov/quickfacts/fact/table/US/PST045223

2. Davis, T. C., Long, S. W., Jackson, R. H., Mayeaux, E. J., George, R. B., Murphy, P. W., and Crouch, M. A. Rapid Estimate of Adult Literacy in Medicine: A Shortened Screening Instrument. Family Medicine 1993;25:391-396.

3. Investigator's Brochure Lebrikizumab LY3650150 (through October 2023).

4. Medical Device Investigator's Brochure (Device IB) for Lebrikizumab 2 mL Pen (through May 2023).

5. E6(R2) Good Clinical Practice: Integrated Addendum to ICH E6(R1) Guidance for Industry U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research (CDER) Center for Biologics Evaluation and Research (CBER) March 2018

6. Code of Federal Regulations, Title 21 Food and Drugs, Food and Drug Administration, Health, and Human Services. https://www.ecfr.gov/current/title-21

7. Eli Lilly and Company Pharmacy Manual (October 2023)

8. Dose Preparation Instructions for LY3650150 Prefilled Pen 250 mg/2 mL for J2T-MC-KGBY Clinical Trial (April 2024)

9. Callis Duffin K, Bukhalo M, Bobonich MA, et al. Usability of a novel disposable autoinjector device for ixekizumab: results from a qualitative study and an open-label clinical trial, including patient-reported experience. Med Devices (Auckl). 2016;9:361-369. Published 2016 Oct 12. doi:10.2147/MDER.S113752

10. Ease of Use and Confidence with an Autoinjector to Administer Ixekizumab in a Phase 3 Trial Evaluated with the Subcutaneous Administration Assessment Questionnaire (SQAAQ). Journal of the American Academy of Dermatology, vol. 74, no. 5, Elsevier BV, May 2016, p. AB245. Crossref, doi:10.1016/j.jaad.2016.02.958.

14 APPENDICES

14.1 INSTRUCTIONS FOR USE

Instructions for Use

Clinical Trial J2T-MC-KGBY

Study Drug (LY3650150)

Prefilled Pen

Injection for use in injection pad only

Single-Dose Prefilled Pen

This Instructions for Use contains information on how to inject Study Drug.

Before you use the Study Drug Prefilled Pen (Pen), read and carefully follow all the step-by-step instructions.

Your Pen may look different than the Pen in the pictures in this document.

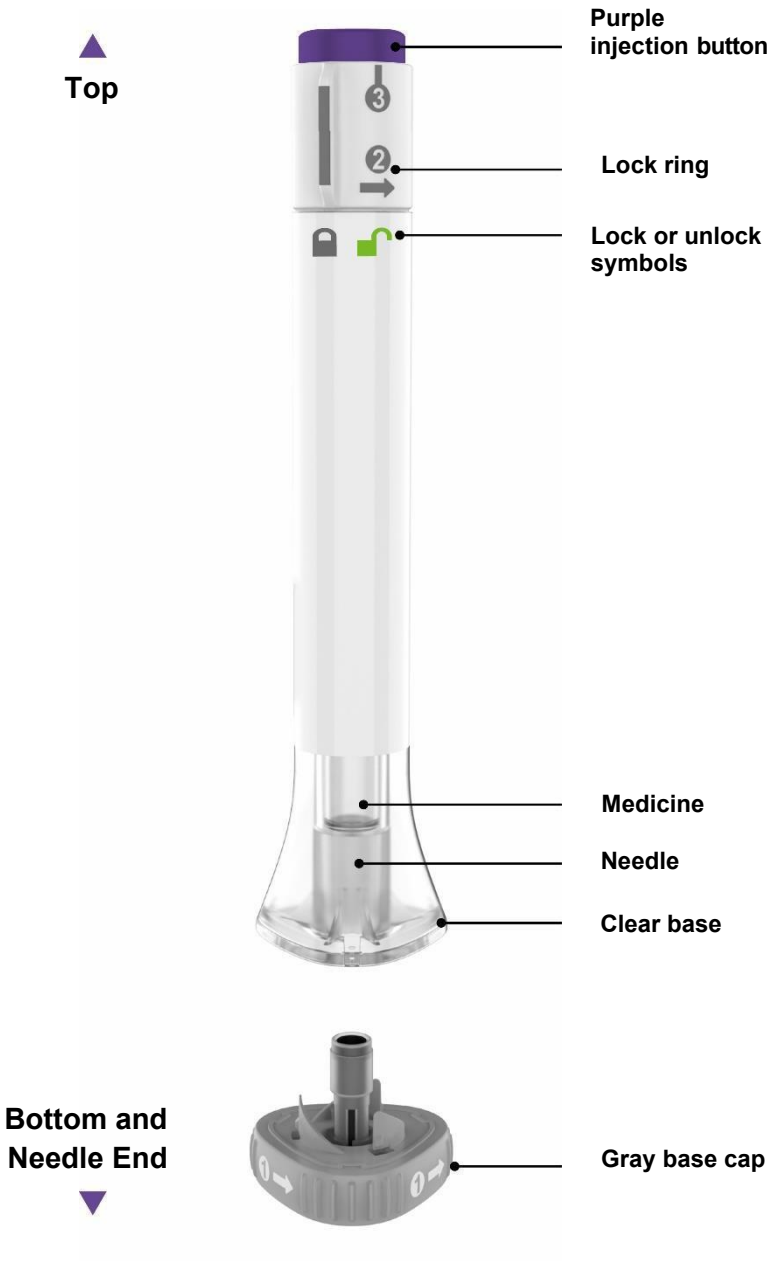
Important information you need to know before injecting Study Drug

- You will be informed on how to prepare and inject Study Drug into the injection pad using the Pen. **Do not** inject yourself or someone else. **Do not** inject into the injection pad until you have been shown how to inject Study Drug.
- Keep this Instructions for Use and read it as needed.
- Each Study Drug Pen contains 1 dose of Study Drug. **The Pen is for one-time use only.**
- The Study Drug Pen contains glass parts. Handle it carefully. If you drop it on a hard surface, **do not** use it and contact study staff.
- The study staff will instruct you how to prepare the injection pad.
- If you have vision or hearing problems, **do not** use Study Drug Pen without help from study staff.

INSTRUCTIONS FOR USE

Before you use the Study Drug Pen, read and carefully follow all the step-by-step instructions.

Parts of the Study Drug Pen



Preparing to inject Study Drug

From the study staff, gather supplies and Study Drug Pen:

- Study Drug Pen
- 1 injection pad
- 1 alcohol wipe
- 1 sharps disposal container (See **Disposing of Study Drug**)

Warm to room temperature

Study staff will have already allowed the Pen to warm to room temperature. Do not remove the gray base cap until you are ready to inject.

- **Do not** warm up the Pen with a microwave, or hot water, or direct sunlight.
- **Do not** use the Pen if the medicine is frozen.

Inspect the Pen and the medicine

Make sure you have the right medicine. The medicine inside should be clear. It may be colorless to slightly yellow to slightly brown.

Do not use the Pen (see **Disposing of Study Drug**) if the:

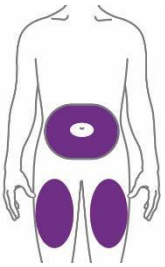
- Pen looks damaged
- Medicine is cloudy, is discolored, or has particles

Wash your hands with soap and water

Prepare injection pad

Your study staff will help you prepare the injection pad for injection. To better simulate a self-injection, you will secure the injection pad to your body, on your abdomen or your thigh.

Clean the injection pad with an alcohol wipe and let dry.



You or another person may inject into these areas.

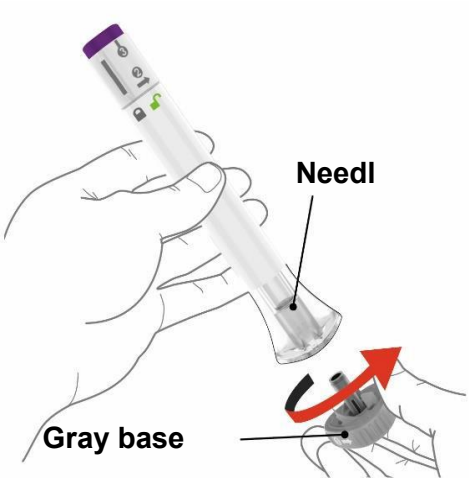
- **Stomach area (abdomen) —**
  At least 2 inches away from the belly button (navel).
- **Front of thigh —**
  At least 2 inches above the knee and 2 inches below the groin.

.

Injecting Study Drug

Figures below illustrate injecting in your body. For this study, all injections are into an injection pad that is secured to your body. **Do not** inject yourself or anyone else.

1 Uncap the Pen



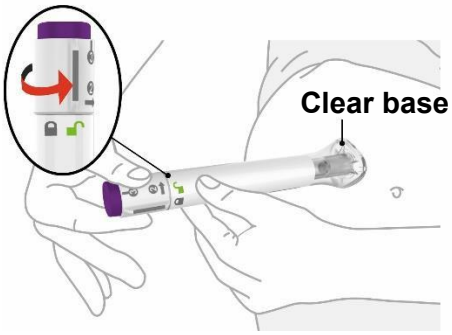
Make sure the Pen is **locked**.

When you are ready to inject, twist off the gray base cap and throw it away in the trash.

Do not put the gray base cap back on; this could damage the needle.

Do not touch the needle inside the clear base.

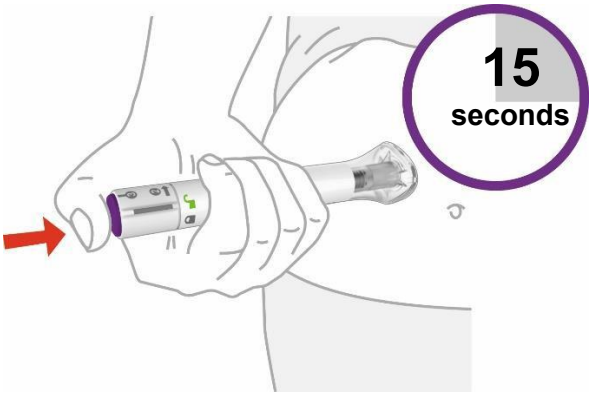
2 Place and unlock



Place and hold the clear base flat and firmly against the injection pad.

Keep the clear base on the injection pad, then turn the lock ring to the **unlock** position.

3 Press and hold for 15 seconds



Press and hold the purple injection button and **listen** for 2 loud clicks:

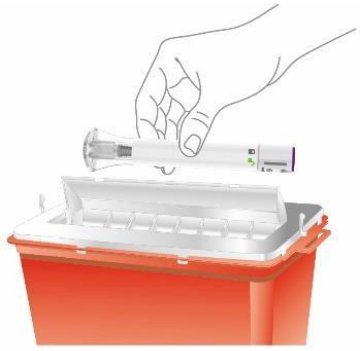
- First click: injection started
- Second click: injection completed

The injection may take up to 15 seconds.

You will know the injection is complete when the gray plunger is visible.

Disposing of Study Drug

Dispose of (throw away) the used Pen



Put the used Study Drug Pen in a sharps disposal container right away after use, as directed by study staff.

Do not throw away (dispose of) the Study Drug Pen in the trash.

Commonly asked questions

Q. What if I see bubbles in the Pen?

A. Air bubbles are normal. They will not harm you or affect your dose.

Q. What if there is a drop of liquid on the tip of the needle when I remove the gray base cap?

A. A drop of liquid on the tip of the needle is normal. This will not harm you or affect your dose.

Q. What if I unlock the Pen and press the purple injection button before twisting off the gray base cap?

A. **Do not** remove the gray base cap. Throw away (dispose of) the Pen and contact study staff to get a replacement. Use a new pen for the injection.

Q. Do I need to hold the purple injection button down until the injection is complete?

A. You do not need to hold the purple injection button down, but it may help you keep the Pen steady and firm against the injection pad.

Q. What if the needle did not retract after my injection?

A. **Do not** touch the needle or replace the gray base cap. Put the Pen in a safe place to avoid an accidental needlestick and contact your study staff.

Q. How can I tell if my injection is complete?

A. After you press the purple injection button, you will hear 2 loud clicks. The second loud click tells you that your injection is complete. You will also see the gray plunger at the top of the clear base. The injection may take up to 15 seconds.

Q. What if I remove the Prefilled Pen before the second loud click or before the gray plunger stops moving?

A. You may not have given the full dose. Contact study staff.

Q. What if I heard more than 2 clicks during my injection, 2 loud clicks and 1 soft one. Did I give a complete injection?

A. Some people may hear a soft click right before the second loud click. That is the normal operation of the Prefilled Pen. **Do not** remove the Prefilled Pen from the injection pad until you hear the second loud click.

Keep your Pen and all medicines out of the reach of children.

2024APR12_23037 J2T-MC-KGBY Lebrikizumab Pen Ease of Use Study Protocol v1.0_FINAL_with Appendices

Final Audit Report 2024-04-15

Created:	2024-04-15
By:	PPD
Status:	Signed
Transaction ID:	PPD

"2024APR12_23037 J2T-MC-KGBY Lebrikizumab Pen Ease of Use Study Protocol v1.0_FINAL_with Appendices" History

Document created by PPD
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2024-04-15 - 1:16:01 PM GMT

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Challenge: The user opened the agreement.
2024-04-15 - 1:22:14 PM GMT

PPD authenticated with Adobe Acrobat Sign.
Challenge: The user opened the agreement.
2024-04-15 - 1:22:44 PM GMT

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Challenge: The user clicked on the signature field: 'Signature 2'.

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Signer PPD entered name at signing as PPD

2024-04-15 - 1:23:42 PM GMT

Document e-signed by PPD

Signing reason: Approved

Signature Date: 2024-04-15 - 1:23:44 PM GMT - Time Source: server

PPD authenticated with Adobe Acrobat Sign.

Challenge: The user clicked on the signature field: 'Signature 1'.

2024-04-15 - 1:24:23 PM GMT

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Challenge: The user opened the agreement.

2024-04-15 - 1:26:16 PM GMT

PPD authenticated with Adobe Acrobat Sign.

Challenge: The user clicked on the signature field: 'Signature 1'.

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Signing reason: Approved

Signature Date: 2024-04-15 - 1:28:11 PM GMT - Time Source: server

Email viewed by PPD

2024-04-15 - 2:33:59 PM GMT

PPD authenticated with phone by verifying one-time code sent to the phone number +X XXX-XXX-PPD

Challenge: The user opened the agreement.

2024-04-15 - 2:34:30 PM GMT

PPD authenticated with phone by verifying one-time code sent to the phone number +X XXX-XXX-PPD

Challenge: The user clicked on the signature field: 'Signature 3'.

2024-04-15 - 2:35:09 PM GMT

Document e-signed by PPD

Signing reason: Approved

Signature Date: 2024-04-15 - 2:35:23 PM GMT - Time Source: server

Agreement completed.

2024-04-15 - 2:35:23 PM GMT