CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

125521Orig1s000

LABELING

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use TALTZ safely and effectively. See full prescribing information for TALTZ.

TALTZ (ixekizumab) injection, for subcutaneous use
Initial U.S. Approval: 2016

----------INDICATIONS AND USAGE----------
TALTZ™ is a humanized interleukin-17A antagonist indicated for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy. (1)

----------DOSAGE AND ADMINISTRATION----------
- Administer by subcutaneous injection. (2.1)
- Recommended dose is 160 mg (two 80 mg injections) at Week 0, followed by 80 mg at Weeks 2, 4, 6, 8, 10, and 12, then 80 mg every 4 weeks. (2.1)

----------DOSAGE FORMS AND STRENGTHS----------
Autoinjector
- Injection: 80 mg/mL solution in a single-dose prefilled autoinjector. (3)

Prefilled Syringe
- Injection: 80 mg/mL solution in a single-dose prefilled syringe. (3)

----------CONTRAINDICATIONS----------
Serious hypersensitivity reaction to ixekizumab or to any of the excipients. (4)

----------WARNINGS AND PRECAUTIONS----------
- Infections: Serious infections have occurred. Instruct patients to seek medical advice if signs or symptoms of clinically important chronic or acute infection occur. If a serious infection develops, discontinue TALTZ until the infection resolves. (5.1)
- Tuberculosis (TB): Evaluate for TB prior to initiating treatment. (5.2)
- Hypersensitivity: If a serious allergic reaction occurs, discontinue TALTZ immediately and initiate appropriate therapy. (5.3)
- Inflammatory Bowel Disease: Crohn's disease and ulcerative colitis, including exacerbations, occurred during clinical trials. Patients who are treated with TALTZ and have inflammatory bowel disease should be monitored closely. (5.4)

----------ADVERSE REACTIONS----------
Most common (≥1%) adverse reactions associated with TALTZ treatment are injection site reactions, upper respiratory tract infections, nausea, and tinea infections. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Eli Lilly and Company at 1-800-545-5979 (1-800-LillyRx) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

---------- DRUG INTERACTIONS ----------
Live Vaccines: Live vaccines should not be given with TALTZ. (7.1)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved Medication Guide.

Revised: 03/2016

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

TALTZ™ is indicated for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

2 DOSAGE AND ADMINISTRATION

2.1 Dosage

TALTZ is administered by subcutaneous injection. The recommended dose is 160 mg (two 80 mg injections) at Week 0, followed by 80 mg at Weeks 2, 4, 6, 8, 10, and 12, then 80 mg every 4 weeks.

2.2 Tuberculosis Assessment Prior to Initiation of TALTZ

Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with TALTZ *[see Warnings and Precautions (5.2)]*.

2.3 Important Administration Instructions

There are two presentations for TALTZ (i.e., autoinjector and prefilled syringe). The TALTZ "Instructions for Use" for each presentation contains more detailed instructions on the preparation and administration of TALTZ *[see Instructions for Use]*.

TALTZ is intended for use under the guidance and supervision of a physician. Patients may self-inject after training in subcutaneous injection technique using the autoinjector or prefilled syringe. Administer each injection at a different anatomic location (such as upper arms, thighs or any quadrant of abdomen) than the previous injection, and not into areas where the skin is tender, bruised, erythematous, indurated or affected by psoriasis. Administration of TALTZ in the upper, outer arm may be performed by a caregiver or healthcare provider.

If a dose is missed, administer the dose as soon as possible. Thereafter, resume dosing at the regular scheduled time.

2.4 Preparation for Use of TALTZ Autoinjector and Prefilled Syringe

Before injection, remove TALTZ autoinjector or TALTZ prefilled syringe from the refrigerator and allow TALTZ to reach room temperature (30 minutes) without removing the needle cap.

Inspect TALTZ visually for particulate matter and discoloration prior to administration. TALTZ is a clear and colorless to slightly yellow solution. Do not use if the liquid contains visible particles, is discolored or cloudy (other than clear and colorless to slightly yellow). TALTZ does not contain preservatives, therefore discard any unused product remaining in the autoinjector or prefilled syringe.

Instruct patients using the autoinjector or prefilled syringe to inject the full amount (1 mL), which provides 80 mg of TALTZ, according to the directions provided in the Instructions for Use *[see Instructions for Use]*.

3 DOSAGE FORMS AND STRENGTHS

TALTZ is a clear and colorless to slightly yellow solution available as:

Autoinjector

- Injection: 80 mg/mL solution of TALTZ in a single-dose prefilled autoinjector

Prefilled Syringe

- Injection: 80 mg/mL solution of TALTZ in a single-dose prefilled syringe

4 CONTRAINDICATIONS

TALTZ is contraindicated in patients with a previous serious hypersensitivity reaction, such as anaphylaxis, to ixekizumab or to any of the excipients *[see Warnings and Precautions (5.3)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Infections

TALTZ may increase the risk of infection. In clinical trials, the TALTZ group had a higher rate of infections than the placebo group (27% vs. 23%). Upper respiratory tract infections, oral candidiasis, conjunctivitis and tinea infections occurred more frequently in the TALTZ group than in the placebo group *[see Adverse Reactions (6.1)]*.

Instruct patients treated with TALTZ to seek medical advice if signs or symptoms of clinically important chronic or acute infection occur. If a patient develops a serious infection or is not responding to standard therapy, monitor the patient closely and discontinue TALTZ until the infection resolves.

5.2 Pre-treatment Evaluation for Tuberculosis

Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with TALTZ. Do not administer to patients with active TB infection. Initiate treatment of latent TB prior to administering TALTZ. Consider anti-TB therapy

prior to initiating TALTZ in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Patients receiving TALTZ should be monitored closely for signs and symptoms of active TB during and after treatment.

5.3 Hypersensitivity

Serious hypersensitivity reactions, including angioedema and urticaria (each ≤0.1%), occurred in the TALTZ group in clinical trials. If a serious hypersensitivity reaction occurs, discontinue TALTZ immediately and initiate appropriate therapy *[see Adverse Reactions (6.1)]*.

5.4 Inflammatory Bowel Disease

Crohn's disease and ulcerative colitis, including exacerbations, occurred at a greater frequency in the TALTZ group (Crohn's disease 0.1%, ulcerative colitis 0.2%) than the placebo group (0%) during the 12-week, placebo-controlled period. During TALTZ treatment, monitor for onset or exacerbation of inflammatory bowel disease.

5.5 Immunizations

Prior to initiating therapy with TALTZ, consider completion of all age appropriate immunizations according to current immunization guidelines. Avoid use of live vaccines in patients treated with TALTZ. No data are available on the response to live or inactive vaccines.

6 ADVERSE REACTIONS

The following adverse drug reactions are discussed in greater detail in other sections of the label:

- Infections *[see Warnings and Precautions (5.1)]*
- Hypersensitivity Reactions *[see Contraindications (4) and Warnings and Precautions (5.3)]*
- Inflammatory Bowel Disease *[see Warnings and Precautions (5.4)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying and controlled conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Weeks 0 to 12:

Three placebo-controlled trials in subjects with plaque psoriasis were integrated to evaluate the safety of TALTZ compared to placebo for up to 12 weeks. A total of 1167 subjects (mean age 45 years; 66% men; 94% White) with plaque psoriasis received TALTZ (160 mg at Week 0, 80 mg every two weeks [Q2W] for 12 weeks) subcutaneously. In two of the trials, the safety of TALTZ (use up to 12 weeks) was also compared with an active comparator, U.S. approved etanercept *[see Clinical Studies (14)]*.

In the 12-week, placebo-controlled period, adverse events occurred in 58% of the TALTZ Q2W group (2.5 per subject-year of follow-up) compared with 47% of the placebo group (2.1 per subject-year of follow-up). Serious adverse events occurred in 2% of the TALTZ group (0.07 per subject-year of follow-up), and in 2% of the placebo group (0.07 per subject-year of follow-up).

Table 1 summarizes the adverse reactions that occurred at a rate of at least 1% and at a higher rate in the TALTZ group than in the placebo group during the 12-week placebo-controlled period of the pooled clinical trials.

Table 1: Adverse Reactions Occurring in ≥1% of the TALTZ Group and More Frequently than in the Placebo Group in the Plaque Psoriasis Clinical Trials through Week 12

Adverse Reactions	TALTZ 80 mg Q2W (N=1167) (n%)	Etanercept[b] (N=287) (n%)	Placebo (N=791) (n%)
Injection site reactions	196 (17)	32 (11)	26 (3)
Upper respiratory tract infections[a]	163 (14)	23 (8)	101 (13)
Nausea	23 (2)	1 (<1)	5 (1)
Tinea infections	17 (2)	0	1 (<1)

[a] Upper respiratory tract infections cluster includes nasopharyngitis and rhinovirus infection.
[b] U.S. approved etanercept.

Adverse reactions that occurred at rates less than 1% in the TALTZ group and more frequently than in the placebo group during the 12-week induction period included rhinitis, oral candidiasis, urticaria, influenza, conjunctivitis, inflammatory bowel disease, and angioedema.

Weeks 13 to 60:

A total of 332 subjects received the recommended maintenance regimen of TALTZ 80 mg dosed every 4 weeks.

During the maintenance period (Weeks 13 to 60), adverse events occurred in 80% of subjects treated with TALTZ (1.0 per subject-year of follow-up) compared to 58% of subjects treated with placebo (1.1 per subject-year of follow-up). Serious adverse events were reported in 4% of subjects treated with TALTZ (0.05 per subject-year of follow-up) and none in the subjects treated with placebo.

Weeks 0 to 60:

Over the entire treatment period (Weeks 0 to 60), adverse events were reported in 67% of subjects treated with TALTZ (1.4 per subject-year of follow-up) compared to 48% of subjects treated with placebo (2.0 per subject-year of follow-up). Serious adverse events were reported in 3% of subjects treated with TALTZ (0.06 per subject-year of follow-up), and in 2% of subjects treated with placebo (0.06 per subject-year of follow-up).

Specific Adverse Drug Reactions:

Injection Site Reactions

The most frequent injection site reactions were erythema and pain. Most injection site reactions were mild-to-moderate in severity and did not lead to discontinuation of TALTZ.

Infections

In the 12-week, placebo-controlled period of the clinical trials in plaque psoriasis, infections occurred in 27% of subjects treated with TALTZ (1.2 per subject-year of follow-up) compared to 23% of subjects treated with placebo (1.0 per subject-year of follow-up). Serious infections occurred in 0.4% of subjects treated with TALTZ (0.02 per subject-year of follow-up) and in 0.4% of subjects treated with placebo (0.02 per subject-year of follow-up) *[see Warnings and Precautions (5.1)]*.

During the maintenance treatment period (Weeks 13 to 60), infections occurred in 57% of subjects treated with TALTZ (0.70 per subject-year of follow-up) compared to 32% of subjects treated with placebo (0.61 per subject-year of follow-up). Serious infections occurred in 0.9% of subjects treated with TALTZ (0.01 per subject-year of follow-up) and none in the subjects treated with placebo.

Over the entire treatment period (Weeks 0 to 60), infections were reported in 38% of subjects treated with TALTZ (0.83 per subject-year of follow-up) compared to 23% of subjects treated with placebo (1.0 per subject-year of follow-up). Serious infections occurred in 0.7% of subjects treated with TALTZ (0.02 per subject-year of follow-up), and in 0.4% of subject treated with placebo (0.02 per subject-year of follow-up).

Laboratory Assessment of Cytopenia

Neutropenia

Over the entire treatment period (Weeks 0 to 60), neutropenia occurred in 11% of subjects treated with TALTZ (0.24 per subject-year of follow-up) compared to 3% of subjects treated with placebo (0.14 per subject-year of follow-up). In subjects treated with TALTZ, the incidence rate of neutropenia during Weeks 13 to 60 was lower than the incidence rate during Weeks 0 to 12.

In the 12-week, placebo-controlled period, neutropenia ≥ Grade 3 (<1,000 cells/mm^3) occurred in 0.2% of the TALTZ group (0.007 per subject-year of follow-up) compared to 0.1% of the placebo group (0.006 per subject-year of follow-up). The majority of cases of neutropenia were either Grade 2 (2% for TALTZ 80 mg Q2W versus 0.3% for placebo; ≥1,000 to <1,500 cells/mm^3) or Grade 1 (7% for TALTZ 80 mg Q2W versus 3% for placebo; ≥1,500 cells/mm^3 to <2,000 cells/mm^3). Neutropenia in the TALTZ group was not associated with an increased rate of infection compared to the placebo group.

Thrombocytopenia

Ninety eight percent of cases of thrombocytopenia were Grade 1 (3% for TALTZ 80 mg Q2W versus 1% for placebo; ≥75,000 cells/mm^3 to <150,000 cells/ mm^3). Thrombocytopenia in subjects treated with TALTZ was not associated with an increased rate of bleeding compared to subjects treated with placebo.

Active Comparator Trials

In the two clinical trials that included an active comparator, the rate of serious adverse events during weeks zero to twelve was 0.7% for U.S. approved etanercept and 2% for TALTZ 80 mg Q2W, and the rate of discontinuation from adverse events was 0.7% for U.S. approved etanercept and 2% for TALTZ 80 mg Q2W. The incidence of infections was 18% for U.S. approved etanercept and 26% for TALTZ 80 mg Q2W. The rate of serious infections was 0.3% for both TALTZ 80 mg Q2W and U.S. approved etanercept.

6.2 Immunogenicity

As with all therapeutic proteins there is the potential for immunogenicity with TALTZ. By Week 12, approximately 9% of subjects treated with TALTZ every 2 weeks developed antibodies to ixekizumab. Approximately 22% of subjects treated with TALTZ at the recommended dosing regimen developed antibodies to ixekizumab during the 60-week treatment period. The clinical effects of antibodies to ixekizumab are dependent on the antibody titer; higher antibody titers were associated with decreasing drug concentration and clinical response.

Of the subjects who developed antibodies to ixekizumab during the 60-week treatment period, approximately 10%, which equates to 2% of subjects treated with TALTZ at the recommended dosing regimen, had antibodies that were classified as neutralizing. Neutralizing antibodies were associated with reduced drug concentrations and loss of efficacy.

However, the assay to test for neutralizing antibodies has limitations detecting neutralizing antibodies in the presence of ixekizumab; therefore, the incidence of neutralizing antibodies development could be underestimated.

The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of incidence of antibodies to TALTZ with the incidences of antibodies to other products may be misleading.

7 DRUG INTERACTIONS

7.1 Live Vaccinations

Avoid use of live vaccines in patients treated with TALTZ *[see Warnings and Precautions (5.5)]*.

7.2 Cytochrome P450 Substrates

The formation of CYP450 enzymes can be altered by increased levels of certain cytokines (e.g., IL-1, IL-6, IL-10, TNFα, IFN) during chronic inflammation. Thus, TALTZ, an antagonist of IL-17A, could normalize the formation of CYP450 enzymes.

Therefore, upon initiation or discontinuation of TALTZ in patients who are receiving concomitant drugs which are CYP450 substrates, particularly those with a narrow therapeutic index, consider monitoring for effect (e.g., for warfarin) or drug concentration (e.g., for cyclosporine) and consider dosage modification of the CYP450 substrate.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available data on TALTZ use in pregnant women to inform any drug associated risks. Human IgG is known to cross the placental barrier; therefore, TALTZ may be transmitted from the mother to the developing fetus. An embryofetal development study conducted in pregnant monkeys at doses up to 19 times the maximum recommended human dose (MRHD) revealed no evidence of harm to the developing fetus. When dosing was continued until parturition, neonatal deaths were observed at 1.9 times the MRHD *[see Data]*. The clinical significance of these nonclinical findings is unknown.

The background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

Data

Animal Data

An embryofetal development study was conducted in cynomolgus monkeys administered ixekizumab. No malformations or embryofetal toxicity were observed in fetuses from pregnant monkeys administered ixekizumab weekly by subcutaneous injection during organogenesis to near parturition at doses up to 19 times the MRHD (on a mg/kg basis of 50 mg/kg/week). Ixekizumab crossed the placenta in monkeys.

In a pre- and post-natal development toxicity study, pregnant cynomolgus monkeys were administered weekly subcutaneous doses of ixekizumab up to 19 times the MRHD from the beginning of organogenesis to parturition. Neonatal deaths occurred in the offspring of two monkeys administered ixekizumab at 1.9 times the MRHD (on a mg/kg basis of 5 mg/kg/week) and two monkeys administered ixekizumab at 19 times the MRHD (on a mg/kg basis of 50 mg/kg/week). These neonatal deaths were attributed to early delivery, trauma, or congenital defect. The clinical significance of these findings is unknown. No ixekizumab-related effects on functional or immunological development were observed in the infants from birth through 6 months of age.

8.2 Lactation

Risk Summary

There are no data on the presence of ixekizumab in human milk, the effects on the breastfed infant, or the effects on milk production. Ixekizumab was detected in the milk of lactating cynomolgus monkeys. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for TALTZ and any potential adverse effects on the breastfed infant from TALTZ or from the underlying maternal condition.

8.4 Pediatric Use

The safety and effectiveness of TALTZ in pediatric patients (<18 years of age) have not been evaluated.

8.5 Geriatric Use

Of the 4204 psoriasis subjects exposed to TALTZ, a total of 301 were 65 years or older, and 36 subjects were 75 years or older. Although no differences in safety or efficacy were observed between older and younger subjects, the

number of subjects aged 65 and over is not sufficient to determine whether they respond differently from younger subjects *[see Clinical Pharmacology (12.3)]*.

10 OVERDOSAGE

In the event of overdosage, monitor the patient for any signs or symptoms of adverse reactions and institute appropriate symptomatic treatment immediately.

11 DESCRIPTION

Ixekizumab is a humanized immunoglobulin G subclass 4 (IgG4) monoclonal antibody (mAb) with neutralizing activity against IL-17A. Ixekizumab is produced by recombinant DNA technology in a recombinant mammalian cell line and purified using standard technology for bioprocessing. Ixekizumab is comprised of two identical light chain polypeptides of 219 amino acids each and two identical heavy chain polypeptides of 445 amino acids each, and has a molecular weight of 146,158 Daltons for the protein backbone of the molecule.

TALTZ injection is a sterile, preservative free, clear and colorless to slightly yellow solution, for subcutaneous use available as 80 mg of ixekizumab in a 1 mL single-dose prefilled autoinjector or a single-dose prefilled syringe. The prefilled autoinjector and prefilled syringe each contain a 1 mL glass syringe with a fixed 27 gauge ½ inch needle. The TALTZ 80 mg prefilled autoinjector and prefilled syringe are manufactured to deliver 80 mg of ixekizumab.

Each mL is composed of ixekizumab (80 mg); Citric Acid Anhydrous, USP (0.51 mg); Polysorbate 80, USP (0.3 mg); Sodium Chloride, USP (11.69 mg); Sodium Citrate Dihydrate, USP (5.11 mg); and Water for Injection, USP. The TALTZ solution has a pH of 5.3 – 6.1.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Ixekizumab is a humanized IgG4 monoclonal antibody that selectively binds with the interleukin 17A (IL-17A) cytokine and inhibits its interaction with the IL-17 receptor. IL-17A is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. Ixekizumab inhibits the release of proinflammatory cytokines and chemokines.

12.2 Pharmacodynamics

No formal pharmacodynamic studies have been conducted with TALTZ.

12.3 Pharmacokinetics

Absorption

Following a single subcutaneous dose of 160 mg in subjects with plaque psoriasis, ixekizumab reached peak mean (±SD) serum concentrations (C_{max}) of 16.2 ±6.6 mcg/mL by approximately 4 days post dose.

Steady-state concentrations were achieved by Week 8 following the 160 mg starting dose and 80 mg every 2 weeks dosing regimen; the mean ±SD steady-state trough concentration was 9.3 ±5.3 mcg/mL. Steady-state concentrations were achieved approximately 10 weeks after switching from the 80 mg every 2 weeks dosing regimen to the 80 mg every 4 weeks dosing regimen at Week 12. The mean ±SD steady-state trough concentration was 3.5 ±2.5 mcg/mL.

In studies of subjects with plaque psoriasis, ixekizumab bioavailability ranged from 60% to 81% following subcutaneous injection. Administration of ixekizumab via injection in the thigh achieved a higher bioavailability relative to that achieved using other injection sites including the arm and abdomen.

Distribution

The mean (geometric CV%) volume of distribution at steady-state was 7.11 L (29%) in subjects with plaque psoriasis.

Elimination

The metabolic pathway of ixekizumab has not been characterized. As a humanized IgG4 monoclonal antibody ixekizumab is expected to be degraded into small peptides and amino acids via catabolic pathways in the same manner as endogenous IgG.

The mean systemic clearance was 0.39 L/day (37%)and the mean (geometric CV%) half-life was 13 days (40%) in subjects with plaque psoriasis.

Weight

Ixekizumab clearance and volume of distribution increase as body weight increases.

Dose Linearity

Ixekizumab exhibited dose-proportional pharmacokinetics in subjects with plaque psoriasis over a dose range from 5 mg (not the recommended dose) to 160 mg following subcutaneous administration.

Specific Populations

Age: Geriatric Population

Population pharmacokinetic analysis indicated that age did not significantly influence the clearance of ixekizumab in adult subjects with plaque psoriasis. Subjects who are 65 years or older had a similar ixekizumab clearance as compared to subjects less than 65 years old.

Renal or Hepatic Impairment

No formal trial of the effect of hepatic or renal impairment on the pharmacokinetics of ixekizumab was conducted.

Drug Interaction Studies

Drug interaction studies have not been conducted with TALTZ.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Animal studies have not been conducted to evaluate the carcinogenic or mutagenic potential of TALTZ. Moreover published literature is mixed on potential effects on malignancy risk due to the inhibition of IL-17A activity, the pharmacological action of TALTZ. Some published literature suggests that IL-17A directly promotes cancer cell invasion, suggesting a potential beneficial effect by TALTZ, whereas other reports indicate IL-17A promotes T-cell mediated tumor rejection, suggesting a potential adverse effect by TALTZ. However, neutralization of IL-17A with TALTZ has not been studied in these models. Depletion of IL-17A with a neutralizing antibody inhibited tumor development in mice, suggesting a potential beneficial effect by TALTZ. The relevance of experimental findings in mouse models for malignancy risk in humans is unknown.

No effects on fertility parameters such as reproductive organs, menstrual cycle length, or sperm analysis were observed in sexually mature cynomolgus monkeys that were administered ixekizumab for 13 weeks at a subcutaneous dose of 50 mg/kg/week (19 times the MRHD on a mg/kg basis). The monkeys were not mated to evaluate fertility.

14 CLINICAL STUDIES

Three multicenter, randomized, double-blind, placebo-controlled trials (Trials 1, 2, and 3) enrolled a total of 3866 subjects 18 years of age and older with plaque psoriasis who had a minimum body surface area involvement of 10%, a static Physician Global Assessment (sPGA) score of ≥3 in the overall assessment (plaque thickness/induration, erythema, and scaling) of psoriasis on a severity scale of 0 to 5, a Psoriasis Area and Severity Index (PASI) score ≥12, and who were candidates for phototherapy or systemic therapy.

In all three trials, subjects were randomized to either placebo or TALTZ (80 mg every two weeks [Q2W]) for 12 weeks, following a 160 mg starting dose. In the two active comparator trials (Trials 2 and 3), subjects were also randomized to receive U.S. approved etanercept 50 mg twice weekly for 12 weeks.

All three trials assessed the changes from baseline to Week 12 in the two co-primary endpoints: 1) PASI 75, the proportion of subjects who achieved at least a 75% reduction in the PASI composite score that takes into consideration both the percentage of body surface area affected and the nature and severity of psoriatic changes (induration, erythema and scaling) within the affected regions, and 2) sPGA of “0” (clear) or “1” (minimal), the proportion of subjects with an sPGA 0 or 1 and at least a 2-point improvement.

Other evaluated outcomes included the proportion of subjects with an sPGA score of 0 (clear), a reduction of at least 90% in PASI (PASI 90), a reduction of 100% in PASI (PASI 100), and an improvement of itch severity as measured by a reduction of at least 4 points on an 11-point itch Numeric Rating Scale.

Subjects in all treatment groups had a median baseline PASI score ranging from approximately 17 to 18. Baseline sPGA score was severe or very severe in 51% of subjects in Trial 1, 50% in Trial 2, and 48% in Trial 3.

Of all subjects, 44% had received prior phototherapy, 49% had received prior conventional systemic therapy, and 26% had received prior biologic therapy for the treatment of psoriasis. Of the subjects who had received prior biologic therapy, 15% had received at least one anti-TNF alpha agent, and 9% had received an anti-IL 12/IL23. A total of 23% of study subjects had a history of psoriatic arthritis.

Clinical Response at Week 12

The results of Trials 1, 2, and 3 are presented in Table 2.

Table 2: Efficacy Results at Week 12 in Adults with Plaque Psoriasis in Trials 1, 2, and 3; NRI[a]

	Trial 1		Trial 2		Trial 3	
	TALTZ 80 mg[c] Q2W (N=433) n (%)	**Placebo (N=431) n (%)**	**TALTZ 80 mg[c] Q2W (N=351) n (%)**	**Placebo (N=168) n (%)**	**TALTZ 80 mg[c] Q2W (N=385) n (%)**	**Placebo (N=193) n (%)**
sPGA of “0” (clear) or “1” (minimal)[b]	354 (82)	14 (3)	292 (83)	4 (2)	310 (81)	13 (7)
sPGA of “0” (clear)	160 (37)	0	147 (42)	1 (1)	155 (40)	0

PASI 75[b]	386 (89)	17 (4)	315 (90)	4 (2)	336 (87)	14 (7)
PASI 90	307 (71)	2 (1)	248 (71)	1 (1)	262 (68)	6 (3)
PASI 100	153 (35)	0	142 (40)	1 (1)	145 (38)	0

[a] Abbreviations: N = number of patients in the intent-to-treat population; NRI = Non-Responder Imputation.
[b] Co-primary endpoints.
[c] At Week 0, subjects received 160 mg of TALTZ.

Examination of age, gender, race, body weight, and previous treatment with a biologic did not identify differences in response to TALTZ among these subgroups at Week 12.

Subjects treated with TALTZ 80 mg Q2W experienced improvement in itch severity when compared to placebo at Week 12.

An integrated analysis of the U.S. sites in the two active comparator studies using U.S. approved etanercept, TALTZ demonstrated superiority to U.S. approved etanercept (50 mg twice weekly) on sPGA and PASI scores during the 12 week treatment period. The respective response rates for TALTZ 80 mg Q2W and U.S. approved etanercept 50 mg twice weekly were: sPGA of 0 or 1 (73% and 27%); PASI 75 (87% and 41%); sPGA of 0 (34% and 5%); PASI 90 (64% and 18%), and PASI 100 (34% and 4%).

Maintenance and Durability of Response

To evaluate the maintenance and durability of response, subjects originally randomized to TALTZ and who were responders at Week 12 (i.e., sPGA of 0 or 1) in Trial 1 and Trial 2 were re-randomized to an additional 48 weeks of either a maintenance dose of TALTZ 80 mg Q4W (every four weeks) or placebo. Non-responders (sPGA >1) at Week 12 and subjects who relapsed (sPGA ≥3) during the maintenance period were placed on TALTZ 80 mg Q4W.

For responders at Week 12, the percentage of subjects who maintained this response (sPGA 0 or 1) at Week 60 (48 weeks following re-randomization) in the integrated trials (Trial 1 and Trial 2) was higher for subjects treated with TALTZ 80 mg Q4W (75%) compared to those treated with placebo (7%).

For responders at Week 12 who were re-randomized to treatment withdrawal (i.e., placebo), the median time to relapse (sPGA ≥3) was 164 days in the integrated trials. Among these subjects, 66% regained a response of at least 0 or 1 on the sPGA within 12 weeks of restarting treatment with TALTZ 80 mg Q4W.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

TALTZ injection is a sterile, preservative free, clear and colorless to slightly yellow solution available in a single-dose prefilled autoinjector or a single-dose prefilled syringe to deliver 80 mg ixekizumab.

TALTZ is supplied as:

	Pack Size	NDC Code
Autoinjector		
80 mg single-dose	Carton of 1	0002-1445-11
80 mg single-dose	Carton of 2	0002-1445-27
80 mg single-dose	Carton of 3	0002-1445-09
Prefilled syringe		
80 mg single-dose	Carton of 1	0002-7724-11
80 mg single-dose	Carton of 2	0002-7724-27
80 mg single-dose	Carton of 3	0002-7724-09

16.2 Storage and Handling

TALTZ is sterile and preservative-free. Discard any unused portion.

- TALTZ must be protected from light until use.
- Store refrigerated at 2°C to 8°C (36°F to 46°F).
- Do not freeze. Do not use TALTZ if it has been frozen.
- Do not shake.
- Discard the TALTZ single-dose autoinjector or syringe after use in a puncture-resistant container.
- Not made with natural rubber latex.

17 PATIENT COUNSELING INFORMATION

Advise the patient and/or caregiver to read the FDA-approved patient labeling *(Medication Guide and Instructions for Use)* before the patient starts using TALTZ, and each time the prescription is renewed, as there may be new information they need to know.

Instructions on Self-Administration: Provide guidance to patients and caregivers on proper subcutaneous injection technique, including aseptic technique, and how to use the autoinjector or prefilled syringe correctly *[see Instructions for Use]*.

Infection: Inform patients that TALTZ may lower the ability of their immune system to fight infections. Instruct patients of the importance of communicating any history of infections to the healthcare provider, and contacting their healthcare provider if they develop any symptoms of infection *[see Warnings and Precautions (5.1)]*.

Allergic Reactions: Advise patients to seek immediate medical attention if they experience any symptoms of serious hypersensitivity reactions *[see Warnings and Precautions (5.3)]*.

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A6.01-TAL-0000-USPI-YYYYMMDD

Medication Guide
TALTZ™ (tȯl(t)s)
(ixekizumab)
injection, for subcutaneous use

What is the most important information I should know about TALTZ?

TALTZ is a medicine that affects your immune system. TALTZ may lower the ability of your immune system to fight infections and may increase your risk of infections, which can sometimes become serious.

- Your healthcare provider should check you for tuberculosis (TB) before you start treatment with TALTZ.
- Your healthcare provider may treat you with medicine for TB before you begin treatment with TALTZ if you have a past history of TB or have TB.
- Your healthcare provider should watch you closely for signs and symptoms of TB during and after treatment with TALTZ.

Before starting TALTZ, tell your healthcare provider if you:

- are being treated for an infection
- have an infection that does not go away or that keeps coming back
- have TB or have been in close contact with someone with TB
- think you have an infection or have symptoms of an infection such as:
  - fever, sweats, or chills
  - muscle aches
  - cough
  - shortness of breath
  - blood in your phlegm (mucus)
  - weight loss
  - warm, red, or painful skin or sores on your body
  - diarrhea or stomach pain
  - burning when you urinate or urinate more often than normal

After starting TALTZ, call your healthcare provider right away if you have any of the symptoms of infection listed above.

Do not use TALTZ if you have any symptoms of infection unless you are instructed to by your healthcare provider.
See **"What are the possible side effects of TALTZ?"** for more information about side effects.

What is TALTZ?

TALTZ is a prescription medicine used to treat adults:

- with moderate to severe plaque psoriasis, **and**
- who may benefit from taking injections or pills (systemic therapy) or phototherapy (treatment using ultraviolet or UV light)

It is not known if TALTZ is safe and effective in children under 18 years of age.

Do not use TALTZ if you have had a severe allergic reaction to ixekizumab or any of the other ingredients in TALTZ. See the end of this Medication Guide for a complete list of ingredients in TALTZ.

Before using TALTZ, tell your healthcare provider about all of your medical conditions, including if you:

- have any of the conditions or symptoms listed in the section **"What is the most important information I should know about TALTZ?"**
- have Crohn's disease or ulcerative colitis
- have recently received or are scheduled to receive an immunization (vaccine). You should avoid receiving live vaccines during treatment with TALTZ.
- are pregnant or plan to become pregnant. It is not known if TALTZ can harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if TALTZ passes into your breast milk.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How should I use TALTZ?

See the detailed "Instructions for Use" that comes with your TALTZ for information on how to prepare and inject a dose of TALTZ, and how to properly throw away (dispose of) used TALTZ autoinjectors and prefilled syringes.

- Use TALTZ exactly as prescribed by your healthcare provider.
- If your healthcare provider decides that you or a caregiver may give your injections of TALTZ at home, you should receive training on the right way to prepare and inject TALTZ. Do not try to inject TALTZ yourself, until you or your caregiver have been shown how to inject TALTZ.
- TALTZ comes in an autoinjector and a prefilled syringe that you or your caregiver may use at home to give injections. Your healthcare provider will decide which type of TALTZ is best for you to use at home.
- TALTZ is given as an injection under your skin (subcutaneous injection), in your thighs or stomach area (abdomen) by you or a caregiver. A caregiver may also give you an injection of TALTZ in the back of your arm.
- **Do not** give an injection in an area of the skin that is tender, bruised, red or hard, or in an area of skin that is affected by

psoriasis.
- Each TALTZ injection should be given at an alternate site. **Do not** use the 1 inch area around your navel (belly button).

If you forget to take your dose:
- Do not miss any doses of TALTZ unless your healthcare provider says it is okay. If you forget to take your TALTZ dose, inject a dose as soon as you remember. Then, take your next dose at your regular scheduled time.
- If you inject more TALTZ than prescribed, call your healthcare provider or go to the nearest emergency room right away.

What are the possible side effects of TALTZ?

TALTZ may cause serious side effects, including:

- **See "What is the most important information I should know about TALTZ?"**
- **Serious allergic reactions. If you have a severe allergic reaction, do not give another injection of TALTZ.**

Get emergency medical help right away if you get any of the following symptoms of a serious allergic reaction:
- o feel faint
- o swelling of your face, eyelids, lips, mouth, tongue, or throat
- o trouble breathing or throat tightness
- o chest tightness
- o skin rash

- **Crohn's disease or ulcerative colitis (Inflammatory bowel disease) can happen during treatment with TALTZ, including worsening symptoms**. Tell your healthcare provider if you have new or worsening symptoms of inflammatory bowel disease during treatment with TALTZ, including:
  - o stomach (abdomen) pain
  - o diarrhea with or without blood
  - o weight loss

The most common side effects of TALTZ include:
- injection site reactions
- upper respiratory infections
- nausea
- fungal infections

These are not all of the possible side effects of TALTZ. Tell your healthcare provider about any side effect that bothers you or that does not go away. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store TALTZ?
- Store TALTZ in the refrigerator between 36°F to 46°F (2°C to 8°C).
- Protect TALTZ from light.
- Do not freeze TALTZ. Do not use if TALTZ has been frozen.
- Do not shake TALTZ.

Keep TALTZ and all medicines out of the reach of children.

General information about the safe and effective use of TALTZ.
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use TALTZ for a condition for which it was not prescribed. Do not give TALTZ to other people, even if they have the same symptoms you have. It may harm them. You can ask your healthcare provider or pharmacist for information about TALTZ that is written for health professionals.

What are the ingredients in TALTZ?

Active ingredient: ixekizumab
Inactive ingredients: Citric Acid Anhydrous, Polysorbate 80, Sodium Chloride, Sodium Citrate Dihydrate, and Water for Injection
Not made with natural rubber latex.

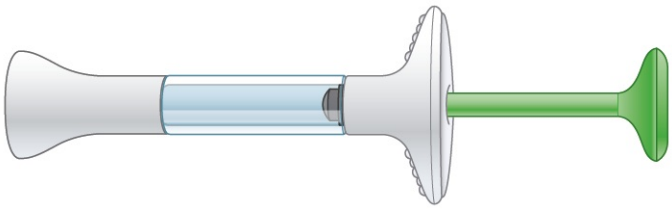
For more information about TALTZ, call 1-800-545-5979 (1-800-LillyRx) or go to the following website: www.taltz.com.

A3.01-TAL-0000-MG-YYYMMDD

This Medication Guide has been approved by the U.S. Food and Drug Administration. Issued: March 2016

INSTRUCTIONS FOR USE

TALTZ™ (tȯl(t)s)
(ixekizumab)
injection, for subcutaneous use
Prefilled Syringe



Lilly

Before you use the TALTZ prefilled syringe, read and carefully follow all the step-by-step instructions.

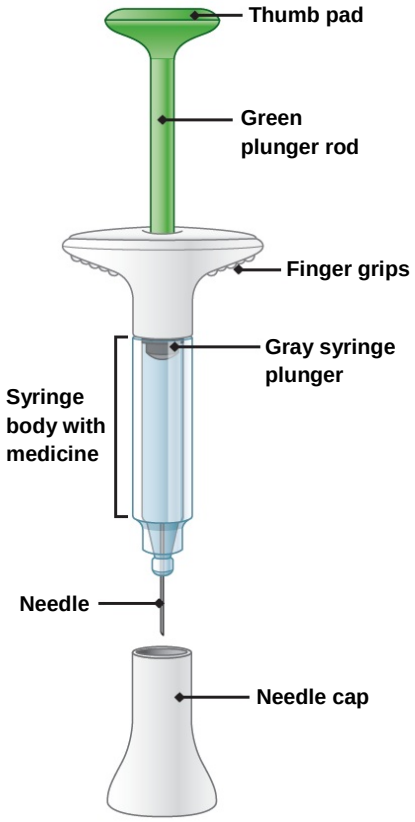
Important information:

- Your healthcare provider or nurse should show you how to prepare and inject TALTZ using the prefilled syringe. Do not inject yourself or someone else until you have been shown how to inject TALTZ.
- You and your caregiver should read this Instructions for Use before you start using TALTZ and each time you get a refill. Keep the Instructions for Use and refer to them as needed.
- Each TALTZ prefilled syringe contains 1 dose of TALTZ. **The syringe is for one-time use only. Do not** share or reuse your TALTZ prefilled syringe. You may give or get an infection.
- Your healthcare provider may help you decide where on your body to inject your dose. **Do not** give an injection in an area of the skin that is tender, bruised, red or hard, or in an area of skin that is affected by psoriasis. Read the **"Choose your injection site"** section of these instructions to help you choose which area can work best for you.
- If you have vision problems, **do not** use TALTZ prefilled syringe without help from a caregiver.

INSTRUCTIONS FOR USE

Before you use the TALTZ prefilled syringe, read and carefully follow all the step-by-step instructions.

Parts of the TALTZ prefilled syringe



1 Get Ready

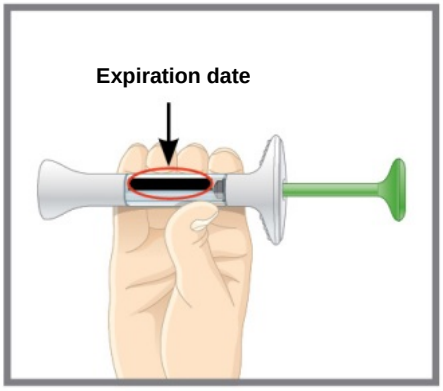
1a

- **Take the TALTZ prefilled syringe from the refrigerator.**
- Remove the prefilled syringe from the package. Put the original package with any unused syringes back in the refrigerator.
- **Wait 30 minutes** to let the prefilled syringe warm to room temperature before you use it.
- **Do not** microwave the syringe, run hot water over it, or leave it in direct sunlight.
- **Do not** shake the prefilled syringe.

1b Gather the supplies needed for your injection:

- 1 alcohol wipe
- 1 cotton ball or piece of gauze
- 1 sharps disposal container. See **"Dispose of the used prefilled syringe."**

1c



Inspect the syringe. Do not uncap the syringe until you are ready to inject.

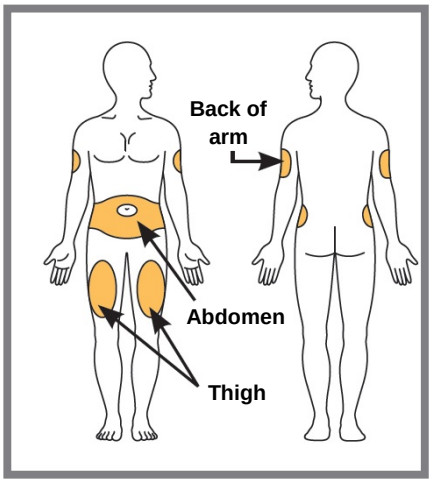
- Make sure the name **TALTZ** appears on the label.
- The medicine inside should be clear. Its color may be colorless to slightly yellow.

Do not use the prefilled syringe, and dispose of as directed by your healthcare provider or pharmacist if:

- the expiration date printed on the label has passed.
- it looks damaged.
- the medicine is frozen.
- the medicine is cloudy, discolored, or has small particles. The medicine should look clear and colorless to slightly yellow.

1d **Wash your hands with soap and water before you inject TALTZ.**

1e



Choose your injection site.

You may inject in your stomach area (abdomen) or in your thigh, or in the back of your arm. To inject in your arm, you will need someone to help you.

Do not give an injection into areas where the skin is tender, bruised, red or hard, or in an area of skin that is affected by psoriasis.

Do not inject within 1 inch of the navel (belly button).

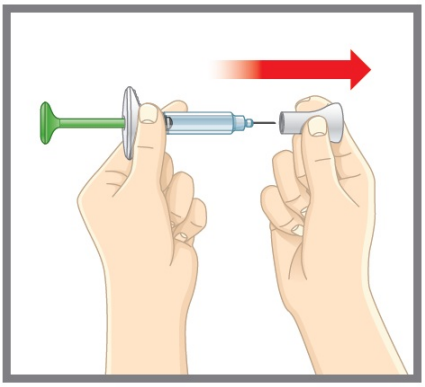
Alternate your injection sites.

- **Do not** inject in the exact same spot every time. For example, if your last injection was in your left thigh, your next injection should be in your right thigh, your abdomen, or the back of either arm.
- Talk with your healthcare provider about where on your body to best inject TALTZ.

1f **Prepare your skin.** Clean your injection site with an alcohol wipe. Let the injection site dry before you inject TALTZ.

2 Inject TALTZ

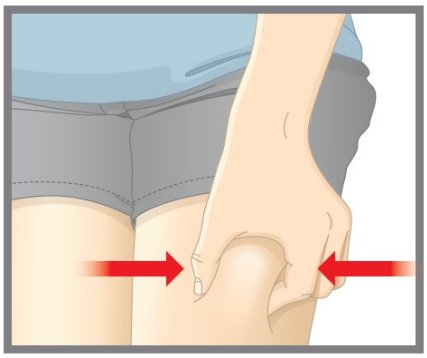
2a



Pull the needle cap off and throw it away.

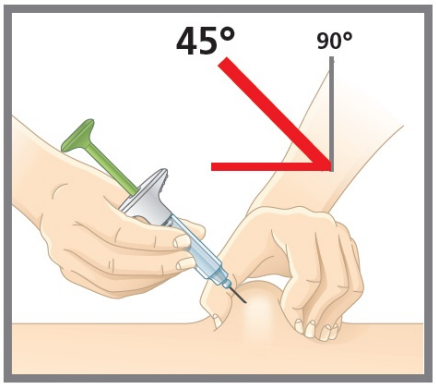
- **Do not** put the needle cap back on. You could damage the needle or stick yourself by accident.
- **Do not** touch the needle.

2b

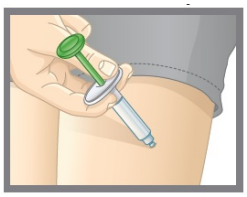


Gently pinch and hold a fold of skin where you will inject.

2c

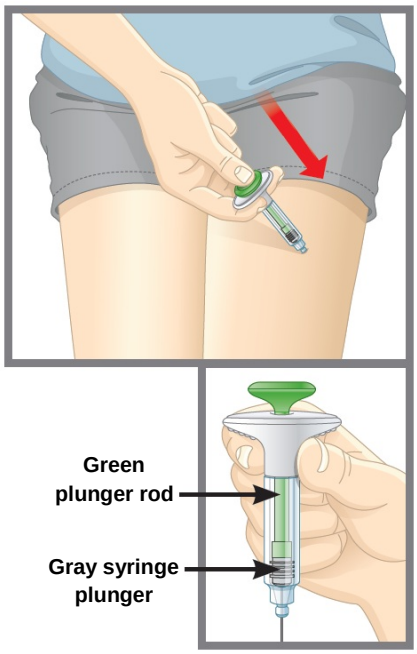


Insert the needle at a 45-degree angle. Then gently let go of your skin. Make sure to keep the needle in place.



Let go of your skin before you push the plunger in.

2d



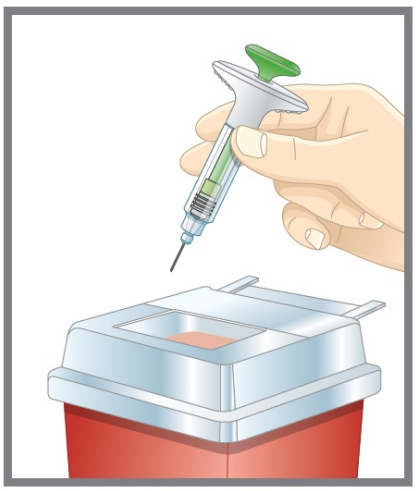
Push in the plunger.

- Slowly push on the thumb pad to push the plunger all the way in until all the medicine is injected.
- The gray syringe plunger should be pushed all the way to the needle end of the syringe.
- **You should see the green plunger rod show through the syringe body when the injection is complete.**
- Gently remove the needle from your skin.
- Press a cotton ball or gauze over the injection site. **Do not** rub the injection site, as this may cause bruising. You may have slight bleeding. This is normal.

Do not put the needle cap back on the prefilled syringe.

3 Dispose of the used prefilled syringe.

3a



Dispose of (throw away) the used prefilled syringe.

- Put the used TALTZ prefilled syringe in a FDA-cleared sharps disposal container right away after use. **Do not** throw away (dispose of) the TALTZ prefilled syringe in your household trash.

- If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
  - made of a heavy-duty plastic,
  - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
  - upright and stable during use,
  - leak-resistant, and
  - properly labeled to warn of hazardous waste inside the container.

- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away needles and syringes. For more information about safe sharps disposal, and for specific information about sharps disposal in the state you live in, go to the FDA's website at:

http://www.fda.gov/safesharpsdisposal

- **Do not** recycle your used sharps disposal container.

Commonly asked questions and answers.

Q. What if I see air bubbles in my TALTZ prefilled syringe?

A. It is normal to have air bubbles in the prefilled syringe.

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

A. It is okay to see a drop of liquid on the tip of the needle.

Q. What if I cannot push in the plunger?

A. If the plunger is stuck or damaged:

- **Do not** continue to use the syringe
- Remove the needle from your skin
- Dispose of the syringe and get a new one

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

A. When your injection is complete:

- The green plunger rod should show through the body of the syringe.
- The gray syringe plunger should be pushed all the way to the needle end of the syringe.

If you have more questions about how to use the TALTZ prefilled syringe:

- Call your healthcare provider
- Call Lilly at 1-800-545-5979 (1-800-Lilly-Rx)
- Visit www.taltz.com

How should I store TALTZ prefilled syringe?

- Store TALTZ in the refrigerator between 36°F to 46°F (2°C to 8°C).
- Protect TALTZ from light.
- Do not freeze TALTZ. Do not use if TALTZ has been frozen.
- Do not shake TALTZ.

Keep TALTZ and all medicines out of the reach of children.

Read the full Prescribing Information and Medication Guide for TALTZ inside this box to learn more about your medicine.

This Instructions for Use has been approved by the U.S. Food and Drug Administration.

Eli Lilly and Company
Indianapolis, IN 46285, USA
US License Number 1891
Product of Ireland

3.01-IXEPFS-0000-IFU-YYYYMMDD

Issued: March 2016

INSTRUCTIONS FOR USE

TALTZ™ (tȯl(t)s)
(ixekizumab)
injection, for subcutaneous use
Autoinjector

Before you use the TALTZ autoinjector, read and carefully follow all the step-by-step instructions.

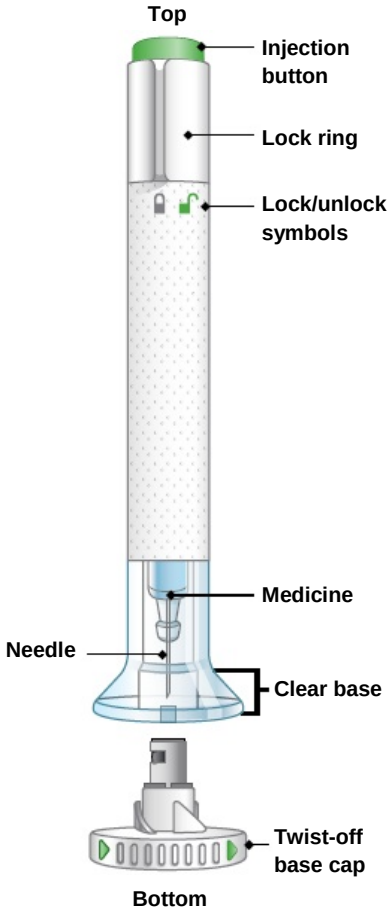
Important information:

- Your healthcare provider or nurse should show you how to prepare and inject TALTZ using the autoinjector. Do not inject yourself or someone else until you have been shown how to inject TALTZ.
- You and your caregiver should read this Instructions for Use before you start using TALTZ and each time you get a refill. Keep the Instructions for Use and refer to them as needed.
- Each TALTZ autoinjector contains 1 dose of TALTZ. **The autoinjector is for one-time use only.**
- The autoinjector contains glass parts. Handle autoinjector carefully. If you drop it on a hard surface, do not use it. Use a new TALTZ autoinjector for your injection.
- Your healthcare provider may help you decide where on your body to inject your dose. **Do not** give an injection in an area of the skin that is tender, bruised, red or hard, or in an area of skin that is affected by psoriasis. Read the **"Choose your injection site"** section of these instructions to help you choose which area can work best for you.
- If you have vision or hearing problems, **do not** use TALTZ autoinjector without help from a caregiver.

INSTRUCTIONS FOR USE

Before you use the TALTZ autoinjector, read and carefully follow all the step-by-step instructions.

Parts of the TALTZ autoinjector



1 Get Ready

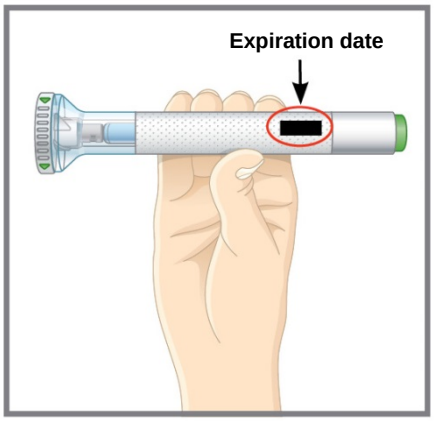
1a

- **Take the TALTZ autoinjector from the refrigerator.**
- Remove the autoinjector from the package. Put the original package with any unused autoinjectors back in the refrigerator.
- **Wait 30 minutes** to let the autoinjector warm to room temperature before you use it.
- **Do not** microwave the autoinjector, run hot water over it, or leave it in direct sunlight.
- **Do not** shake the autoinjector.

1b Gather the supplies needed for your injection:

- 1 alcohol wipe
- 1 cotton ball or piece of gauze
- 1 sharps disposal container. See **"Dispose of the used autoinjector."**

1c



Inspect the autoinjector.

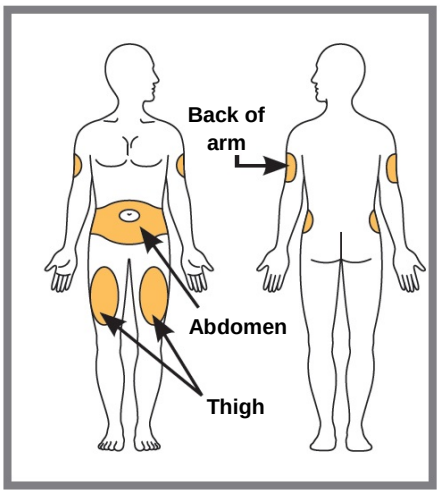
- Make sure the name **TALTZ** appears on the label.
- The medicine inside should be clear. Its color may be colorless to slightly yellow.

Do not use the autoinjector, and dispose of as directed by your healthcare provider or pharmacist if:

- the expiration date printed on the label has passed.
- it looks damaged.
- the medicine is frozen.
- the medicine is cloudy, discolored, or has small particles. The medicine should look clear and colorless to slightly yellow.

1d Wash your hands with soap and water before you inject TALTZ.

1e



Choose your injection site.

You may inject in your stomach area (abdomen) or in your thigh, or in the back of your arm. To inject in your arm, you will need someone to help you.

Do not give an injection into areas where the skin is tender, bruised, red or hard, or in an area of skin that is affected by psoriasis.

Do not inject within 1 inch of the navel (belly button).

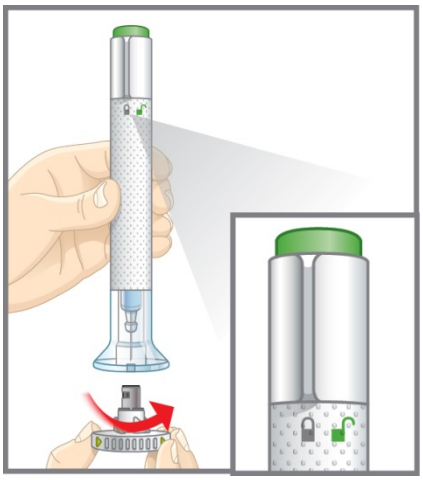
Alternate your injection sites.

- **Do not** inject in the exact same spot every time. For example, if your last injection was in your left thigh, your next injection should be in your right thigh, your abdomen, or the back of either arm.
- Talk with your healthcare provider about where on your body to best inject TALTZ.

1f Prepare your skin. Clean your injection site with an alcohol wipe. Let the injection site dry before you inject TALTZ.

2 Inject TALTZ

2a



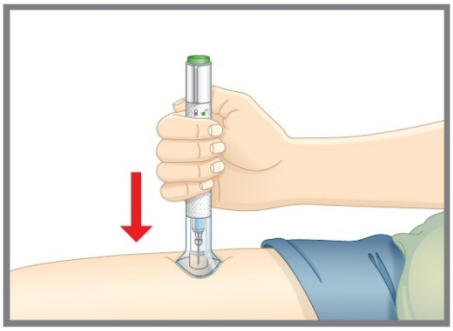
Make sure the lock ring is in the lock position.

- **Do not** remove the base cap until you are ready to inject.
- **Do not** touch the needle.

Twist off the base cap in the direction of the arrows.

- Throw the base cap in the trash. You will not need to put the base cap back on. If you do, you could damage the needle or stick yourself by accident.

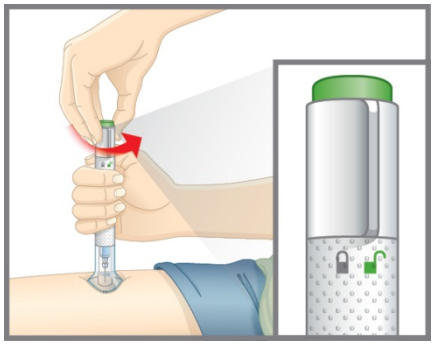
2b



Thigh injection

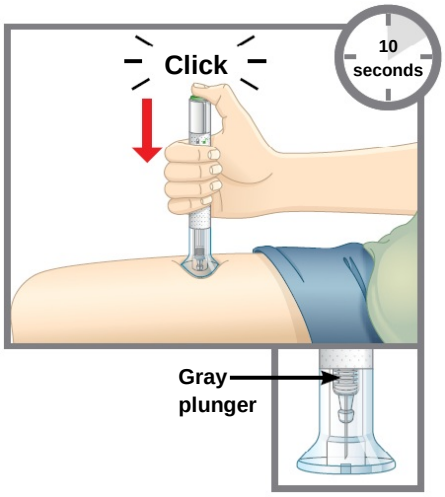
Place the clear base flat and firmly against your skin at the injection site.

2c



While holding the clear base against your skin, turn the lock ring to the unlock position. You are now ready to inject.

2d



Press the green injection button. There will be a loud click.

- **Keep holding the clear base** firmly against your skin.
- You will hear a **second click** in about 10 seconds after the first one. **The second click tells you that your injection is complete.**
- You will see the gray plunger at the top of the clear base.

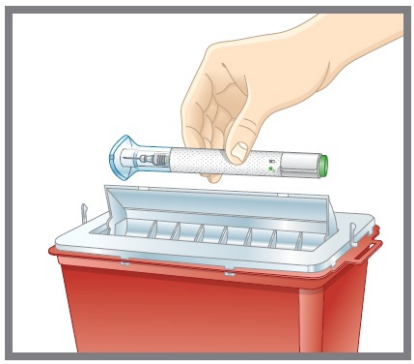
Remove the autoinjector from your skin.

- Press a cotton ball or gauze over the injection site. **Do not** rub the injection site, as this may cause bruising. You may have slight bleeding. This is normal.

Do not put the base cap back on the autoinjector.

3 Dispose of the used autoinjector.

3a



Dispose of (throw away) the used autoinjector.

- Put the used TALTZ autoinjector in a FDA-cleared sharps disposal container right away after use. **Do not** throw away (dispose of) the TALTZ autoinjector in your household trash.

- If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
  - made of a heavy-duty plastic,
  - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
  - upright and stable during use,
  - leak-resistant, and
  - properly labeled to warn of hazardous waste inside the container.

- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away needles and syringes. For more information about safe sharps disposal, and for specific information about sharps disposal in the state you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal

- **Do not** recycle your used sharps disposal container.

Commonly asked questions and answers.

Q. What if I see bubbles in the TALTZ autoinjector?

A. It is normal to have air bubbles in the autoinjector.

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

A. It is okay to see a drop of liquid on the tip of the needle.

Q. What if I unlocked the autoinjector and pressed the green injection button before I twisted off the base cap?

A. Do not remove the base cap. Dispose of the autoinjector and get a new one.

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

A. You do not need to hold the injection button down, but it may help you keep the autoinjector steady and firm against your skin.

Q. What if the needle did not retract after my injection or I am not sure that the autoinjector worked in the right way?

A. Do not touch the needle or replace the base cap. Store the autoinjector in a safe place (e.g., a household container as described in "**Dispose of the used autoinjector.**") to avoid an accidental needlestick and contact Lilly (1-800-545-5979) for instructions on how to return the autoinjector.

Q. What if I hear more than 2 clicks during my injection? Did I get my complete dose?

A. You may hear a soft click right before the second loud click. This is the normal operation of the autoinjector. Do not remove the autoinjector from your skin until you hear the second loud click.

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

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

If you have more questions about how to use the TALTZ autoinjector:

- Call your healthcare provider
- Call Lilly at 1-800-545-5979 (1-800-Lilly-Rx)
- Visit www.taltz.com

How should I store TALTZ autoinjector?

- Store TALTZ in the refrigerator between 36°F to 46°F (2°C to 8°C).
- Protect TALTZ from light.
- Do not freeze TALTZ. Do not use if TALTZ has been frozen.
- Do not shake TALTZ.

Keep TALTZ and all medicines out of the reach of children.

Read the full Prescribing Information and Medication Guide for TALTZ inside this box to learn more about your medicine.

This Instructions for Use has been approved by the U.S. Food and Drug Administration.

Eli Lilly and Company
Indianapolis, IN 46285, USA
US License Number 1891
Product of Ireland

The TALTZ autoinjector meets the current dose accuracy and functional requirements of ISO 11608-1 and 11608-5.

3.01-IXEAI-0000-IFU-YYYYMMDD

Issued: March 2016

packaging line Datamatrix code create using 10 mil with -2 X & Y barwidth reduction.

* If this is not possible due to country or regulatory requirements, place as close as possible to this area.

(b) (4)

Spot Glue-
Typ. 2 Places

1/8

R 2

3 2

45

45

open here

1 27/32

1/32

taltz™
(ixekizumab)
injection
80 mg/mL

1 Single-Dose
prefilled autoinjector

For Subcutaneous Use Only
Single-Dose Only

R 5/16

7/16

TE seal.
no ink
under
non-varnish
area

WS

NDC 0002-1445-11

Each prefilled autoinjector
contains 80 mg of TALTZ.

Rx Only

**Dispense enclosed Medication
Guide to each patient.**

Lilly

(b) (4)

taltz™
(ixekizumab)
injection
80 mg/mL

NDC 0002-1445-11

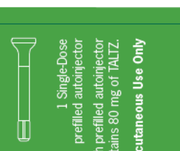
1 Single-Dose prefilled autoinjector
Each prefilled autoinjector contains 80 mg of TALTZ.
For Subcutaneous Use Only

R 7/16

1/32

taltz™
(ixekizumab)
injection
80 mg/mL

NDC 0002-1445-11



1 Single-Dose
prefilled autoinjector
Each prefilled autoinjector
contains 80 mg of TALTZ.
For Subcutaneous Use Only

taltz™
(ixekizumab)
injection
80 mg/mL

DO NOT FREEZE OR SHAKE
Store refrigerated at 2° to 8°C (36° to 46°F).
Protect from light.
Keep out of reach of children.
See package insert for dosing information.
Carton Contents:
1 Single-Dose prefilled autoinjector
Package Insert
Medication Guide
Instructions for Use

Each mL of TALTZ contains 80 mg ixekizumab; Citric Acid Anhydrous, USP (0.51 mg); Polysorbate 80, USP (0.3 mg); Sodium Chloride, USP (11.69 mg); Sodium Citrate Dihydrate, USP (5.11 mg); and Water for Injection, USP.

No preservative.
No U.S. standard of potency.
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Indianapolis, IN 46285, USA
US License Number 1891
Product of Ireland
www.taltz.com

Lilly

EPO
3 0002-1445-11 9

**PHARMACY
LABEL HERE**

<<<<< GRAIN >>>>>

1/32

1/8

1/4

45

taltz™
(ixekizumab)
injection
80 mg/mL

0.8268

If the seal is broken before
first use, contact pharmacist.

TE seal.
no ink
under
non-varnish
area

WS

EPO
NL02-4DAAM03

Imprint/Expires here

45

1/8 x 1/8
Perf-Typ. 4 Places

R 1/4

Reference ID: 3906227

Spot Glue-
Typ. 2 Places

1/8

R 21

1 1/32

1 1/32

3

0.5599

45

open here

45

1

R 5/16

TE seal.
no ink
under
non-varnish
area

taltz™
(ixekizumab)
injection
80 mg/mL

1 Single-Dose
prefilled syringe

For Subcutaneous Use Only
Single-Dose Only

NDC 0002-7724-11

Each prefilled syringe
contains 80 mg of TALTZ.

Rx Only

**Dispense enclosed Medication
Guide to each patient.**

Lilly

1/32

taltz™
(ixekizumab)
injection
80 mg/mL

NDC 0002-7724-11

1 Single-Dose prefilled syringe
Each prefilled syringe contains 80 mg of TALTZ.
For Subcutaneous Use Only

DO NOT FREEZE OR SHAKE
Store refrigerated at 2° to 8°C (36° to 46°F).
Protect from light.
Keep out of reach of children.
See package insert for dosing information.
Carton Contents:
1 Single-Dose prefilled syringe
Package Insert
Medication Guide
Instructions for Use
Each mL of TALTZ contains 80 mg ixekizumab; Citric Acid Anhydrous, USP (0.51 mg); Polysorbate 80, USP (0.3 mg); Sodium Chloride, USP (11.69 mg); Sodium Citrate Dihydrate, USP (5.11 mg); and Water for Injection, USP.

No preservative.
No U.S. standard of potency.
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www.taltz.com

Lilly

3 0002-7724-11 9

**PHARMACY
LABEL HERE**

taltz™
(ixekizumab)
injection
80 mg/mL

NDC 0002-7724-11

1 Single-Dose prefilled syringe
Each prefilled syringe contains 80 mg of TALTZ.
For Subcutaneous Use Only

1/32

1/4

1/8

GRAIN

taltz™ (ixekizumab) injection **80 mg/mL**

TE seal. no ink under non-varnish area

If the seal is broken before first use, contact pharmacist.

Lot/Exp: imprint legend goes here

NL027DAAM03

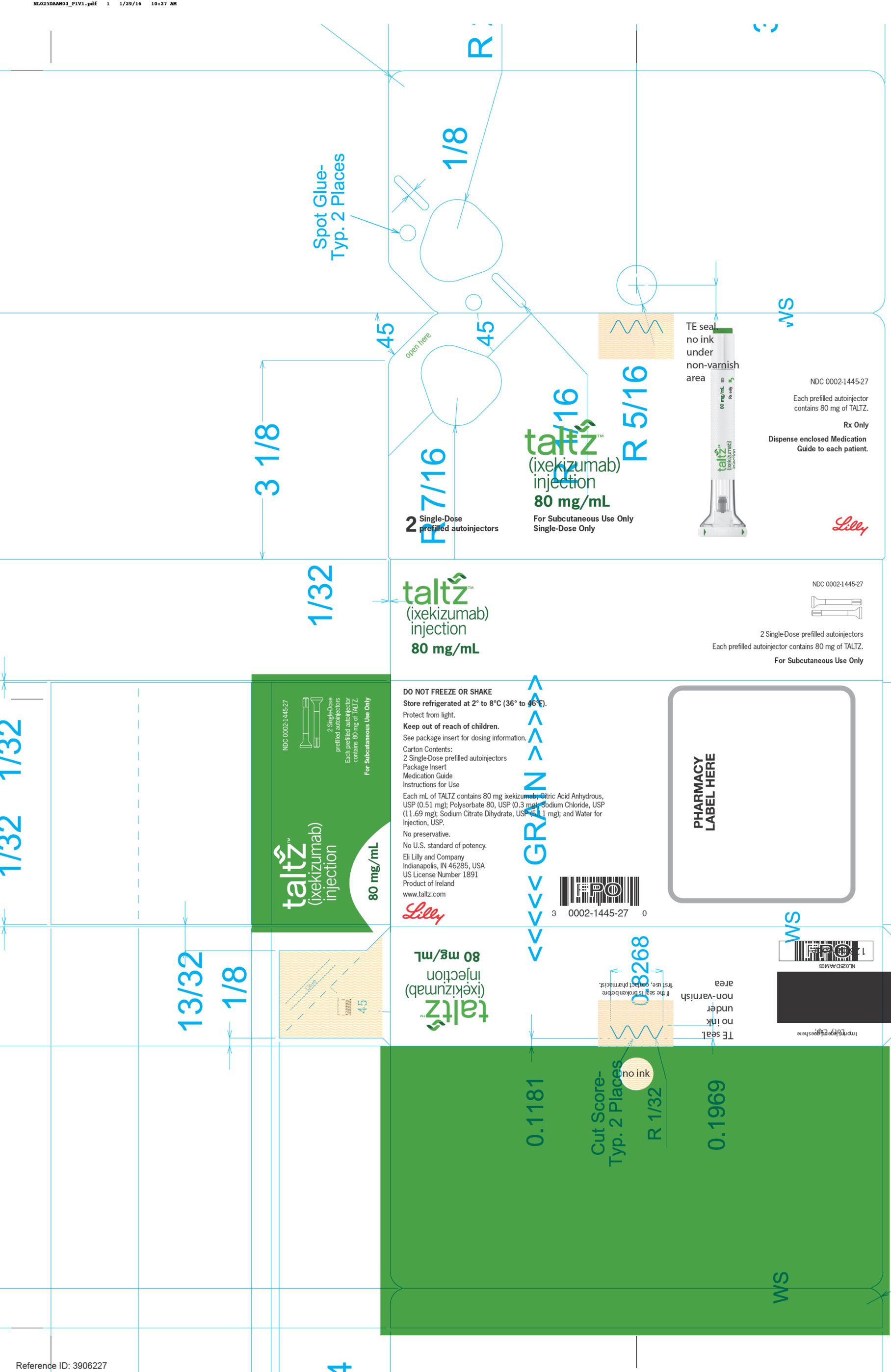
45

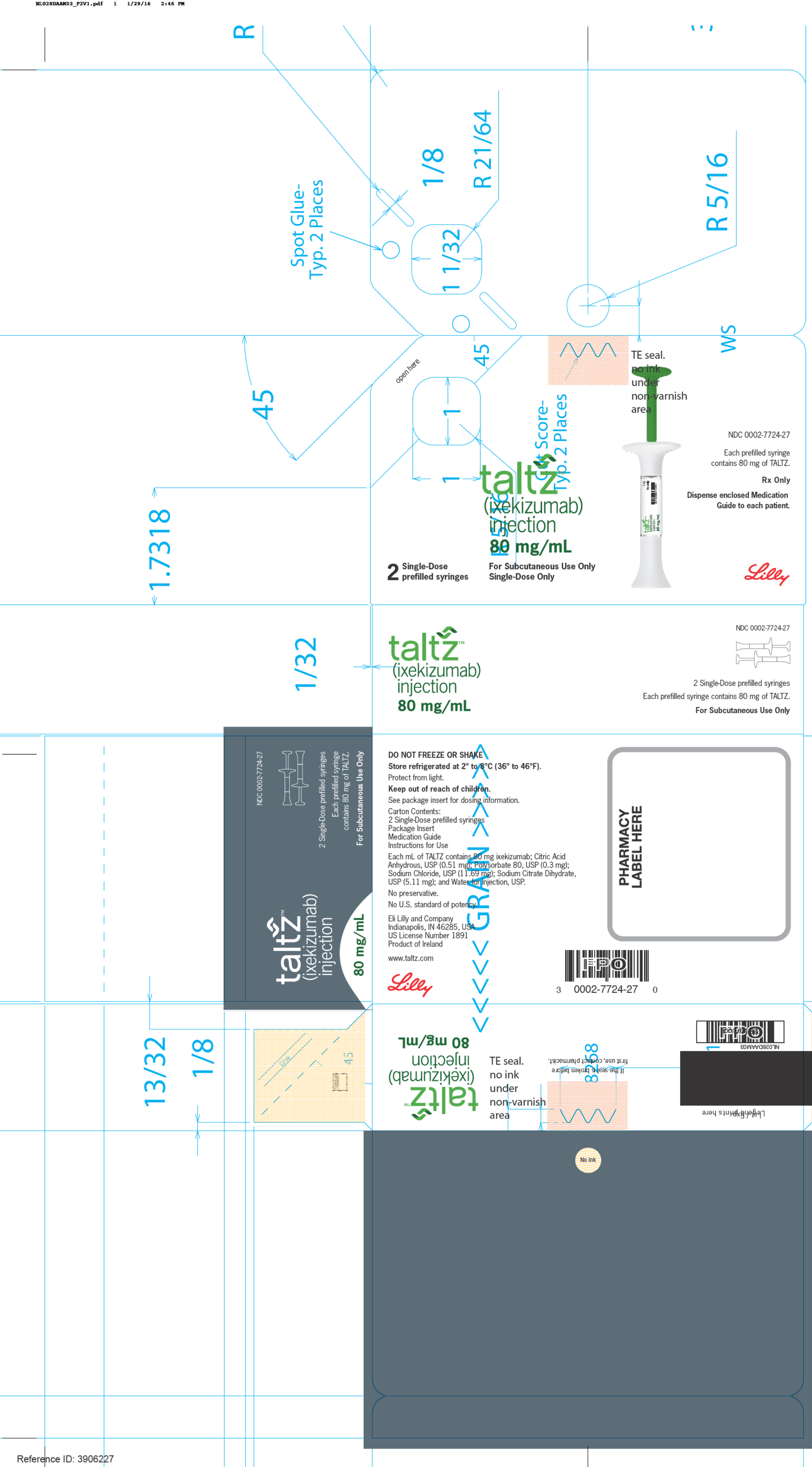
45

no ink

R 1/4

1/8 x 1/8
Perf-Typ. 4 Places





DO NOT FREEZE OR SHAKE
Store refrigerated at 2° to 8°C (36° to 46°F).
Protect from light.
Keep out of reach of children.
See package insert for dosing information.

Carton Contents:
2 Single-Dose prefilled syringes
Package Insert
Medication Guide
Instructions for Use

Each mL of TALTZ contains 80 mg ixekizumab; Citric Acid Anhydrous, USP (0.51 mg); Polysorbate 80, USP (0.3 mg); Sodium Chloride, USP (11.69 mg); Sodium Citrate Dihydrate, USP (5.11 mg); and Water for Injection, USP.

No preservative.

No U.S. standard of potency.

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www.taltz.com

PHARMACY
LABEL HERE

3 0002-7724-27 0

Spot Glue-
Typ. 2 Places

R 29/64

1/8

45

open here

45

R 1/16

R 5/16

TE seal.
no ink
under
non-varnish
area

WS

taltz™
(ixekizumab)
injection
80 mg/mL

3 Single-Dose prefilled autoinjectors

For Subcutaneous Use Only
Single-Dose Only

R 7/16

2.9036

NDC 0002-1445-09

Each prefilled autoinjector contains 80 mg of TALTZ.

Rx Only

Dispense enclosed Medication Guide to each patient.

Lilly

(b) (4)

1/32

taltz™
(ixekizumab)
injection
80 mg/mL

NDC 0002-1445-09

3 Single-Dose prefilled autoinjectors
Each prefilled autoinjector contains 80 mg of TALTZ.

For Subcutaneous Use Only

1/32

1/32

NDC 0002-1445-09

3 Single-Dose prefilled autoinjectors
Each prefilled autoinjector contains 80 mg of TALTZ.

For Subcutaneous Use Only

taltz™
(ixekizumab)
injection
80 mg/mL

DO NOT FREEZE OR SHAKE

Store refrigerated at 2° to 8°C (36° to 46°F).

Protect from light.

Keep out of reach of children.

See package insert for dosing information.

Carton Contents:
3 Single-Dose prefilled autoinjectors
Package Insert
Medication Guide
Instructions for Use

Each mL of TALTZ contains 80 mg ixekizumab; Citric Acid Anhydrous, USP (0.51 mg); Polysorbate 80, USP (0.3 mg); Sodium Chloride, USP (11.69 mg); Sodium Citrate Dihydrate, USP (5.11 mg); and Water for Injection, USP.

No preservative.

No U.S. standard of potency.

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Product of Ireland

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Lilly

<<<<< CUT AGAIN >>>>>

PHARMACY
LABEL HERE

Score-
Typ. 2 Places

FPO

3 0002-1445-09 6

13/32

1/8

45

taltz™
(ixekizumab)
injection
80 mg/mL

TE seal.
no ink
under
non-varnish
area

If the seal is broken before first use, contact pharmacist.

WS

FPO

NL026DAAM03

Lot / Exp:
Imprint legend goes here

45

1/8 x 1/8
Perf-Typ. 4 Places

1 3/4

0.1181

0.8260

0.1969

R 1/4

WS

Reference ID: 3906227

Reference ID: 3906227

13/32

1/8

3/4

1/32

2.9193

45

R

Spot Glue-
Typ. 2 Places

R 1/16

1 1/32

1/8

R 21/64

1 1/32

0.8268

0.1969

R 1/4

1/8 x 1/8
Perf-Typ. 4 Places

R 5/16

3 7

WS

taltz™
(ixekizumab)
injection

80 mg/mL

NDC 0002-7724-09

3 Single-Dose prefilled syringes

Each prefilled syringe contains 80 mg of TALTZ.

For Subcutaneous Use Only

PHARMACY
LABEL HERE

DO NOT FREEZE OR SHAKE

Store refrigerated at 2° to 8°C (36° to 46°F).

Protect from light.

Keep out of reach of children.

See package insert for dosing information.

Carton Contents:
3 Single-Dose prefilled syringes
Package Insert
Medication Guide
Instructions for Use

Each mL of TALTZ contains 80 mg ixekizumab; Citric Acid Anhydrous, USP (0.51 mg); Polysorbate 80, USP (0.51 mg); Sodium Chloride, USP (11.69 mg); Sodium Citrate Dihydrate, USP (5.11 mg); and Water for Injection, USP.

No preservative.

No U.S. standard of potency.

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www.taltz.com

<<<<GRAN>>>>

TE seal.
no ink
under
non-varnish
area

Lot

Exp

Peel tab here

3 Single-Dose prefilled syringes

For Subcutaneous Use Only
Single-Dose Only

Each prefilled syringe contains 80 mg of TALTZ.

Rx Only

Dispense enclosed Medication Guide to each patient.

NDC 0002-7724-09

Lilly

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/s/

JULIE G BEITZ
03/22/2016