

## FULL PRESCRIBING INFORMATION

### 1. NAME OF THE MEDICINAL PRODUCT ILUMYA

### 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each pre-filled syringe contains 100 mg of tildrakizumab in 1 mL.

For the full list of excipients, see section 11.

#### Excipient with known effect:

Each pre-filled syringe of Ilumya 100 mg contains 0.5 mg of polysorbate 80.

### 3. PHARMACEUTICAL FORM

Solution for injection (injection)

The solution is clear to slightly opalescent, colorless to slightly yellow solution.

### 4. CLINICAL PARTICULARS

#### 4.1 Therapeutic indications

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

### 5. DOSAGE AND ADMINISTRATION

#### **Dosage**

ILUMYA is intended for use under the guidance and supervision of a physician experienced in the diagnosis and treatment of plaque psoriasis.

#### Posology

The recommended dose of ILUMYA is 100 mg by subcutaneous injection at weeks 0, and 4 and every 12 weeks thereafter.

Consideration should be given to discontinuing treatment in patients who have shown no response after 28 weeks of treatment. Some patients with initial partial response may subsequently improve with continued treatment beyond 28 weeks.

#### Missed dose

If a dose is missed, the dose should be administered as soon as possible. Thereafter, dosing should be resumed at the regular scheduled time.

#### Special populations

##### *Elderly*

No dose adjustment is required [see 9.4].

##### *Renal or hepatic impairment*

ILUMYA has not been studied in these patient populations. No dose recommendations can be made. For further information on elimination of tildrakizumab, see 12.3.

### *Paediatric population*

The safety and efficacy of ILUMYA in children and adolescents below the age of 18 years have not yet been established. No data are available.

### **Preparation and Administration of ILUMYA**

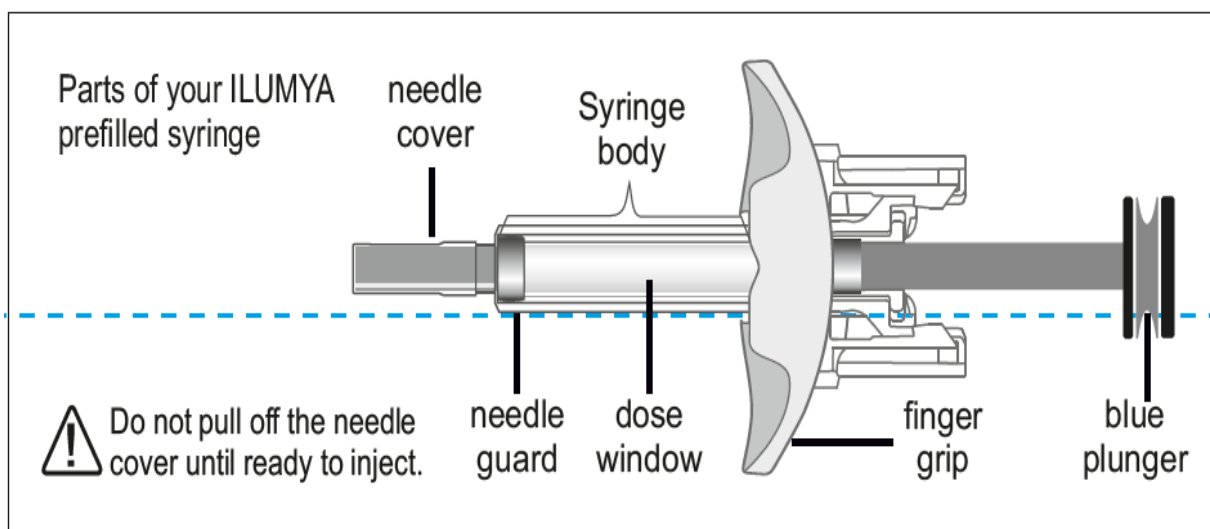
Before injection, remove ILUMYA carton from the refrigerator, and let the prefilled syringe (in the ILUMYA carton with the lid closed) sit at room temperature for 30 minutes. The prefilled syringe must not be shaken.

Follow the instructions on the ILUMYA leaflet to remove the prefilled syringe correctly, and remove only when ready to inject. Do not pull off the needle cover until you are ready to inject. Each pre-filled syringe is for single use only.

Inspect ILUMYA visually for particulate matter and discoloration prior to administration. ILUMYA is a clear to slightly opalescent, colorless to slightly yellow solution. Do not use if the liquid contains visible particles or the syringe is damaged. Air bubbles may be present; there is no need to remove them.

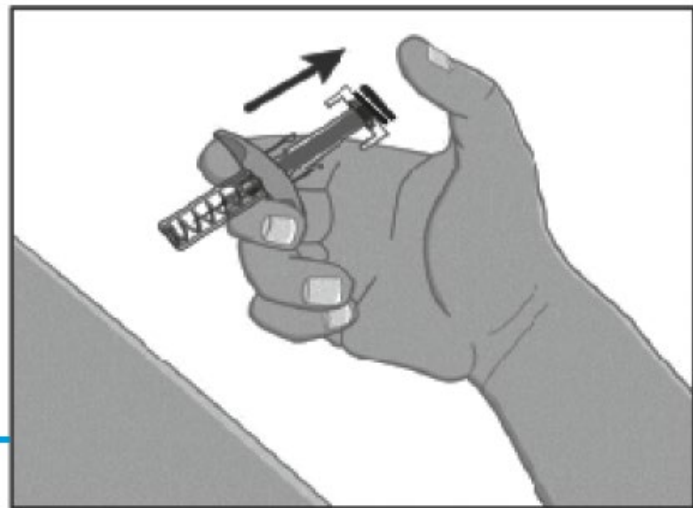
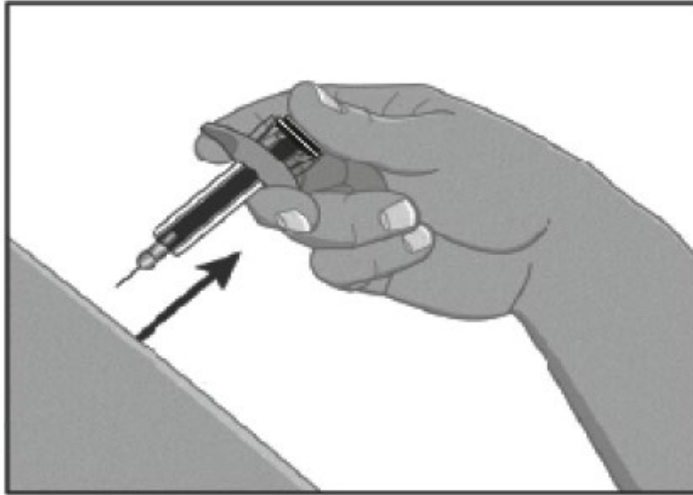
Choose an injection site with clear skin and easy access (such as abdomen, thighs, or upper arm). Injection sites should be alternated. Do not administer 2 inches around the navel or where the skin is tender, bruised, erythematous, indurated, or affected by psoriasis. Also do not inject into scars, stretch marks, or blood vessels.

After proper training in subcutaneous injection technique, patients may self-inject Ilumya if a physician determines that it is appropriate. However, the physician should ensure appropriate follow-up of patients. Patients should be instructed to inject the full amount of tildrakizumab according to the instructions provided in the package leaflet. Comprehensive instructions for administration are given in the package leaflet.



- While holding the body of the syringe, pull the needle cover straight off (do not twist) and discard.
- Inject ILUMYA subcutaneously as recommended [see Dosage (5)].
- Press down the blue plunger until it can go no further. This activates the safety mechanism that will ensure full retraction of the needle after the injection is given. Remove the needle

from the skin entirely before letting go of the blue plunger. After the blue plunger is released, the safety lock will draw the needle inside the needle guard.



- Discard any unused portion. Dispose of used syringe.

## 6. CONTRAINDICATIONS

ILUMYA is contraindicated in patients with a previous serious hypersensitivity reaction to tildrakizumab or to any of the excipients [see *Warnings and Precautions (7.1)*].

## 7. WARNINGS AND PRECAUTIONS

### 7.1 Hypersensitivity

Cases of angioedema and urticaria occurred in ILUMYA treated subjects in clinical trials. If a serious hypersensitivity reaction occurs, discontinue ILUMYA immediately and initiate appropriate therapy [see *Adverse Reactions (8)*].

### 7.2 Infections

ILUMYA may increase the risk of infection. Although infections were more common in the ILUMYA group (23%), the difference in frequency of infections between the ILUMYA group and the placebo group (22%) was less than 1% during the placebo-controlled period.

However, subjects with active infections or a history of recurrent infections were not included in clinical trials. Upper respiratory infections occurred more frequently in the ILUMYA group than in the placebo group [*see Adverse Reactions (8)*].

The rates of serious infections for the ILUMYA group and the placebo group were  $\leq 0.3\%$ . Treatment with ILUMYA should not be initiated in patients with any clinically important active infection until the infection resolves or is adequately treated.

In patients with a chronic infection or a history of recurrent infection, consider the risks and benefits prior to prescribing ILUMYA. Instruct patients to seek medical help if signs or symptoms of clinically important chronic or acute infection occur. If a patient develops a clinically important or serious infection or is not responding to standard therapy, monitor the patient closely and consider discontinuation of ILUMYA until the infection resolves [*see Adverse Reactions (8)*].

### **7.3 Pretreatment Evaluation for Tuberculosis**

Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with ILUMYA. Initiate treatment of latent TB prior to administering ILUMYA. In clinical trials, of 55 subjects with latent TB who were concurrently treated with ILUMYA and appropriate TB prophylaxis, no subjects developed active TB (during the mean follow-up of 56.5 weeks). One other subject developed TB while receiving ILUMYA. Monitor patients for signs and symptoms of active TB during and after ILUMYA treatment. Consider anti-TB therapy prior to initiation of ILUMYA in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Do not administer ILUMYA to patients with active TB infection.

### **7.4 Immunizations**

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

### **7.5 Excipients**

Ilumya contains 0.5 mg of polysorbate 80 in each pre-filled syringe of 100 mg, which is equivalent to 0.5mg/ml. Polysorbate may cause allergic reactions.

### **7.6 Traceability**

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

## **8. ADVERSE REACTIONS**

The following serious adverse reactions are discussed elsewhere in the labeling:

Hypersensitivity Reactions [*see Warnings and Precautions (7.1)*]

Infections [*see Warnings and Precautions (7.2)*]

### **Reporting of suspected adverse reactions**

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form <https://sideeffects.health.gov.il>

## 8.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying 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.

### Plaque Psoriasis

In clinical trials, a total of 1994 subjects with plaque psoriasis were treated with ILUMYA, of which 1083 subjects were treated with ILUMYA 100 mg. Of these, 672 subjects were exposed for at least 12 months, 587 for 18 months, and 469 for 24 months.

Data from three placebo-controlled trials (Trials 1, 2, and 3) in 705 subjects (mean age 46 years, 71% males, 81% white) were pooled to evaluate the safety of ILUMYA (100 mg administered subcutaneously at Weeks 0 and 4, followed by every 12 weeks [Q12W]) [*see Clinical Studies (14)*].

*Placebo-Controlled Period (Weeks 0-16 of Trial 1 and Weeks 0-12 of Trials 2 and 3)*  
Table 1 summarizes the adverse reactions that occurred at a rate of at least 1% and at a higher rate in the ILUMYA group than in the placebo group.

**Table 1: Adverse Reactions Occurring in  $\geq 1\%$  of Subjects in the ILUMYA Group and More Frequently than in the Placebo Group in the Plaque Psoriasis Trials 1, 2, and 3**

Adverse Reaction	ILUMYA 100 mg (N=705) N (%)	Placebo (N=355) N (%)
Upper respiratory infections*	98 (14)	41 (12)
Injection site reactions <sup>†</sup>	24 (3)	7 (2)
Diarrhea	13 (2)	5 (1)

\* Upper respiratory infections include nasopharyngitis, upper respiratory tract infection, viral upper respiratory tract infection, and pharyngitis.

<sup>†</sup>Injection site reactions include injection site urticaria, pruritus, pain, reaction, erythema, inflammation, edema, swelling, bruising, hematoma, and hemorrhage.

Gastrointestinal disorders include gastroenteritis and nausea adverse reactions that occurred at rates more than 1%.

Nervous system disorders include headache adverse reactions that occurred at rates more than 1%.

Cases of back pain were also reported at rates more than 1%.

During the placebo-controlled period of Trials 1, 2, and 3, adverse reactions that occurred at rates less than 1% but greater than 0.1% in the ILUMYA group and at a higher rate than in the placebo group included dizziness and pain in extremity.

Cases of angioedema and urticaria were reported in ILUMYA-treated subjects in clinical trials.

*Safety through Week 52/64*

Through Week 52 (Trials 1 and 3) and Week 64 (Trial 2), no new adverse reactions were identified with ILUMYA use and the frequency of the adverse reactions was similar to that observed during the placebo-controlled period.

#### Psoriasis of the Scalp

The safety of ILUMYA was assessed in a multicenter, randomized, double-blind, placebo-controlled trial (Trial 4) in 231 subjects with psoriasis of the scalp [*see Clinical Studies (14)*]. No new safety signals were identified through follow-up to Week 72.

#### Psoriasis of the Nail

The safety of ILUMYA was assessed in a multicenter, randomized, double-blind, placebo controlled trial (Trial 5) in 99 subjects with psoriasis of the nail [*see Clinical Studies (14)*]. No new safety signals were identified through Week 28.

### **8.2 Immunogenicity**

The observed incidence of anti-drug antibodies is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of anti-drug antibodies in the studies described below with the incidence of anti-drug antibodies in other studies.

Up to Week 64, approximately 6.5% of subjects treated with ILUMYA 100 mg developed antibodies to tildrakizumab. Of the subjects who developed antibodies to tildrakizumab, approximately 40% (2.5% of all subjects receiving ILUMYA) had antibodies that were classified as neutralizing. Development of neutralizing antibodies to tildrakizumab was associated with lower serum tildrakizumab concentrations and reduced efficacy.

## **9. USE IN SPECIFIC POPULATIONS**

### **9.1 Pregnancy**

#### Risk Summary

Limited available data with ILUMYA use in pregnant women are insufficient to inform a drug associated risk of adverse developmental outcomes.

Monoclonal antibodies are actively transported across the placenta (see Clinical Considerations). An embryofetal developmental study conducted with tildrakizumab in pregnant monkeys revealed no treatment-related effects to the developing fetus when tildrakizumab was administered subcutaneously during organogenesis to near parturition at doses up to 159 times the maximum recommended human dose (MRHD). When dosing was continued until parturition, an increase in neonatal death was observed at 59 times the MRHD [*see Data below*]. The clinical significance of this nonclinical finding is unknown.

All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. The background risk of major birth defects and miscarriage for the indicated population is unknown.

#### Clinical Considerations

##### *Fetal/Neonatal Adverse Reactions*

Transport of endogenous IgG antibodies across the placenta increases as pregnancy progresses, and peaks during the third trimester. Therefore, ILUMYA may be present in infants exposed *in utero*. The potential clinical impact of tildrakizumab exposure in infants exposed *in utero* should be considered.

## Data

### *Animal Data*

In an embryofetal developmental study, subcutaneous doses up to 300 mg/kg tildrakizumab were administered to pregnant cynomolgus monkeys once every two weeks during organogenesis to gestation day 118 (22 days from parturition). No maternal or embryofetal toxicities were observed at doses up to 300 mg/kg (159 times the MRHD of 100 mg, based on AUC comparison). Tildrakizumab crossed the placenta in monkeys.

In a pre- and postnatal developmental study, subcutaneous doses up to 100 mg/kg tildrakizumab were administered to pregnant cynomolgus monkeys once every two weeks from gestation day 50 to parturition. Neonatal deaths occurred in the offspring of one control monkey, two monkeys at 10 mg/kg dose (6 times the MRHD based on AUC comparison), and four monkeys at 100 mg/kg dose (59 times the MRHD based on AUC comparison). The clinical significance of these nonclinical findings is unknown. No tildrakizumab-related adverse effects were noted in the remaining infants from birth through 6 months of age.

## **9.2 Lactation**

### Risk Summary

There are no data on the presence of tildrakizumab in human milk, the effects on the breastfed infant, or the effects on milk production. Human IgG is known to be present in human milk. Tildrakizumab was detected in the milk of monkeys [*see Data*].

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for ILUMYA and any potential adverse effects on the breastfed child from ILUMYA or from the underlying maternal condition.

## Data

### *Animal Data*

Tildrakizumab was detected in breast milk of monkeys in the pre- and postnatal developmental study described in 8.1. The mean tildrakizumab concentrations in milk were approximately 0.09 – 0.2% of that in serum on postpartum days 28 and 91.

## **9.3 Pediatric Use**

Safety and effectiveness of ILUMYA in pediatric patients (<18 years of age) have not been established.

## **9.4 Geriatric Use**

A total of 1083 subjects were exposed to ILUMYA 100 mg during Phase 2 and 3 trials. A total of 92 subjects were 65 years or older, and 17 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 responded 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, administer appropriate symptomatic treatment immediately, and contact Poison Control.

## **11. DESCRIPTION**

Tildrakizumab is a humanized IgG1/k monoclonal antibody that specifically binds to the p19 subunit of interleukin-23 (IL-23).

Tildrakizumab is produced in a recombinant Chinese hamster ovary (CHO) cell line and has an approximate molecular mass of 147 kilodaltons.

ILUMYA (tildrakizumab) injection, for subcutaneous use, is a sterile, clear to slightly opalescent, colorless to slightly yellow solution. ILUMYA is supplied in a single-dose prefilled syringe with a glass barrel and 29-gauge fixed, 1/2-inch needle.

The syringe is fitted with a passive needle guard and a needle cover.

Each 1 mL single-dose prefilled syringe contains 100 mg of tildrakizumab formulated in: sucrose, L-Histidine hydrochloride monohydrate, polysorbate 80, L-histidine and Water for Injections.

## 12. CLINICAL PHARMACOLOGY

### 12.1 Mechanism of Action

Tildrakizumab is a humanized IgG1/k monoclonal antibody that selectively binds to the p19 subunit of IL-23 and inhibits its interaction with the IL-23 receptor. IL-23 is a naturally occurring cytokine that is involved in inflammatory and immune responses. Tildrakizumab inhibits the release of proinflammatory cytokines and chemokines.

### 12.2 Pharmacodynamics

No formal pharmacodynamics studies have been conducted with ILUMYA.

### 12.3 Pharmacokinetics

Tildrakizumab pharmacokinetics increases proportionally over a dose range from 50 mg to 200 mg (0.5 to 2 times the approved recommended dosage) following subcutaneous administration in subjects with plaque psoriasis. Steady-state concentrations were achieved by Week 16 following subcutaneous administration of tildrakizumab at Weeks 0, 4, and every 12 weeks thereafter. At the 100 mg dose at Week 16, the mean ( $\pm$  SD) steady-state trough concentrations ranged from  $1.22 \pm 0.94$  mcg/mL to  $1.47 \pm 1.12$  mcg/mL. The geometric mean (CV%) steady-state  $C_{max}$  was 8.1 mcg/mL (34%).

#### Absorption

The absolute bioavailability of tildrakizumab was estimated to be 73-80% following subcutaneous injection. The peak concentration ( $C_{max}$ ) was reached by approximately 6 days.

#### Distribution

The geometric mean (CV%) volume of distribution is 10.8 L (24%).

#### Elimination

The geometric mean (CV%) systemic clearance was 0.32 L/day (38%) and the half-life was approximately 23 days (23%).

#### Metabolism

The metabolic pathway of tildrakizumab has not been characterized. As a humanized IgG1/k monoclonal antibody, tildrakizumab is expected to be degraded into small peptides and amino acids via catabolic pathways in a manner similar to endogenous IgG.

#### Specific Populations

No clinically significant differences in the pharmacokinetics of tildrakizumab were observed based on age ( $\geq 18$  years). No specific studies have been conducted to determine the effect of renal or hepatic impairment on the pharmacokinetics of tildrakizumab.

#### *Body Weight*

Tildrakizumab concentrations were lower in subjects with higher body weight.

#### Drug Interaction Studies

##### *Cytochrome P450 Substrates*

The AUC<sub>inf</sub> of dextromethorphan (CYP2D6 substrate) increased by 20% when used concomitantly with tildrakizumab 200 mg (two times the approved recommended dose) administered subcutaneously at Weeks 0 and 4 in subjects with plaque psoriasis. No clinically significant changes in AUC<sub>inf</sub> of caffeine (CYP1A2 substrate), warfarin (CYP2C9 substrate), omeprazole (CYP2C19 substrate), and midazolam (CYP3A4 substrate) were observed.

### **13. NONCLINICAL TOXICOLOGY**

#### **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

Animal studies have not been conducted to evaluate the carcinogenic or mutagenic potential of ILUMYA.

No effects on fertility parameters were observed in male or female cynomolgus monkeys that were administered tildrakizumab at subcutaneous or intravenous doses up to 140 mg/kg once every two weeks for 3 months (133 or 155 times the MRHD, respectively, based on AUC comparison). The monkeys were not mated to evaluate fertility.

### **14. CLINICAL STUDIES**

#### Plaque Psoriasis

In two multicenter, randomized, double-blind, placebo-controlled trials (Trial 2 [NCT01722331] and Trial 3 [NCT01729754]), 926 subjects were treated with ILUMYA 100 mg (N=616) or placebo (N=310). Subjects had a Physician Global Assessment (PGA) score of  $\geq 3$  (moderate) on a 5-point scale of overall disease severity, Psoriasis Area and Severity Index (PASI) score  $\geq 12$ , and a minimum body surface area (BSA) involvement of 10%. Subjects with guttate, erythrodermic, or pustular psoriasis were excluded.

In both trials, subjects were randomized to either placebo or ILUMYA (100 mg at Week 0, Week 4, and every twelve weeks thereafter [Q12W]) up to 64 weeks.

Trials 2 and 3 assessed the changes from baseline to Week 12 in the two co-primary endpoints:

- PASI 75, the proportion of subjects who achieved at least a 75% reduction in the PASI composite score.
- PGA of 0 (“cleared”) or 1 (“minimal”), the proportion of subjects with a PGA of 0 or 1 and at least a 2-point improvement.

Other evaluated outcomes in Trials 2 and 3 included the proportion of subjects who achieved a reduction from baseline in PASI score of at least 90% (PASI 90) and a reduction of 100% in PASI score (PASI 100) at Week 12 and maintenance of efficacy up to Week 64.

In both trials, subjects in the ILUMYA 100 mg and placebo treatment groups were predominantly men (69%) and White (80%), with a mean age of 46 years. At baseline, these subjects had a median affected BSA of 27%, a median PASI score of 17.8, and approximately 33% had a PGA score of 4 (“marked”) or 5 (“severe”). Approximately 34% had received prior phototherapy, 39% had received prior conventional systemic therapy, and 18% had received prior biologic therapy for the treatment of psoriasis. Approximately 16% of subjects had a history of psoriatic arthritis.

### Clinical Response at Week 12

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

**Table 2: Efficacy Results at Week 12 in Adults with Plaque Psoriasis in Trials 2 and 3 (NRI\*)**

	Trial 2 (NCT01722331)		Trial 3 (NCT01729754)	
	ILUMYA 100 mg (N=309) n (%)	Placebo (N=154) n (%)	ILUMYA 100 mg (N=307) n (%)	Placebo (N=156) n (%)
<b>PGA of 0 or 1<sup>†,‡</sup></b>	179 (58)	11 (7)	168 (55)	7 (4)
<b>PASI 75</b>	197 (64)	9 (6)	188 (61)	9 (6)
<b>PASI 90</b>	107 (35)	4 (3)	119 (39)	2 (1)
<b>PASI 100</b>	43 (14)	2 (1)	38 (12)	0 (0)

\* NRI = Non-Responder Imputation

† Co-Primary Endpoints

‡ PGA score of 0 (“cleared”) or 1 (“minimal”)

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

### *Maintenance of Response and Durability of Response*

In Trial 2, subjects originally randomized to ILUMYA and who were responders at Week 28 (i.e., PASI 75) were re-randomized to an additional 36 weeks of either maintaining the same dose of ILUMYA Q12W (every twelve weeks) or placebo.

At Week 28, 229 (74%) subjects treated with ILUMYA 100 mg were PASI 75 responders.

At Week 64, 84% of subjects who continued on ILUMYA 100 mg Q12W maintained PASI 75 compared to 22% of subjects who were re-randomized to placebo. In addition, for subjects who were re-randomized and also had a PGA score of 0 or 1 at Week 28, 69% of subjects who continued on ILUMYA 100 mg Q12W maintained this response (PGA 0 or 1) at Week 64 compared to 14% of subjects who were re-randomized to placebo.

For PASI 75 responders at Week 28 who were re-randomized to treatment withdrawal (i.e., placebo), the median time to loss of PASI 75 was approximately 20 weeks.

In addition, for subjects who were re-randomized to placebo and also had a PGA score of 0 or 1 at Week 28, the median time to loss of PGA score of 0 or 1 was approximately 16 weeks.

### Psoriasis of the Scalp

In a multicenter, randomized, double-blind, placebo-controlled trial (Trial 4 [NCT03897088]) 231 subjects with moderate to severe psoriasis of the scalp (IGA Scalp score of 3 or 4) were treated subcutaneously with ILUMYA 100 mg (n=117) or placebo (n=114) at Weeks 0 and 4. Of the 231 randomized subjects, 217 subjects completed Part 1 (Day 1 to Week 16). In Part 2 of the trial, subjects previously randomized to placebo were switched to ILUMYA 100 mg at Weeks 16, 20, 32, and 44, and those in the ILUMYA 100 mg arm continued to receive ILUMYA 100 mg at Weeks 16, 28, 40, and 52.

The trial population was 79% White, 8% Black or African American, 6% Asian, 3% Native Hawaiian or Other Pacific Islander, 2% American Indian or Alaska Native, and 2% Other; for ethnicity, 65% of subjects identified as Not Hispanic or Latino. The trial population was 60% male and the mean age was 45 years. At baseline, these subjects had a median affected scalp surface area of 50%, a median PASI score of 16.7, and IGA Scalp score of 3 (“moderate”) or 4 (“severe”) in 81% and 16%, respectively.

The primary endpoint was the proportion of subjects with IGA Scalp score of “clear” and “almost clear” with at least 2-point reduction from Baseline at Week 16.

Other evaluated outcomes included the proportion of subjects achieving a) Psoriasis Scalp Severity Index (PSSI) 90 ( $\geq 90\%$  improvement from Baseline in PSSI) at Week 16; b) PSSI 90 at Week 12; and c) IGA Scalp score of “clear” or “almost clear” with at least 2-point reduction from Baseline at Week 12.

The efficacy results from Trial 4 are presented in Table 3.

**Table 3: Efficacy Results for Primary and Secondary Endpoints in Subjects with Moderate to Severe Psoriasis of the Scalp in Trial 4 (mITT, NRI\*)**

	<b>Trial 4 (NCT03897088)</b>	
	<b>ILUMYA 100 mg (N=89) n (%)</b>	<b>Placebo (N=82) n (%)</b>
<b>Primary Endpoint</b>		
<b>IGA Scalp Response Rate for score 0 or 1 (clear or almost clear) at Week 16 with at least 2-point reduction from baseline score</b>	44 (49)	6 (7)
<b>Secondary Endpoints</b>		
<b>PSSI 90 Response Rate at Week 16</b>	54 (61)	4 (5)

<b>IGA Scalp Response Rate for score 0 or 1 (clear or almost clear) at Week 12 with at least 2-point reduction from baseline score</b>	41 (46)	4 (5)
<b>PSSI 90 Response Rate at Week 12</b>	43 (48)	2 (2)

Note: IGA = Investigator Global Assessment. PSSI = psoriasis scalp severity index.

\* NRI = Non-responder imputation; mITT = modified Intent-to-treat, all randomized subjects, excluding subjects enrolled early in the trial evaluated under a different IGA Scalp scale.

### Psoriasis of the Nail

In a randomized, multicenter, double-blind, placebo-controlled trial (Trial 5 [NCT03897075]), 99 subjects with moderate to severe psoriasis of the nail received subcutaneous ILUMYA 100 mg (N=51) or placebo (N=48) at Weeks 0, 4, and 16. Of the 99 randomized subjects, 78 subjects completed Part 1 (Day 1 to Week 28) of the trial.

The trial population was 79% White, 2% Black or African American, 15% Asian and 4% Other; for ethnicity, 62% of subjects identified as Not Hispanic or Latino. The trial population was 71% male and the mean age was 46 years. At baseline, these subjects had a median Modified Nail Psoriasis Severity Index (mNAPSI) score of 34 and a median PASI score of 16.

The primary endpoint was the proportion of subjects who achieved at least a 75% improvement from baseline in total mNAPSI at Week 28.

The efficacy results from Trial 5 are presented in Table 4.

**TABLE 4: Efficacy Results for the Modified Nail Psoriasis Severity Index in Subjects with Moderate to Severe Psoriasis of the Nail in Trial 5 (ITT, NRI\*)**

	Trial 5	
	ILUMYA 100mg N=51 n (%)	Placebo N=48 n (%)
<b>Proportion of subjects who achieve at least a 75% improvement from baseline in total mNAPSI at Week 28</b>	13 (26)	2 (4)

ITT = Intent to Treat.

mNAPSI = modified Nail Psoriasis Severity Index

\* NRI = Non-responder Imputation

## **15. HOW SUPPLIED/STORAGE AND HANDLING**

### **How Supplied**

ILUMYA (tildrakizumab) injection is a sterile, preservative-free, clear to slightly opalescent, colorless to slightly yellow solution.

ILUMYA is supplied as one single-dose prefilled syringe with safety device syringe barrel per carton that delivers 1 mL of a 100 mg/mL solution.

The safety device components include a needle guard, plunger rod and finger flange.

**Shelf life**

The expiry date of the product is indicated on the package materials.

**Storage and Handling**

Store refrigerated at 2°C to 8°C in the original carton to protect from light until the time of use. Do not freeze. Do not shake.

ILUMYA can be kept at room temperature at up to 25°C for up to 30 days in the original carton to protect from light. Once stored at room temperature, do not place back in the refrigerator. If not used within 30 days, discard ILUMYA. Do not store ILUMYA above 25°C.

**16. MANUFACTURER:**

Sun Pharmaceutical Industries Europe B.V.  
Polaris Avenue 87, 2132 JH Hoofddorp, The Netherlands

**17. MARKETING AUTHORISATION HOLDER**

Taro International Ltd.  
14 Hakitor St., Haifa Bay 2624761

**18. MARKETING AUTHORISATION NUMBER**

167-49-36455-00

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