▼This medicinal product is subject to additional monitoring in Australia. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at https://www.tga.gov.au/reporting-problems.

AUSTRALIAN PRODUCT INFORMATION

ILUMYA™

100 mg /1 mL solution for injection

(tildrakizumab)

1. NAME OF THE MEDICINE

Tildrakizumab (rch)

2. QUANTITATIVE AND QUALITATIVE COMPOSITION

The single-use pre-filled syringe contains 100 mg/mL of tildrakizumab.

Tildrakizumab is a humanised IgG1/k monoclonal antibody produced by recombinant DNA technology in a Chinese hamster ovary (CHO) cells.

For a full list of excipients, see section 6.1 LIST OF EXCIPIENTS.

3. PHARMACEUTICAL FORM

Solution for injection in a single-use pre-filled syringe.

The solution is clear to slightly opalescent and colourless to slightly yellow.

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.

4.2 DOSE AND METHOD OF ADMINISTRATION

ILUMYA is intended for use under the guidance and supervision of a physician experienced in the diagnosis and treatment of psoriasis. It is administered by subcutaneous injection.

Dosage:

Adults

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

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

Method of administration:

ILUMYA (1mL) is administered by subcutaneous injection. Full instructions for use are provided in the Consumer Medicine Information.

After proper training in subcutaneous injection technique, patients may self-inject ILUMYA if a healthcare professional determines that it is appropriate. However, the physician should ensure appropriate follow-up of patients.

Sites for injection include abdomen, thighs, or upper arm. Do not administer 5 cm around the navel or where the skin is tender, bruised, abnormally red, indurated or affected by psoriasis. Do not inject into scars, stretch marks, or blood vessels.

The pre-filled syringe should be visually inspected for particulate matter and discolouration prior to administration. Product exhibiting particulate matter or discolouration must not be used. Do not shake.

ILUMYA does not contain any antimicrobial preservatives. Discard any unused product remaining in the pre-filled syringe. ILUMYA pre-filled syringes are for single-use in one patient only.

Dosage adjustments in:

Renal or hepatic impairment

ILUMYA has not been studied in these patient populations. No dose recommendations can be made.

Elderly (≥ 65 years)

No dose adjustment is required (see section 5.2 PHARMACOKINETIC PROPERTIES**)**.

Paediatric population

The safety and efficacy of ILUMYA in children and adolescents under 18 years of age has not yet been evaluated.

4.3 CONTRAINDICATIONS

- Hypersensitivity to the active substance or to any of the excipients (see section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE and 6.1 LIST OF EXCIPIENTS).
- Clinically important active infection (e.g. active tuberculosis, see section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Infections

In clinical trials, there was no increased risk of infection in subjects treated with ILUMYA, however patients with active infections or a history of recurrent infections were not included in clinical trials. Caution should be exercised when considering the use of ILUMYA in patients with a chronic infection or a history of recurrent infection. If a patient develops a serious infection whilst on treatment with ILUMYA, the patient should be closely monitored.

ILUMYA must not be given to patients with active tuberculosis (TB).

Pre-treatment evaluation for tuberculosis

Prior to initiating treatment with ILUMYA, patients should be evaluated for tuberculosis (TB) infection. Patients receiving ILUMYA should be monitored for signs and symptoms of active TB during and after treatment. Anti-TB therapy should be considered prior to initiating ILUMYA in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed.

Hypersensitivity

Non-serious cases of urticaria occurred in ILUMYA-treated subjects in clinical trials. If a serious hypersensitivity reaction occurs, administration of ILUMYA should be discontinued immediately and appropriate therapy initiated.

Immunisations

Prior to initiating treatment with ILUMYA, consider completion of all appropriate immunisations according to current immunisation guidelines. If a patient has received live viral or bacterial vaccination it is recommended to wait at least 4 weeks prior to starting treatment with tildrakizumab. Patients treated with ILUMYA should not receive live vaccines during treatment and for at least 17 weeks after treatment (see section 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS).

Malignancy

In the initial placebo-controlled period of the Phase 2 and Phase 3 studies, a non-significant numerical imbalance between tildrakizumab-treated patients and those receiving placebo with malignancies was reported (see section 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)). As patients with prior or concurrent malignancy were excluded from the clinical trials, caution should be observed when treating patients with a history of malignancy or those who develop a malignancy during therapy.

Use in the elderly

See section 5.2 PHARMACOKINETIC PROPERTIES.

Paediatric Use

The safety and efficacy of ILUMYA in children and adolescents under 18 years of age has not yet been evaluated.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Live vaccines should not be given concurrently with ILUMYA (see section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

Results from a drug-drug interactions study conducted in psoriasis subjects suggest that ILUMYA had no clinically relevant effect on cytochrome p450 (CYP) enzymes CYP1A2, CYP2C9, CYP2C19, CYP2D6 and CYP3A4 (see section 5.2 PHARMACOKINETIC PROPERTIES – Drug interactions).

The safety of ILUMYA in combination with other immunomodulatory agents or phototherapy has not been evaluated.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on Fertility

The effect of ILUMYA on human fertility has not been evaluated.

The effects of tildrakizumab were not directly assessed in dedicated animal fertility studies. However, no effects on fertility parameters such as reproductive organs, menstrual cycle length, and/or hormones were observed in male and female cynomolgus monkeys that were administered tildrakizumab at up to 100 mg/kg by subcutaneous injections once every 14 days (>100 times the human exposure at the recommended dose based on AUC) for 9 months.

Use in Pregnancy (Category B1)

There is limited information regarding the use of ILUMYA in pregnant women. As a precautionary measure, it is preferable to avoid the use of ILUMYA during pregnancy. Women of childbearing potential should use an effective method of contraception during treatment and for at least 17 weeks after treatment.

Animal studies do not indicate direct or indirect harmful effect with respect to pregnancy, embryonic/fetal development, parturition or post-natal development. In a pre- and postnatal development toxicity study in monkeys given up to 100 mg/kg tildrakizumab by subcutaneous injections once every 14 days (>100 times the human exposure at the recommended dose), no related increase in pregnancy loss was observed.

Tildrakizumab was shown to distribute across the placental barrier. After repeated dosing to pregnant cynomolgus monkeys, serum concentrations were quantifiable in the fetus however the reproduction toxicity studies did not reveal any untoward effects. No harmful effects were noted in neonates at maternal exposures up to 19 times the human exposure at the recommended dose. Two neonatal deaths from monkeys administered tildrakizumab at maternal exposure of >100 times the human exposure at the recommended dose were attributed to possible viral infection and considered of uncertain relationship to the treatment. The clinical significance of these findings is unknown.

Use in Lactation

It is not known whether tildrakizumab is excreted in human milk. In a pre-/postnatal development study tildrakizumab was detected at low levels in breast milk in monkeys dosed with tildrakizumab from gestation day 50 to parturition. The milk/serum ratio was ≤0.002. In the same study, serum levels of tildrakizumab in infants up to 91 days old were similar to, or exceed maternal serum levels.

A decision should be made whether to discontinue breast-feeding or to discontinue ILUMYA taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

ILUMYA has no or negligible influence on the ability to drive and use machines.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

The most common adverse reactions observed with ILUMYA in the pooled data from one Phase 2 and two Phase 3 studies in psoriasis patients for the placebo controlled period (16 weeks for the Phase 2 study and 12 weeks for the Phase 3 studies) were nasopharyngitis, headache, and site injection pain.

Most adverse reactions were considered mild and no adverse reaction led to discontinuation of treatment in >1% of patients. For clinical management of specific adverse reactions, see section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE.

The frequency of adverse reactions is defined using the following convention: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); and not known (cannot be estimated from available data).

Table 1 provides a summary of the adverse reactions that were reported at a frequency of >1% and at a higher rate in the ILUMYA group than in the placebo group.

Table 1: Adverse reactions experienced at an incidence of ≥ 1% by patients treated with ILUMYA 100 mg during the placebo-controlled phase of the Phase 2 and Phase 3 studies

System organ class	Preferred term	Frequency category	Frequency	
			ILUMYA 100 mg (N=705) n (%)	Placebo (N=355) n (%)
Gastrointestinal disorders	Diarrhoea	Common	13 (1.8)	5 (1.4)
	Nausea	Common	7 (1.0)	3 (0.8)
General disorders and administration site conditions	Fatigue	Common	17 (2.4)	6 (1.7)
	Injection site pain	Common	10 (1.4)	3 (0.8)
Infections and infestations	Nasopharyngitis	Common	78 (11.1)	29 (8.2)
	Sinusitis	Common	11 (1.6)	5 (1.4)
Muscoskeletal and connective tissue disorders	Arthralgia	Common	15 (2.1)	7 (2.0)
	Back pain	Common	9 (1.3)	4 (1.1)
	Pain in extremity	Common	7 (1.0)	2 (0.6)

Immunogenicity

In the Phase 2 and Phase 3 psoriasis clinical studies 6.5% of patients treated continuously with ILUMYA 100 mg developed antibodies to ILUMYA. In the subset of these patients with treatment emergent neutralising antibodies, a small decrease in serum tildrakizumab concentrations and a corresponding increase in clearance was observed. Those patients who developed neutralising antibodies reported minor decreases in some efficacy parameters. No apparent association between the development of antibodies to ILUMYA and the development of treatment emergent adverse events was seen.

Hypersensitivity reactions

Non-serious cases of urticaria occurred in ILUMYA-treated subjects in clinical trials. If a serious hypersensitivity reaction occurs, administration of ILUMYA should be discontinued immediately and

appropriate therapy initiated. See section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE - Hypersensitivity.

Malignancy

In the initial placebo-controlled period of the Phase 2 and Phase 3 studies, a non-significant numerical imbalance in malignancy was reported between tildrakizumab-treated patients (0.2%) and those receiving placebo (0.0%). This imbalance was not observed in the controlled-data period (exposure-adjusted incidence rate of 1.2/100 patient years of exposure for tildrakizumab 100 mg, 1.7/100 patient years 200 mg, 2.6/100 patient years with etanercept, 0.9/100 patient years with placebo) or in the data collected in the open label extensions to the pivotal studies following up to 5 years of treatment (exposure adjusted rates of 0.7/100 patient with tildrakizumab 100 mg and 0.8/100 patient years with tildrakizumab 200 mg). The overall rate of malignancies reported with tildrakizumab across all studies was 0.422/100 patient years exposure (excluding non-melanoma skin cancer (NMSC)) and 0.348/100 patient years for non-melanoma skin cancer.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at http://www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

Intravenous doses up to 10 mg/kg have been safely administered in clinical trials.

In the event of overdose, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions and appropriate symptomatic treatment be instituted immediately.

For information on the management of overdose, contact the Poison Information Centre on 131 126 (Australia).

5. PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

The expression of mRNA for IL-23p19 is elevated in psoriatic lesions compared to normal skin. In exploratory studies in patients with psoriasis, inflammatory infiltrates were decreased in lesional tissue biopsies after dosing with tildrakizumab. A decrease in expression of IL-23p19 was observed in lesional skin biopsies measured at baseline and up to two weeks post-treatment. Gene expression patterns of inflammation were normalised following treatment with tildrakizumab.

Mechanism of Action

Tildrakizumab is a humanized IgG1/κ monoclonal antibody that specifically binds to the p19 protein subunit of the interleukin 23 (IL-23) cytokine and inhibits its interaction with the IL-23 receptor.

IL-23 is a naturally occurring cytokine composed of 2 subunits (IL-23p19 and IL-12/23p40), that is involved in inflammatory and immune responses. Tildrakizumab inhibits the release of proinflammatory cytokines and chemokines. In *in vitro* models, tildrakizumab was shown to disrupt IL-23 mediated signalling and cytokine cascades by disrupting the interaction of IL-23 binding to its specific receptor, IL-23R without binding to IL-12 (composed of 2 subunits IL-12p35 and IL-12/23p40).

Clinical Trials

The multicenter, randomized, double-blind, placebo-controlled trials reSURFACE 1 and reSURFACE 2 enrolled a total of 1862 patients 18 years of age and older with plaque psoriasis who had a minimum body surface area involvement of 10%, a Physician Global Assessment (PGA) score of ≥3 in the overall assessment (plaque thickness, 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 these studies, there was an initial 12 week placebo controlled period where patients were randomized to ILUMYA (including 100 mg and 200 mg at 0, 4 and every twelve weeks thereafter [Q12W]) or placebo. In the active comparator study (reSURFACE 2), patients were also randomized to receive etanercept 50 mg twice weekly for 12 weeks, and weekly thereafter up to 28 weeks. After the initial 12 week treatment period, patients previously receiving placebo were randomized to either 100 mg or 200 mg ILUMYA through week 28. After week 28, those patients receiving ILUMYA from week 0 were eligible for dosage adjustment based on PASI response. In reSURFACE 2, non-responding or partial-responding patients receiving etanercept were switched to ILUMYA 200 mg. The total treatment period was 52 or 64 weeks for the base studies, each study also incorporated an optional long-term extension phase.

Results obtained at Weeks 12, 28 and beyond (up to Week 64 in reSURFACE 1 and up to Week 52 in reSURFACE 2) are presented in **Table 2**.

Patients in all treatment groups (reSURFACE 1 and re SURFACE 2) had a median baseline PASI score ranging from 17.6 to 18.4. The baseline PGA score was marked or severe in 33.4% of patients. Of all patients enrolled, 35.8% had received prior phototherapy, 41.1% had received prior conventional systemic therapy, 16.7% had received prior biologic therapy for the treatment of psoriasis, and 7.7% had received at least one anti-TNF alpha agent. A total of 15.4% of study patients had a history of psoriatic arthritis. Baseline Dermatology Life Quality Index (DLQI) ranged from 13.2 to 14.8.

Studies reSURFACE 1 and reSURFACE 2 assessed the changes from baseline at Week 12 in the two co-primary endpoints: 1) PASI 75 and 2) PGA of "0" (cleared) or "1" (minimal), with at least a 2-point improvement from baseline. Other evaluated outcomes in reSURFACE 1 and reSURFACE 2 included the proportion of patients who achieved PASI 90 and PASI 100, the proportion of patients with DLQI 0 or 1, and maintenance of efficacy up to 64 weeks.

Examination of age, race, previous treatment with a biologic or traditional systemic therapy did not identify significant differences in PASI 75 response to ILUMYA 100 mg among these subgroups at Week 12.

Table 2: Summary of Response Rates in Studies reSURFACE 1 and reSURFACE 2

	Week 12 (2 doses)				Week 28 (3 doses)			Long term response [a]	
	100 mg	200 mg	Placebo	Etanercept	100 mg	200 mg	Etanercept	100 mg	200 mg
reSURFACE 1									
Number of patients	309	308	154	-	299	298	-	112	114
PASI 75[b], n (%)	197 (63.8) [†c]	192 (62.3) [†c]	9 (5.8) [c]	-	229 (80.4) [d]	236 (81.9) [d]	-	98 (87.5) [d]	107 (93.9) [d]
PGA of "clear" or "minimal" with ≥ 2 grade improvement from Baseline [b], n (%)	179 (57.9) [†c]	182 (59.1) [†c]	11 (7.1) [c]	-	188 (66.0) [d]	199 (69.1) [d]	-	69 (61.6) [d]	87 (76.3) [d]
PASI 90, n (%)	107 (34.6) [†c]	109 (35.4) [†c]	4 (2.6) [c]	-	147 (51.6) [d]	170 (59.0) [d]	-	65 (58.0) [d]	85 (74.6) [d]
PASI 100, n (%)	43 (13.9) [†c]	43 (14.0) [†c]	2 (1.3) [c]	-	67 (23.5) [d]	91 (31.5) [d]	-	36 (32.1) [d]	46 (40.4) [d]

	Week 12 (2 doses)				Week 28 (3 doses)			Long term response [a]	
	100 mg	**200 mg**	**Placebo**	**Etanercept**	**100 mg**	**200 mg**	**Etanercept**	**100 mg**	**200 mg**
DLQI Score 0 or 1, n (%)	126 (41.5) [†]	132 (44.2) [†]	8 (5.3)	-	152 (52.4) [d]	164 (56.7) [d]	-	59 (52.2) [d]	78 (68.4) [d]
reSURFACE 2									
Number of patients	307	314	156	313	294	299	289	204	105
PASI 75[b], n (%)	188 (61.2) [†‡c]	206 (65.6) [†‡c]	9 (5.8) [c]	151 (48.2) [c]	216 (73.5) [‡c]	217 (72.6) [‡c]	155 (53.6) [c]	191 (93.6) [d]	102 (97.1) [d]
PGA of "clear" or "minimal" with ≥ 2 grade improvement from Baseline [b], n (%)	168 (54.7) [†c]	186 (59.2) [†¥c]	7 (4.5) [c]	149 (47.6) [c]	190 (64.6) [‡c]	207 (69.2) [‡c]	131 (45.3) [c]	162 (79.4) [d]	89 (84.8) [d]
PASI 90, n (%)	119 (38.8) [†‡c]	115 (36.6) [†‡c]	2 (1.3) [c]	67 (21.4) [c]	161 (55.5) [‡d]	169 (57.7) [‡d]	85 (29.4) [d]	160 (78.4) [d]	86 (81.9) [d]
PASI 100, n (%)	38 (12.4) [†‡c]	37 (11.8) [†‡c]	0	15 (4.8) [c]	66 (22.8) [‡d]	79 (27.0) [‡d]	31 (10.7) [d]	72 (35.3) [d]	49 (46.7) [d]
DLQI Score 0 or 1, n (%)	119 (40.2) [†]	145 (47.4) [†¥]	12 (8.0)	108 (35.5)	157 (54.1) [‡d]	193 (65.0) [‡d]	111 (39.4) [d]	141 (68.8) [d]	76 (72.4) [d]

[a] Long-term response in patients who were responders (had achieved at least PASI 75) to ILUMYA at Week 28. (64 weeks in reSURFACE 1 and 52 weeks in reSURFACE 2)

[b] Co-primary efficacy endpoint at week 12.

[c] Non-responder imputation for missing data

[d] No imputation for missing data

n = number of patients in the full analysis set for which data was available, after imputation when applicable.

p-values calculated using the Cochran-Mantel-Haenszel (CMH) test stratified by body weight (≤90kg, >90kg) and prior exposure to biologic therapy for psoriasis (yes/no).

[†] p≤0.001 versus placebo; [‡] p≤0.001 versus etanercept; [¥] p≤0.05 versus etanercept.

Maintenance of Response

To evaluate the maintenance and durability of response, patients originally randomized to ILUMYA who were responders at Week 28 (i.e. had achieved PASI 75 response) in reSURFACE 1 were re-randomized to an additional 36 weeks of either maintaining the same dose of ILUMYA Q12W (every twelve weeks) or placebo.

Of the patients continuing with the same dose of ILUMYA, 87.5% of patients treated with ILUMYA 100 mg maintained PASI 75 response at week 64. Of the patients re-randomized to receive placebo, 49% of patients originally treated with 100 mg tildrakizumab maintained PASI 75 response at Week 64.

Retreatment after Relapse

In patients re-randomized to placebo in reSURFACE 1, 54.4% (who were originally treated with 100 mg) experienced relapse (defined as a reduction in maximum PASI response by 50%). These patients were restarted on their original dose of ILUMYA upon relapse. After a minimum of 12 weeks from re-initiation of therapy, over 85% had regained a PASI 75 response by Week 64.

Quality of Life/Patient-reported Outcomes

At Week 12 and across studies, ILUMYA was associated with statistically significant improvement in Health-related Quality of Life as assessed by the Dermatology Life Quality Index (DLQI). The proportion of patients treated with ILUMYA who achieved DLQI 0 or 1 at W12 was 41% and 40%, in reSURFACE 1 and 2 respectively. Improvements were maintained over a year with DLQI 0/1 achieved by 64 % and 69% of patients treated with 100 mg in reSURFACE 1 and 2 respectively. At Week 52, 82% (reSURFACE 1) and 87% (reSURFACE 2) of the patients on ILUMYA 100mg had a DLQI score < 5 points.

In reSURFACE 1, the physical and mental component summary scores of the Short Form Health Survey (SF-36) were significantly improved in patients treated with ILUMYA compared with placebo.

Treatment maintenance in partial responders

68.4% patients (reSURFACE 2) originally randomized to ILUMYA 100 mg who achieved a PASI response of ≥50% but <75% improvement from Baseline at Week 28 (3 doses) and remained on ILUMYA 100 mg (n ~ 20), achieved a PASI 75 response at Week 52 (i.e. 3 additional doses).

5.2 PHARMACOKINETIC PROPERTIES

Absorption

The subcutaneous formulation of tildrakizumab was characterized with an absolute bioavailability of 73-90% and slow absorption with time to reach maximum concentration at 6.2 days after injection. Steady-state was achieved by 16 weeks with the clinical regimen of 0, 4, and every 12 weeks thereafter, with 1.1-fold accumulation in exposure between Week-1 and Week-12 independent of dose.

At steady state, following administration of 100 mg of tildrakizumab in subjects with moderate to severe psoriasis geometric means (% CV) of $AUC_{0-\tau}$ and C_{max} values were 305 μg*day/ml (41%) and 8.1 μg /ml (34%), respectively.

Tildrakizumab pharmacokinetics exhibited low to moderate variability (33-41%).

Distribution

Tildrakizumab has limited extravascular distribution with volume of distribution (Vd) values ranging from 76.9 to 106 mL/kg.

Metabolism

Tildrakizumab is catabolized into component amino acids by general protein degradation processes.

Small-molecule metabolic pathways (e.g., cytochrome P450 enzymes (CYPs), glucuronosyltransferases) do not contribute to its clearance.

Excretion

The geometric mean systemic clearance (CV %) was 0.32 L/day (38%) and the half-life was 23.4 days (23%) in subjects with plaque psoriasis.

Dose linearity

Tildrakizumab exhibited dose-proportional pharmacokinetics in subjects with plaque psoriasis over a dose range from 50 mg to 200 mg, and in healthy subjects at doses from 50 mg to 400 mg following subcutaneous administration, with clearance being independent of dose.

Special populations

Elderly

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

Renal and Hepatic impairment

No formal trial on the effect of hepatic or renal impairment on the pharmacokinetics of tildrakizumab has been conducted.

Drug interactions

A clinical pharmacology study, administering 200 mg of tildrakizumab subcutaneously on Day 1 and Day 29 demonstrated that tildrakizumab does not have a clinically relevant effect on the pharmacokinetics of caffeine (CYP1A2 probe substrate), warfarin (CYP2C9 probe substrate), omeprazole (2C19 probe substrate), dextromethorphan (CYP2D6 probe substrate) or midazolam (CYP3A4 probe substrate). (See section 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS)

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

ILUMYA has not been evaluated for genotoxic potential.

Carcinogenicity

Animal carcinogenicity studies have not been conducted with tildrakizumab. Studies in mouse tumour models showed that selective inhibition of IL-23p19 does not increase carcinogenic risk.

6. PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Histidine, histidine hydrochloride monohydrate, polysorbate 80, sucrose and water for injections.

6.2 INCOMPATIBILITIES

Not known

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store at 2°C to 8°C. Refrigerate. Do not freeze.

ILUMYA is stable for up to 30 days at 25°C.

Protect from light. Keep the pre-filled syringe in the outer carton until ready to use. Do not shake.

6.5 NATURE AND CONTENTS OF CONTAINER

ILUMYA solution for injection is supplied as a single-use, pre-filled syringe comprising a clear glass barrel with a stainless-steel needle, latex-free rubber plunger stopper and needle shield. Each pre-filled syringe is assembled with a needle safety device for subcutaneous (sc) administration.

Pack size of 1 pre-filled syringe.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

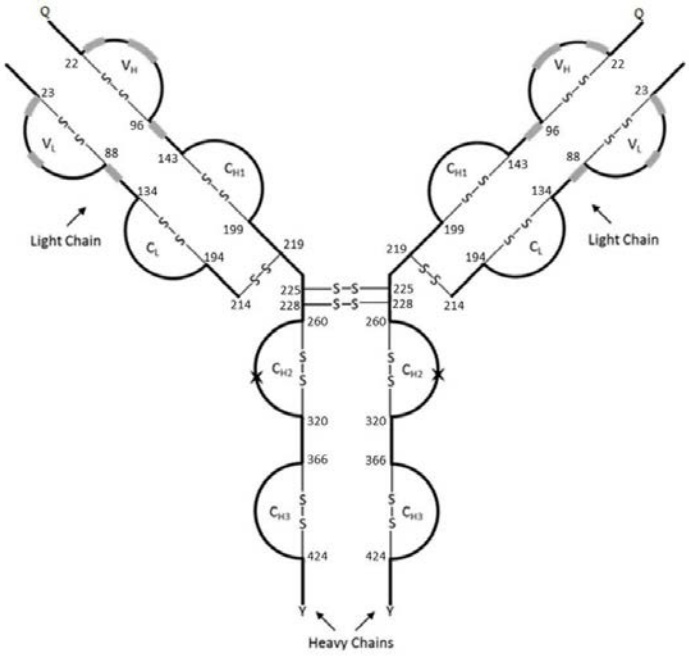
No special requirements for disposal.

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSIOCHEMICAL PROPERTIES

ILUMYA (tildrakizumab) is a humanised IgG1/k monoclonal antibody produced by recombinant DNA technology in a Chinese hamster ovary (CHO) cells. It is composed of two identical heavy chains of 446 amino acids each and two identical light chains of 214 amino acids each linked by interchain disulfide bonds, with an approximate molecular weight of 147.0kDa.

Chemical structure:



CAS Registry No: 1326244-10-3

7. MEDICINE SCHEDULE (POISON STANDARD)

Schedule 4 - Prescription Only Medicine

8. SPONSOR

Sun Pharma ANZ Pty Ltd

Macquarie Park NSW 2113

Australia

Telephone 1 800 726 229

9. DATE OF FIRST APPROVAL

10 September 2018

10. DATE OF REVISION

Summary table of changes

Section changed	Summary of new information
All	1. New