

PRODUCT MONOGRAPH  
INCLUDING PATIENT MEDICATION INFORMATION

**PrADTRALZA®**

Tralokinumab injection

Single-use pre-filled syringe

150 mg/1 mL

Solution for subcutaneous injection

Immunomodulator, Interleukin inhibitor  
ATC Code: D11AH07

LEO Pharma Inc.  
Thornhill, Ontario  
L3T 7W8  
[www.leo-pharma.ca](http://www.leo-pharma.ca)

Date of Initial Authorization:  
October 13, 2021

Submission Control Number: 245877

® Registered trademark of LEO Pharma A/S used under license by LEO Pharma Inc.

## TABLE OF CONTENTS

Sections or subsections that are not applicable at the time of authorization are not listed.

<b>TABLE OF CONTENTS</b> .....	<b>2</b>
<b>PART I: HEALTH PROFESSIONAL INFORMATION</b> .....	<b>4</b>
<b>1 INDICATIONS</b> .....	<b>4</b>
1.1 Pediatrics .....	4
1.2 Geriatrics.....	4
<b>2 CONTRAINDICATIONS</b> .....	<b>4</b>
<b>4 DOSAGE AND ADMINISTRATION</b> .....	<b>4</b>
4.1 Dosing Considerations.....	4
4.2 Recommended Dose and Dosage Adjustment .....	4
4.3 Reconstitution.....	5
4.4 Administration.....	5
4.5 Missed Dose.....	5
<b>5 OVERDOSAGE</b> .....	<b>6</b>
<b>6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING</b> .....	<b>6</b>
<b>7 WARNINGS AND PRECAUTIONS</b> .....	<b>7</b>
7.1 Special Populations .....	7
7.1.1 Pregnant Women .....	7
7.1.2 Breast-feeding.....	7
7.1.3 Pediatrics.....	8
7.1.4 Geriatrics.....	8
<b>8 ADVERSE REACTIONS</b> .....	<b>8</b>
8.1 Adverse Reaction Overview.....	8
8.2 Clinical Trial Adverse Reactions.....	8
8.2.1 Clinical Trial Adverse Reactions – Pediatrics .....	10
8.3 Less Common Clinical Trial Adverse Reactions (< 1%).....	10
8.3.1 Less Common Clinical Trial Adverse Reactions – Pediatrics .....	10
8.4 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data .....	11
8.5 Post-Market Adverse Reactions .....	11
<b>9 DRUG INTERACTIONS</b> .....	<b>11</b>
9.2 Drug Interactions Overview.....	11

9.3	Drug-Behavioural Interactions.....	11
9.4	Drug-Drug Interactions.....	11
9.5	Drug-Food Interactions.....	12
9.6	Drug-Herb Interactions.....	12
9.7	Drug-Laboratory Test Interactions.....	12
<b>10</b>	<b>CLINICAL PHARMACOLOGY .....</b>	<b>12</b>
10.1	Mechanism of Action.....	12
10.2	Pharmacodynamics.....	12
10.3	Pharmacokinetics.....	12
<b>11</b>	<b>STORAGE, STABILITY AND DISPOSAL .....</b>	<b>14</b>
<b>12</b>	<b>SPECIAL HANDLING INSTRUCTIONS .....</b>	<b>14</b>
	<b>PART II: SCIENTIFIC INFORMATION .....</b>	<b>15</b>
<b>13</b>	<b>PHARMACEUTICAL INFORMATION .....</b>	<b>15</b>
<b>14</b>	<b>CLINICAL TRIALS .....</b>	<b>16</b>
14.1	Trial Design and Study Demographics.....	16
14.2	Study Results.....	17
<b>15</b>	<b>MICROBIOLOGY.....</b>	<b>19</b>
<b>16</b>	<b>NON-CLINICAL TOXICOLOGY .....</b>	<b>20</b>
	<b>PATIENT MEDICATION INFORMATION .....</b>	<b>22</b>
	<b>INSTRUCTIONS FOR USE.....</b>	<b>27</b>

## **PART I: HEALTH PROFESSIONAL INFORMATION**

### **1 INDICATIONS**

Adtralza (tralokinumab injection) is indicated for the treatment of moderate-to-severe atopic dermatitis in adult patients whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable.

Adtralza can be used with or without topical corticosteroids.

#### **1.1 Pediatrics**

Pediatrics (< 18 years): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

#### **1.2 Geriatrics**

Geriatrics (≥ 65 years): Of the 1605 patients exposed to Adtralza in the initial 16-week treatment period of the atopic dermatitis clinical studies, a total of 77 patients were ≥ 65 years of age. Although the number of patients aged 65 and over is limited, evidence from clinical studies suggests there are no differences in safety and efficacy between older and younger subjects. No dose adjustment is recommended for elderly patients.

### **2 CONTRAINDICATIONS**

Adtralza is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see [\(6\)](#) DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING section of the product monograph.

### **4 DOSAGE AND ADMINISTRATION**

#### **4.1 Dosing Considerations**

- Adtralza can be used with or without topical corticosteroids. Adtralza may be used with topical calcineurin inhibitors.
- Health Canada has not authorized an indication for pediatric use, as no data are available in patients < 18 years of age [see [\(1.1\)](#) INDICATIONS, Pediatrics].

#### **4.2 Recommended Dose and Dosage Adjustment**

- The recommended dose of Adtralza for adult patients is an initial dose of 600 mg (four 150 mg injections) followed by 300 mg (two 150 mg injections) administered every other week as subcutaneous injection.
- At prescriber's discretion, every fourth week dosing may be considered for some patients who achieve clear or almost clear skin after 16 weeks of treatment; however, the probability of maintaining clear or almost clear skin may be decreased with dosing every fourth week.
- Some patients with initial partial response may subsequently improve further with continued treatment every other week beyond 16 weeks. At the prescriber's discretion, discontinuation of treatment may be considered in patients who have shown no response

after 16 weeks of treatment.

#### *Body weight*

For patients with high body weight (>100 kg) who achieve clear or almost clear skin after 16 weeks of treatment, dosage every other week may be more appropriate than every fourth week dosing [see (10.3) CLINICAL PHARMACOLOGY, Pharmacokinetics, Special Populations and Conditions].

#### *Elderly patients (≥ 65 years)*

No dose adjustment is recommended for elderly patients [see (10.3) CLINICAL PHARMACOLOGY, Pharmacokinetics, Special Populations and Conditions].

#### *Hepatic impairment*

No dose adjustment is needed in patients with mild hepatic impairment. Very limited data are available in patients with moderate or severe hepatic impairment [see (10.3) CLINICAL PHARMACOLOGY, Pharmacokinetics, Special Populations and Conditions].

#### *Renal impairment*

No dose adjustment is needed in patients with mild or moderate renal impairment. Very limited data are available in patients with severe renal impairment [see (10.3) CLINICAL PHARMACOLOGY, Pharmacokinetics, Special Populations and Conditions].

### **4.3 Reconstitution**

Adtralza does not require reconstitution prior to injection [see (6) DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING].

### **4.4 Administration**

- Adtralza is administered by subcutaneous injection into the thigh or abdomen, except the 5 cm (2 inches) around the navel. If somebody else administers the injection, the upper arm can also be used. Adtralza should not be administered intramuscularly.
- For the initial 600 mg dose, administer four 150 mg Adtralza injections consecutively in different injection sites within the same body area according to the [PATIENT MEDICATION INFORMATION, INSTRUCTIONS FOR USE](#) section of the product monograph.
- It is recommended to rotate the body area with each subsequent set of injections. Adtralza should not be injected into skin that is tender, damaged or has bruises or scars.
- A patient may self-inject Adtralza or the patient's caregiver may administer Adtralza if their health professional determines that this is appropriate. Proper training should be provided to patients and/or caregivers on the preparation and administration of Adtralza prior to use according to the [PATIENT MEDICATION INFORMATION, INSTRUCTIONS FOR USE](#) section of the product monograph.

### **4.5 Missed Dose**

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

## 5 OVERDOSAGE

There is no specific treatment for Adtralza overdose.

In clinical studies with tralokinumab, single intravenous doses of up to 30 mg/kg and multiple subcutaneous doses of 600 mg every 2 weeks for 12 weeks were found to be well tolerated.

For management of a suspected drug overdose, contact your regional poison control centre.

## 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

To help ensure the traceability of biologic products, health professionals should recognise the importance of recording both the brand name and the non-proprietary (active ingredient) name as well as other product-specific identifiers such as the Drug Identification Number (DIN) and the batch/lot number of the product supplied.

**Table 1-1: Dosage Forms, Strengths, Composition and Packaging**

<b>Route of Administration</b>	<b>Dosage Form/Strength/Composition</b>	<b>Non-medicinal Ingredients</b>
Subcutaneous Injection	<p>Each single-use pre-filled syringe contains 150 mg of tralokinumab in 1 mL solution (150 mg/mL).</p> <p>The pre-filled syringe is composed of Type-1 clear glass with a fixed 27 gauge, ½ inch, 5 bevel needle and a needle guard.</p>	<p>Acetic acid Polysorbate 80 Sodium acetate trihydrate Sodium chloride Water for injection</p>

Adtralza is available in the following pack sizes:

- 1 carton containing 2 pre-filled syringes
- 1 multipack carton containing 4 pre-filled syringes (2 packs of 2)

Not all pack sizes may be marketed.

None of the components of the pre-filled syringe or the needle cover are made with natural rubber latex (NRL), dry natural rubber (DNR), or any derivatives (of NRL or DNR).

Adtralza is supplied as a preservative-free, clear to opalescent, colorless to pale yellow solution.

## 7 WARNINGS AND PRECAUTIONS

### Immune

#### Hypersensitivity

Hypersensitivity reactions have been reported following the use of Adtralza. If a systemic hypersensitivity reaction (immediate or delayed) occurs, administration of Adtralza should be discontinued immediately and appropriate therapy initiated.

Anaphylactic reaction has been reported very rarely in clinical studies following administration of tralokinumab.

#### Helminth infection

Patients with known helminth infections were excluded from participation in clinical studies. It is unknown if Adtralza will influence the immune response against helminth infections by inhibiting IL-13 signaling.

Treat patients with pre-existing helminth infections before initiating Adtralza. If patients become infected while receiving Adtralza and do not respond to anti-helminth treatment, treatment with Adtralza should be discontinued until infection resolves.

#### Conjunctivitis

Conjunctivitis occurred more frequently in subjects with atopic dermatitis who received Adtralza than in subjects who received placebo. Advise patients to report new onset or worsening eye symptoms to their healthcare professional. Patients treated with Adtralza who develop conjunctivitis that does not resolve following standard treatment should undergo ophthalmological examination, as appropriate [see [\(8\)](#) ADVERSE REACTIONS].

### 7.1 Special Populations

#### 7.1.1 Pregnant Women

No studies have been conducted with Adtralza in pregnant women and relevant data from clinical use are very limited.

As a precautionary measure, it is preferable to avoid the use of Adtralza during pregnancy.

Human IgG antibodies are known to cross the placental barrier; therefore, Adtralza may be transmitted from the mother to the developing fetus. In a developmental toxicity study conducted in cynomolgus monkeys, tralokinumab was detected in monkey infant serum following *in utero* exposure, indicating transport across the placenta [see [\(16\)](#) NON-CLINICAL TOXICOLOGY].

#### 7.1.2 Breast-feeding

It is unknown whether Adtralza is excreted in human milk or absorbed systemically after ingestion. A decision must be made whether to discontinue breast-feeding or to discontinue Adtralza therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

### 7.1.3 Pediatrics

No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use [see (1.1) INDICATIONS, Pediatrics].

### 7.1.4 Geriatrics

Evidence from 77 patients  $\geq 65$  years of age that were exposed to Adtralza in clinical studies in atopic dermatitis suggests that use in the geriatric population is not associated with differences in safety or efficacy [see (1.2) INDICATIONS, Geriatrics].

## 8 ADVERSE REACTIONS

### 8.1 Adverse Reaction Overview

The most frequently ( $\geq 10\%$ ) reported adverse drug reactions (ADRs) in the pool of 5 studies were upper respiratory tract infections (23%) compared with 17% in the placebo group. The majority of these were reported as common cold. All of the reactions were mild or moderate in severity.

The proportion of patients who discontinued treatment due to adverse events was 2.3% in the Adtralza group and 2.8% in the placebo group during the initial treatment period of up to 16 weeks.

During the maintenance treatment period of the monotherapy studies (ECZTRA 1 and ECZTRA 2) from 16 to 52 weeks, upper respiratory tract infections were reported at an exposure-adjusted rate of 64 per 100 patient-years for Adtralza 300 mg Q2W and Adtralza 300 mg Q4W compared to 94 per 100 patient-years for Adtralza 300 mg Q2W in the initial treatment period. In the continuation treatment period of ECZTRA 3 (up to 32 weeks), the exposure-adjusted rate was 98 per 100 patient-years for Adtralza 300 mg Q2W + TCS and 63 per 100 patient-years for Adtralza 300 mg Q4W + TCS compared to 120 per 100 patient-years for Adtralza 300 mg Q2W + TCS in the initial treatment period.

Across all treatment periods (up to 52 weeks), the majority ( $>80\%$ ) of the upper respiratory tract infections were classified as mild and non-serious.

### 8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials; therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

The safety of Adtralza was evaluated based on a pool of 5 randomized, double-blind, placebo-controlled studies in patients with moderate-to-severe atopic dermatitis including three phase 3 studies (ECZTRA 1, ECZTRA 2, and ECZTRA 3), a dose-ranging study and a vaccine-response study. The safety population had a mean age of 38 years; 43% of patients were female, 67% were white, 20% were Asian, and 10% were black; in terms of co-morbid conditions, 38% of the patients had asthma, 47% had hay fever, 34% had food allergy, and 20% had allergic conjunctivitis.



In these 5 atopic dermatitis studies, 1991 patients were treated with subcutaneous injections of Adtralza, with or without concomitant topical corticosteroids (TCS). A total of 807 patients were treated with Adtralza for at least 1 year.

The long-term safety of Adtralza was assessed in the 2 monotherapy studies up to 52 weeks and in 1 combination study with TCS up to 32 weeks. The safety profile of Adtralza through week 52 and week 32 respectively was consistent with the safety profile observed up to week 16.

Table 1-2 summarizes the adverse reactions occurring in the atopic dermatitis clinical trials at a rate of  $\geq 1\%$  in the Adtralza 300 mg every other week monotherapy group (ECZTRA 1 and ECZTRA 2), and in the Adtralza 300 mg every other week + TCS study (ECZTRA 3).

**Table 1-2: List of adverse reactions occurring with a frequency of  $\geq 1\%$  in ECZTRA 1, ECZTRA 2 and ECZTRA 3 clinical trials through week 16**

System organ class ADR	Monotherapy <sup>a</sup> (up to 16 weeks)		Adtralza + TCS <sup>b</sup> (up to 16 weeks)	
	Adtralza (N=1194; PYE=354.46)	Placebo (N=396; PYE=114.47)	Adtralza + TCS (N=252; PYE=75.03)	Placebo + TCS (N=126; PYE=37.94)
	N (%)	N (%)	N (%)	N (%)
<b>Infections and infestations</b>				
Upper respiratory tract infections	284 (23.8)	80 (20.2)	73 (29.0)	19 (15.1)
Conjunctivitis (PT)	61 (5.1)	7 (1.8)	28 (11.1)	4 (3.2)
<b>Blood and lymphatic system disorders</b>				
Eosinophilia	17 (1.4)	2 (0.5)	3 (1.2)	0 (0.0)
<b>Eye disorders</b>				
Conjunctivitis allergic (PT)	28 (2.3)	5 (1.3)	5 (2.0)	2 (1.6)
<b>General disorders and administration site conditions</b>				
Injection site reactions (HLT) (i.e., redness, swelling)	87 (7.3)	16 (4.0)	27 (10.7)	1 (0.8)

**Abbreviations:**

ADR = adverse drug reaction; HLT = high-level term; N= number of patients (with events); PT= preferred term; PYE= patient-years of exposure; TCS = topical corticosteroids

<sup>a</sup> Pooled analysis of ECZTRA 1 and 2, <sup>b</sup> Analysis of ECZTRA 3 where subjects were on background TCS treatment.

### Conjunctivitis

Conjunctivitis occurred more frequently in atopic dermatitis patients who received Adtralza (5.4%) compared to placebo (1.9%) in the initial treatment period of up to 16 weeks in the pool of 5 studies. Most patients recovered or were recovering during the treatment period.

### Infections

In the pool of 5 studies in atopic dermatitis, serious infections were reported in 0.4% of patients treated with Adtralza and 1.1% of patients treated with placebo during the initial treatment period of up to 16 weeks.

### Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity with Adtralza.

No immunogenicity related adverse events such as immune-complex disease, serum sickness/serum sickness-like reactions, or anaphylaxis were observed in 1991 patients treated with Adtralza in the pool of 5 studies in atopic dermatitis.

Anti-Drug-Antibody (ADA) responses were not associated with any impact on Adtralza exposure, safety, or efficacy.

In ECZTRA 1, ECZTRA 2, ECZTRA 3, and the vaccine-response study (ECZTRA 5), the incidence of ADA up to 16 weeks was 1.4% for patients treated with Adtralza and 1.3% for patients treated with placebo; neutralizing antibodies were seen in 0.1% of patients treated with Adtralza and 0.2% of patients treated with placebo.

The ADA incidence for patients who received Adtralza up to 52 weeks was 4.4%; 0.7% had persistent ADA and 0.9% had neutralizing antibodies.

The observed incidence of persistent ADA responses and neutralizing activity in the assay are highly dependent on the sensitivity and specificity of the assay used. Additionally, the observed incidence of 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 status of the individual patient. For these reasons, comparison of the incidence of antibodies to Adtralza with the incidence of antibodies to other products may be misleading.

## **8.2.1 Clinical Trial Adverse Reactions – Pediatrics**

No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

## **8.3 Less Common Clinical Trial Adverse Reactions (< 1%)**

Eye disorders: Keratitis

### **8.3.1 Less Common Clinical Trial Adverse Reactions – Pediatrics**

No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

## 8.4 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data

### Clinical Trial Findings

Eosinophilia was reported in 1.3% of patients treated with Adtralza and 0.3% of patients treated with placebo during the initial treatment period of up to 16 weeks in the pool of 5 studies. Adtralza-treated patients had a greater mean initial increase from baseline in eosinophil count compared to patients treated with placebo. However, the increase in the Adtralza-treated patients was transient, and mean eosinophil counts returned to baseline during continued treatment. The safety profile for patients with eosinophilia was comparable to the safety profile for all patients.

## 8.5 Post-Market Adverse Reactions

Not applicable, as post-market adverse reactions have yet to be reported.

## 9 DRUG INTERACTIONS

### 9.2 Drug Interactions Overview

The effects of Adtralza on the pharmacokinetics (PK) of cytochrome P450 (CYP) substrates have not been studied.

### 9.3 Drug-Behavioural Interactions

Drug-behavioural interactions have not been established.

### 9.4 Drug-Drug Interactions

#### Drug-Drug Interactions

Interactions with other drugs have not been established.

#### Drug-Vaccine Interactions

##### *Live Vaccines:*

Adtralza has not been studied with live vaccines. Live vaccines should not be given concurrently with Adtralza.

##### *Non-Live Vaccines:*

Immune responses to non-live vaccines were assessed in a study in which adult patients with atopic dermatitis were treated with an initial dose of 600 mg (four 150 mg injections) followed by 300 mg every second (other) week administered as subcutaneous injection. After 12 weeks of Adtralza administration, patients were vaccinated with a combined tetanus, diphtheria, and acellular pertussis vaccine, and a meningococcal vaccine and immune responses were assessed 4 weeks later. Antibody responses to both tetanus vaccine and meningococcal vaccine were similar in Adtralza-treated and placebo-treated patients.

No adverse interactions between either of the non-live vaccines or Adtralza were noted in the study. Therefore, patients receiving Adtralza may receive concurrent inactivated or non-live vaccinations.

## 9.5 Drug-Food Interactions

Interactions with food have not been established.

## 9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

## 9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

# 10 CLINICAL PHARMACOLOGY

## 10.1 Mechanism of Action

Tralokinumab is a fully human IgG4 monoclonal antibody that specifically binds to the type 2 cytokine interleukin-13 (IL-13) and inhibits its interaction with the IL-13 receptors, IL-13R $\alpha$ 1 and IL-13R $\alpha$ 2. Tralokinumab neutralizes the activity of IL-13 by blocking its interaction with the IL-13R $\alpha$ 1/IL-4R $\alpha$  receptor complex.

IL-13 is a major driver of type 2 inflammation in atopic dermatitis, with atopic dermatitis skin showing overexpression of IL-13. IL-13 signals via the IL-13R $\alpha$ 1/IL-4R $\alpha$  receptor complex and stimulates inflammatory responses, contributes to itch induction, and impairs the expression of proteins necessary for a normal skin barrier.

## 10.2 Pharmacodynamics

In clinical studies, treatment with tralokinumab was associated with decreases from baseline in concentrations of Th2 and Th22 immunity biomarkers in the blood, such as thymus and activation-regulated chemokine (TARC/CCL17), periostin, IL-22, LDH and serum IgE. Furthermore, tralokinumab treatment resulted in reduced epidermal thickness and decreased expression of Keratin 16 and Ki-67 in AD skin. The protein expression of loricrin was upregulated in AD skin, further indicating that the skin barrier was improved with tralokinumab. Finally, tralokinumab suppressed expression of genes in the Th2 pathway, including CCL17, CCL18 and CCL26 as well as markers of Th17- and Th22-regulated genes in lesional skin. In addition, patients treated with tralokinumab achieved a more than 10-fold higher reduction in abundance of *staphylococcus aureus* at week 16 compared to placebo.

## 10.3 Pharmacokinetics

**Absorption:** After subcutaneous (SC) dose of tralokinumab median times to maximum concentration in serum ( $t_{max}$ ) were 5-8 days. The absolute bioavailability of tralokinumab following SC dosing is 76%.

Steady-state concentrations were achieved by week 16 following a 600 mg starting dose and 300 mg every other week. Across clinical studies (ECZTRA 1, ECZTRA 2 and ECZTRA 3), the mean  $\pm$ SD steady-state trough concentration ranged from 98.0 $\pm$ 41.1 mcg/mL to 101.4 $\pm$ 42.7 mcg/mL for 300 mg dose administered every other week.

**Distribution:** A volume of distribution for tralokinumab of approximately 4.2 L was estimated by population PK analysis.

**Metabolism:** Specific metabolism studies were not conducted because tralokinumab is a protein. Tralokinumab is expected to degrade to small peptides and individual amino acids.

**Elimination:** Tralokinumab is eliminated through a non-saturable proteolytic pathway. Half-life is 22 days, consistent with the typical estimate for human IgG4 monoclonal antibodies targeting soluble cytokines.

**Linearity:** Exposure of tralokinumab increases proportionally to the dose of tralokinumab over a range of investigated doses 0.1-10 mg/kg.

### Special Populations and Conditions

- **Pediatrics:** The pharmacokinetics of tralokinumab in pediatric patients has not been studied.
- **Geriatrics:** Age was not found to be associated with clinically relevant impact of systemic exposure of tralokinumab determined by population PK analysis. 131 subjects  $\geq 65$  years were included in the analysis.
- **Sex:** Gender was not found to be associated with any clinically meaningful impact on the systemic exposure of tralokinumab determined by population PK analysis.
- **Ethnic Origin:** Race was not found to be associated with any clinically meaningful impact on the systemic exposure of tralokinumab by population PK analysis.
- **Hepatic Insufficiency:** Tralokinumab, as a monoclonal antibody, is not expected to undergo significant hepatic elimination. No clinical studies have been conducted to evaluate the effect of hepatic impairment on the pharmacokinetics of tralokinumab. Mild hepatic impairment was not found to affect the PK of tralokinumab determined by population PK analysis. Moderate or severe hepatic impairment was not found to affect the PK of tralokinumab. Very limited data are available in patients with moderate or severe hepatic impairment.
- **Renal Insufficiency:** Tralokinumab, as a monoclonal antibody, is not expected to undergo significant renal elimination. No clinical studies have been conducted to evaluate the effect of renal impairment on the pharmacokinetics of tralokinumab. Population PK analysis did not identify mild or moderate renal impairment as having a clinically meaningful influence on the systemic exposure of tralokinumab. Very limited data are available in patients with severe renal impairment.
- **Body Weight:** Tralokinumab trough concentrations were lower in patients with higher body weight.

## 11 STORAGE, STABILITY AND DISPOSAL

Store in a refrigerator (2-8°C). Do not freeze.

Store in the original carton in order to protect from light. The pre-filled syringe should not be exposed to heat or direct sunlight and should not be shaken.

If necessary, pre-filled syringes may be kept at room temperature up to 25°C for a maximum of 14 days, within the expiration date period of the product. Do not store above 25°C.

If the carton needs to be removed permanently from the refrigerator, the date of removal may be recorded on the outer carton. Discard the product if it is not used within 14 days of storage at room temperature.

After removing the pre-filled syringe from the refrigerator, it should be allowed to reach room temperature by waiting for 30 minutes before injecting.

Do not put syringes back in the refrigerator once they have reached room temperature.

The solution should be clear to opalescent, colorless to pale yellow. If the solution is cloudy, discolored or contains visible particulate matter, the solution should not be used. Do not use if the pre-filled syringe is damaged or has been dropped on a hard surface.

Adtralza is sterile and does not contain preservatives; therefore, discard any unused product remaining in the pre-filled syringe.

After injection, safely dispose of the used pre-filled syringes in accordance with local requirements.

## 12 SPECIAL HANDLING INSTRUCTIONS

For special handling instructions on how to properly dispose of Adtralza following an injection, refer to the [PATIENT MEDICATION INFORMATION, INSTRUCTIONS FOR USE](#) section of the product monograph.

## PART II: SCIENTIFIC INFORMATION

### 13 PHARMACEUTICAL INFORMATION

#### Drug Substance

Proper name:	Tralokinumab
Chemical name:	Not applicable. Tralokinumab is an immunoglobulin.
Molecular formula:	C <sub>6374</sub> H <sub>9822</sub> N <sub>1698</sub> O <sub>2014</sub> S <sub>44</sub>
Molecular mass:	Approximately 147 kDa (including oligosaccharides)
Structural formula:	The antibody is composed of two heavy chains, and two light chains covalently linked with four inter-chain disulfide bonds. Tralokinumab has an N-linked oligosaccharide attachment site. The oligosaccharides are predominantly fucosylated biantennary complex-type oligosaccharides.
Physicochemical properties:	Tralokinumab is supplied as a sterile, preservative-free solution for subcutaneous administration. The solution is colorless to pale yellow and clear to opalescent, with pH of 5.5.

#### Product Characteristics:

Tralokinumab is produced in mouse myeloma cells by recombinant DNA technology. No materials of human origin are used in the manufacture of Adtralza. The cell cultivation and harvest process consists of five steps. Following the final harvest step, the clarified conditioned medium containing tralokinumab is further processed through a series of purification steps. Purification involves chromatography steps to remove product- and process-related impurities, and dedicated virus clearance steps. A concentration and diafiltration step, followed by a formulation step and a 0.2 micron filtration step, are then used to generate the final drug substance.

## 14 CLINICAL TRIALS

### 14.1 Trial Design and Study Demographics

The efficacy and safety of Adtralza (tralokinumab injection) as monotherapy and with concomitant topical corticosteroids were evaluated in three pivotal randomized, double-blind, placebo-controlled studies (ECZTRA 1, ECZTRA 2 and ECZTRA 3) in 1976 patients 18 years of age and older with moderate to severe atopic dermatitis (AD) who had a previous inadequate response to topical medication. Disease severity was defined by Investigator's Global Assessment (IGA) score of 3 or 4 (moderate or severe), an Eczema Area and Severity Index (EASI) score of  $\geq 16$  at baseline, and a minimum body surface area (BSA) involvement of  $\geq 10\%$ .

In all three studies (Table 2-1), patients received 1) an initial dose of 600 mg Adtralza (four 150 mg injections) on day 1, followed by 300 mg every two weeks (Q2W) up to week 16, or 2) matching placebo. In ECZTRA 3, patients received concomitant topical corticosteroids (i.e., 0.1% mometasone furoate) on active lesions as needed. Adtralza was administered by subcutaneous (SC) injection in all studies.

In ECZTRA 1 and ECZTRA 2, to evaluate the maintenance of response, patients responding to initial 16-week treatment with Adtralza (i.e., IGA 0 or 1, or EASI-75) were re-randomized to 1) Adtralza 300 mg Q2W, or 2) Adtralza 300 mg Q4W (alternating Adtralza 300 mg and placebo Q2W), or 3) placebo Q2W up to 52 weeks. Patients responding to the initial 16-week treatment with placebo continued on placebo. Patients not achieving IGA 0 or 1 or EASI-75 at week 16 and patients who did not maintain the response during the maintenance period were transferred to open-label treatment with Adtralza 300 mg Q2W with optional use of topical corticosteroids (TCS).

In ECZTRA 3, patients responding to the initial 16-week treatment with Adtralza + TCS were re-randomized to 1) Adtralza 300 mg Q2W + TCS, or 2) Adtralza 300 mg Q4W + TCS (alternating placebo 300 mg Q2W + TCS) up to 32 weeks. Patients responding to the initial 16-week treatment with placebo + TCS continued on placebo + TCS. Patients, who at week 16 did not achieve IGA 0 or 1 or EASI-75, continued on Adtralza 300 mg Q2W + TCS treatment, irrespectively of their initial treatment.

In all three pivotal studies, the co-primary endpoints were achievement of IGA 0 or 1 and EASI-75 from baseline to week 16. Secondary endpoints included the reduction of itch as defined by at least 4-point improvement in the Worst Daily Pruritus Numeric Rating Scale (NRS), reduction in the SCORing Atopic Dermatitis (SCORAD) scale, change in Dermatology Life Quality Index (DLQI), and a reduction of at least 50% and 90% in EASI (EASI-50 and EASI-90) from baseline to week 16.



**Table 2-1: Summary of patient demographics for clinical trials in moderate to severe atopic dermatitis**

Study #	Trial design	Dosage, route of administration and duration	Study patients (n)	Mean age (SD)	Sex
ECZTRA 1	Phase 3 randomized, double-blind, placebo-controlled, monotherapy, efficacy and safety	300 mg Adtralza subcutaneous injection (two 150 mg injections), up to 52 weeks	Adult patients with moderate-to-severe AD (n=802)	38.8 (14.1)	M=474 (59.1%) F=328 (40.9%)
ECZTRA 2	Phase 3 randomized, double-blind, placebo-controlled, monotherapy, efficacy and safety	300 mg Adtralza subcutaneous injection (two 150 mg injections), up to 52 weeks	Adult patients with moderate-to-severe AD (n=794)	36.7 (14.6)	M=473 (59.6%) F=321 (40.4%)
ECZTRA 3	Phase 3 randomized, double-blind, placebo-controlled, combination with TCS, efficacy and safety	300 mg Adtralza subcutaneous injection (two 150 mg injections), up to 32 weeks	Adult patients with moderate-to-severe AD (n=380)	39.1 (15.2)	M=209 (55.0%) F=171 (45.0%)

## 14.2 Study Results

### *Baseline characteristics*

In the monotherapy studies (ECZTRA 1 and ECZTRA 2), across all treatment groups, the mean age was 37.8, the mean weight was 76.0 kg, 40.7% were female, 66.5% were white, 22.9% were Asian, and 7.5% were black. In these studies, 49.9% of patients had a baseline IGA score of 3 (moderate AD), 49.7% of patients had a baseline IGA of 4 (severe AD), the mean baseline EASI score was 32.3, the mean baseline Worst Daily Pruritus NRS was 7.8, the mean baseline DLQI was 17.3, the baseline mean SCORAD score was 70.4, 63.3% of patients had received prior systemic steroids, and 42.5% of patients had received prior other systemic immunosuppressants (cyclosporine, methotrexate, azathioprine and mycophenolate).

In the concomitant TCS study (ECZTRA 3), across both treatment groups, the mean age was 39.1 years, the mean weight was 79.4 kg, 45.0% were female, 75.8% were white, 10.8% were Asian, and 9.2% were black. In this study, 53.2% of patients had a baseline IGA score of 3, 46.3% of patients had a baseline IGA of 4, the mean baseline EASI score was 29.4, the baseline Worst Daily Pruritus NRS was 7.7, the baseline mean DLQI was 17.5, the baseline mean SCORAD score was 67.6, and 39.2% of patients received prior systemic immunosuppressants.

## Clinical response

### Monotherapy Studies (ECZTRA 1 and ECZTRA 2) and Concomitant TCS Study (ECZTRA 3) - Initial Treatment Period (Weeks 0-16)

The efficacy results of the pivotal Phase III trials are included in Table 2-2 below.

**Table 2-2: Efficacy results of Adtralza at week 16 in ECZTRA 1 (monotherapy), ECZTRA 2 (monotherapy) and ECZTRA 3 (combination therapy with TCS) (FAS)**

Monotherapy						
	ECZTRA 1		ECZTRA 2		ECZTRA 3	
	Week 16		Week 16		Week 16	
	Placebo	Adtralza 300 mg Q2W	Placebo	Adtralza 300 mg Q2W	Placebo + TCS	Adtralza 300 mg Q2W + TCS
<b>Number of patients randomized and dosed (FAS)</b>	197	601	201	591	126	252
IGA 0 or 1, % responders <sup>a,b)</sup>	7.1	15.8*	10.9	22.2*	26.2	38.9*
EASI-50, % responders <sup>a)</sup>	21.3	41.6*	20.4	49.9*	57.9	79.4*
EASI-75, % responders <sup>a)</sup>	12.7	25.0*	11.4	33.2*	35.7	56.0*
EASI-90, % responders <sup>a)</sup>	4.1	14.5*	5.5	18.3*	21.4	32.9*
Pruritus NRS ( $\geq$ 4-point improvement, % responders) <sup>a,c)</sup>	10.3 (20/194)	20.0* (119/594)	9.5 (19/200)	25.0* (144/575)	34.1 (43/126)	45.4* (113/249)

LS=least squares; SE=standard error, FAS: Full Analysis Set - includes all patients randomized and dosed.

If needed to control intolerable symptoms of atopic dermatitis, patients were permitted to receive rescue treatment at the discretion of the investigator.

a) Patients who received rescue treatment or had missing data were considered non-responders in the analyses.

b) Responder was defined as a patient with IGA 0 or 1 ("clear" or "almost clear" on a 0-4 IGA scale).

c) The percentage is calculated relative to the number of patients with a baseline value > 4.

\* $p < 0.05$

A numerically greater improvement in Worst Daily Pruritus NRS (mean percent change from baseline) in patients randomized to Adtralza compared to placebo was observed as early as week 1 for ECZTRA 1 and ECZTRA 2 and week 2 for ECZTRA 3 and was maintained at each visit throughout the 16-week period. The improvement in Worst Daily Pruritus NRS occurred in conjunction with the improvement of DLQI and objective signs of atopic dermatitis including SCORAD.

In ECZTRA 3, patients who received Adtralza 300 mg Q2W from week 0 to 16 used 50% less of the supplied TCS at week 16 as compared to patients who received placebo.

### Monotherapy Studies (ECZTRA 1 and ECZTRA 2) – Maintenance Period (Weeks 16-52)

In an analysis of the maintenance period (Weeks 16-52), the findings from the Q2W dosage regimen indicate that the treatment benefit based on both IGA 0 or 1 and EASI-75 was maintained.

Additionally, in patients who switched from Q2W to Q4W dosing at Week 16, a favourable trend was observed on both IGA 0 or 1 and EASI-75 at Week 52; however, the magnitude of effect was numerically less than that observed with the Q2W dosage regimen.

### 32-Week Concomitant TCS Study (ECZTRA 3) - Maintenance Period (Weeks 16-32)

In an analysis of the maintenance period (Weeks 16-32), the findings from the Q2W dosage regimen indicate that the treatment benefit based on both IGA 0 or 1 and EASI-75 was maintained.

Additionally, in patients who switched from Q2W to Q4W dosing at Week 16, a favourable trend was observed on both IGA 0 or 1 and EASI-75 at Week 32; however, the magnitude of effect was numerically less than that observed with the Q2W dosage regimen.

### Quality of Life/Patient-Reported Outcomes

In both monotherapy studies (ECZTRA 1 and ECZTRA 2) and in the TCS combination study (ECZTRA 3), improvements in patient reported outcomes were associated with Adtralza 300 mg Q2W.

A larger proportion of subjects treated with Adtralza had an improvement in eczema-related sleep NRS score, SF-36 (mental and physical components), and a  $\geq 4$  points improvement (corresponding to minimal clinically important difference) in POEM and DLQI in ECZTRA 1, ECZTRA 2, and ECZTRA 3 studies compared to placebo.

In ECZTRA 1, the proportion of Adtralza-treated responders for POEM and DLQI was 43.0% and 44.6%, respectively, compared to 18.0% and 31.6% for placebo at week 16.

In ECZTRA 2, the proportion of Adtralza-treated responders for POEM and DLQI was 54.4% and 56.3%, respectively, compared 22.1% and 27.3% for placebo at week 16.

In ECZTRA 3, the proportion of Adtralza-treated responders for POEM and DLQI was 78.4% and 83.5%, respectively, compared to 59.3% and 65.9% for placebo at week 16.

## **15 MICROBIOLOGY**

No microbiological information is required for this drug product.

## 16 NON-CLINICAL TOXICOLOGY

**General Toxicology:** In a 26-week repeat-dose toxicity study in cynomolgus monkeys, tralokinumab was well tolerated at weekly intravenous doses of 10, 30, and 100 mg/kg body weight. There were no tralokinumab-related adverse effects observed, including on cardiovascular function. At the no observed-adverse-effect level (NOAEL) of 100 mg/kg body weight, the systemic exposure was approximately 41-fold higher than atopic dermatitis patients receiving 300 mg of Adtralza Q2W, based on AUC.

No tralokinumab-related adverse effects, including on cardiovascular function, were observed in cynomolgus monkeys administered tralokinumab by subcutaneous injection at doses of 75, 150, and 300 mg/animal (24.2 to 34.1, 48.4 to 68.2, and 96.8 to 136.4 mg/kg body weight, respectively) once weekly for 13 weeks. At the NOAEL of 300 mg/animal once weekly, the systemic exposure was approximately 64-fold higher than atopic dermatitis patients receiving 300 mg of Adtralza Q2W, based on AUC.

**Genotoxicity:** Genotoxicity studies have not been conducted to evaluate the genotoxic potential of tralokinumab; however monoclonal antibodies are not expected to alter DNA or chromosomes.

**Carcinogenicity:** Carcinogenicity studies have not been conducted to evaluate the carcinogenic potential of tralokinumab.

**Reproductive and Developmental Toxicology:** In an enhanced pre- and post-natal development study, intravenous doses of 30 or 100 mg/kg body weight of tralokinumab (systemic exposure 29-fold higher than atopic dermatitis patients receiving 300 mg of Adtralza Q2W, based on AUC) were administered to pregnant cynomolgus monkeys once every week from the beginning of organogenesis to parturition. No tralokinumab-related adverse effects on embryofetal toxicity, including malformations, or on morphological, functional, or immune function development were observed in the infants from birth through 6 months of age. Thus, the NOAEL for the maternal and developmental toxicity of tralokinumab in this study was 100 mg/kg body weight once weekly (the highest dose tested). Tralokinumab was detected in infant serum during the post-natal period up until post-natal day 91, but generally not by post-natal 180. This finding demonstrates transport across the placenta.

Effects of tralokinumab on fertility-related parameters were assessed in male and female sexually mature cynomolgus monkeys in separate studies. In the female study, animals were subcutaneously administered tralokinumab at doses of 100 or 350 mg/animal (17.5 to 29.4 mg/kg body weight or 55.6 to 134.6 mg/kg body weight, respectively) once a week for three consecutive menstrual cycles (maximum of 15 doses) (systemic exposure 30-fold higher than atopic dermatitis patients receiving 300 mg of Adtralza Q2W, based on AUC). In the male study, animals were subcutaneously administered tralokinumab at doses of 200 or 600 mg/animal (22.0 to 39.2 mg/kg body weight or 67.4 to 101.7 mg/kg body weight, respectively) once a week for 13 weeks (systemic exposure 27-fold higher than atopic dermatitis patients receiving 300 mg of Adtralza Q2W, based on AUC). No effects on fertility-related parameters, such as reproductive organ weights, menstrual cycle, and sperm analysis were observed. There were also no tralokinumab-related histopathological findings in reproductive tissues (epididymides and testes in males and ovaries, uterus/cervix, and vagina in females). The monkeys were not mated to evaluate fertility. The NOAEL for effects on female reproductive

organs was 350 mg/animal and the NOAEL for effects on male reproductive organs was 600 mg/kg (the highest doses tested).

## PATIENT MEDICATION INFORMATION

### READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

#### **PrADTRALZA® (tralokinumab injection)**

Solution for subcutaneous injection  
Single-use pre-filled syringe (150 mg/1 mL)

Read this carefully before you start taking **Adtralza** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **Adtralza**.

#### **What is Adtralza used for?**

Adtralza is used to treat adults who have a moderate-to-severe skin condition called 'atopic dermatitis' (eczema) that causes symptoms such as dry, itchy, scaly skin. Adtralza is used for adults who cannot be adequately treated using therapies that are applied on the surface of the skin (topical).

Adtralza can be used with or without other drugs called topical corticosteroids or topical calcineurin inhibitors (TCIs).

It is not known if Adtralza is safe and effective in children under 18 years old.

#### **How does Adtralza work?**

Adtralza contains the active substance tralokinumab.

Adtralza works by stopping a protein in the body called IL-13, which is found in higher amounts in adults with atopic dermatitis. This can result in reduced inflammation, improved condition of your skin, and reduced itch, redness and scaling.

#### **What are the ingredients in Adtralza?**

Medicinal ingredients: tralokinumab

Non-medicinal ingredients: acetic acid, polysorbate 80, sodium acetate trihydrate, sodium chloride, and water for injection.

#### **Adtralza comes in the following dosage forms:**

Adtralza comes as a single-use pre-filled syringe with needle guard.

Each syringe of Adtralza contains 150 mg of tralokinumab in 1mL solution (150 mg/mL).

The components of the pre-filled syringe or the needle cover are NOT made with natural rubber latex (NRL), dry natural rubber (DNR), or any derivatives (of NRL or DNR).

### Do not use Adtralza if:

You are allergic to tralokinumab or to any of the other ingredients of this medicine.

**To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Adtralza. Talk about any health conditions or problems you may have, including if you:**

- have eye problems (e.g., itching, redness).
- have a parasitic worm (helminth) infection.
- are scheduled to receive any vaccinations. You should **not** receive a “live vaccine” if you are treated with Adtralza.
- are pregnant or plan to become pregnant. It is not known if Adtralza will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if Adtralza will pass into your breast milk and harm your baby.

### Other warnings you should know about:

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. **Do not** use Adtralza for a condition for which it was **not** prescribed. **Do not** give Adtralza to other people, even if they have the same symptoms you have. It may harm them. You can ask your pharmacist or healthcare provider for information about Adtralza that is written for health professionals.

**Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.**

### How to take Adtralza:

- Your healthcare professional may decide if you or a caregiver can give the injections of Adtralza. **Do not** try to inject Adtralza until your healthcare professional shows you the right way.
- See the detailed “Instructions for Use” that comes with Adtralza for information on how to prepare and inject Adtralza. It also shows how to properly store and throw away used Adtralza pre-filled syringes.
- Use Adtralza exactly as your healthcare professional has told you.
- Adtralza is given as an injection under the skin (subcutaneous injection). **Do not** inject into your muscle.
- Your healthcare professional may prescribe other medicines to use with Adtralza. Use the other medicines exactly as your healthcare professional has told you.

### Usual dose:

Each pre-filled syringe contains 150 mg of Adtralza to be injected under the skin (subcutaneously).

Your treatment with Adtralza should be started by a healthcare professional who has experience in the treatment of atopic dermatitis.

- The initial dose is 600 mg (four 150 mg injections).
- Afterwards, a maintenance dose of 300 mg (two 150 mg injections) should be given every other week.

- Your healthcare professional may consider treating you with a maintenance dose every four weeks depending on how you respond to your treatment with Adtralza.

This is a long-term treatment. Your healthcare professional will regularly check your condition to see if the treatment is effective.

### **Overdose:**

There is no specific treatment for Adtralza overdose.

If you think you, or a person you are caring for, have taken too much Adtralza, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

### **Missed Dose:**

If you miss a dose, administer the dose as soon as possible. **Do not** wait for the next planned dose. After that, continue dosing at the regular scheduled time. If you are not sure what to do, contact your healthcare professional for guidance.

### **What are possible side effects from using Adtralza?**

These are not all the possible side effects you may have when taking Adtralza. If you experience any side effects not listed here, tell your healthcare professional.

Very rarely, drugs can cause serious side effects, including allergic (hypersensitivity) reactions and anaphylactic reaction. You must look out for signs of these conditions (which can include breathing problems, swelling of the face, mouth, and tongue, fainting, dizziness, feeling lightheaded (low blood pressure), fever, hives, itching, skin rash) while you are taking Adtralza.

If you notice any of the signs above, stop using Adtralza and get emergency help right away.

### **The most common side effects of Adtralza include:**

- Upper respiratory tract infections (i.e., common cold and sore throat)
- Injection site reactions: itching, pain, redness, tenderness, warmth in the area around the injection
- Eye problems: eye inflammation, including redness, swelling, and itching. Tell your healthcare professional if you have any worsening eye problems, including eye pain or changes in vision.



Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
<b>RARE</b>			
Allergic reactions (hypersensitivity): Breathing problems, difficulty swallowing, swelling of the face, mouth, and tongue, fainting, dizziness, feeling lightheaded (low blood pressure), fever, hives, itching, skin rash			✓

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

### Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

*NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.*

### Storage:

- Store Adtralza in its original carton to protect from light. **Do not** put Adtralza pre-filled syringes into direct sunlight or expose to heat.
- Store Adtralza in a refrigerator between 2°C and 8°C.
  - **Do not** freeze Adtralza pre-filled syringes. **Do not** use syringes if they have been frozen.
- If necessary, you may keep Adtralza pre-filled syringes at room temperature up to 25°C for a maximum of 14 days, within the expiration date period of the product.
  - **Do not** store above 25°C.
  - If the carton needs to be removed permanently from the refrigerator, record the date of removal on the outer carton. Throw away syringes in a puncture resistant container if not used within 14 days of storage at room temperature.
  - **Do not** put syringes back in the refrigerator once they have reached room temperature.
- **Do not** shake Adtralza pre-filled syringes.
- **Do not** use Adtralza after the expiration date shown on the outer box or syringe label. If it has expired, return the whole pack to the pharmacy.

- Keep out of reach and sight of children.

**If you want more information about Adtralza:**

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>); the manufacturer's website [www.leo-pharma.ca](http://www.leo-pharma.ca), or by calling 1-800-668-7234.

This leaflet was prepared by LEO Pharma Inc.

Adtralza® is a registered trademark of LEO Pharma A/S used under license by LEO Pharma Inc.

Last Revised: October 13, 2021

## INSTRUCTIONS FOR USE

### PrADTRALZA® (tralokinumab injection)

Solution for subcutaneous injection  
Single-use pre-filled syringe

Read the following Instructions for Use before you start using Adtralza pre-filled syringes and each time you get a new package. There may be new information. This information does not take the place of talking to your healthcare professional about your medical condition or your treatment.

Keep these Instructions for Use and refer to them as needed.

**Each pre-filled syringe contains 150 mg of Adtralza.**

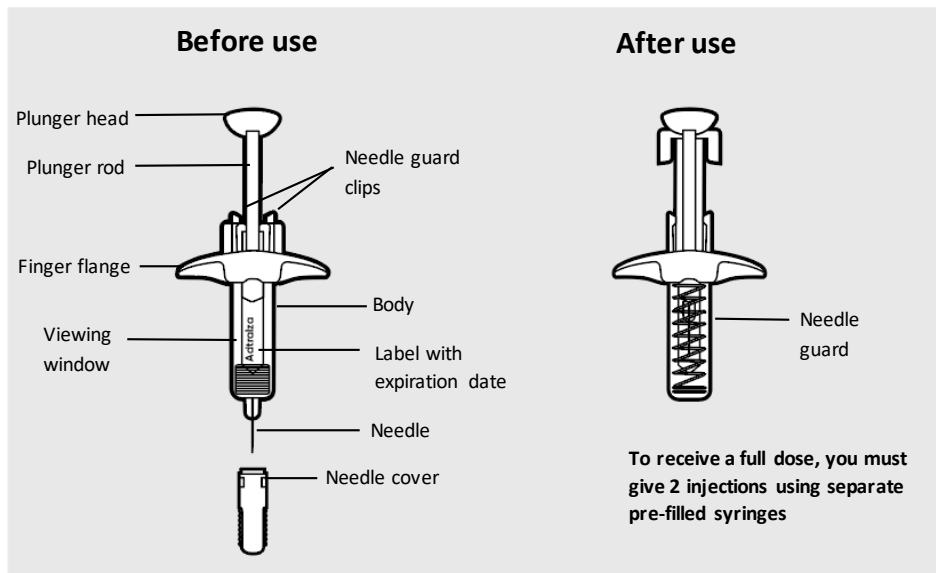
**Adtralza pre-filled syringes are for single-use only.**

### IMPORTANT INFORMATION

Important information you need to know before injecting Adtralza:

- Your healthcare professional should show you how to prepare and inject Adtralza before you make your first injection.
- **Do not** inject yourself or someone else until you have been shown how to inject Adtralza the right way.
- Talk to your healthcare professional if you have any questions about how to inject Adtralza the right way.
- **To receive your full dose, you will need to give more than 1 Adtralza injection.**
  - To get your full initial dose of **600 mg**, you will need to give **4** injections at different injection sites within the same body area.
  - To get your full maintenance dose of **300 mg**, you will need to give **2** injections at different injection sites within the same body area.
- **It is recommended to rotate the injection area (see Figure 2a) with each new set of injections.**
- The Adtralza pre-filled syringes have a needle guard that will automatically cover the needle after the injection is finished.
- For injection directly into the fatty layer under the skin (subcutaneous injection only).
- **Do not** remove the needle cover until just before you give the injection.
- **Do not** share or reuse your Adtralza pre-filled syringes.
- **Do not** inject through clothes.

## ADTRALZA PRE-FILLED SYRINGE PARTS:

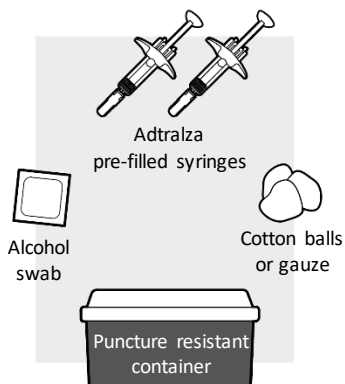


### How to store Adtralza

- Store Adtralza pre-filled syringes in a refrigerator between 2°C and 8°C.
- Store Adtralza pre-filled syringes in the original package and protect from light and heat until you are ready to use them.
- **Do not** freeze Adtralza pre-filled syringes. **Do not** use if they have been frozen.
- Adtralza can be stored at room temperature up to 25°C for up to 14 days, within the expiration date period of the product. Discard syringes if left out of the refrigerator for more than 14 days.
- **Keep Adtralza and all medicines out of the sight and reach of children.**

### STEP 1: SETTING UP ADTRALZA FOR INJECTION

#### 1a: Gather the supplies needed for your injections



**For each Adtralza dose you will need:**

- A clean flat, well-lit work surface, like a table
- 1 Adtralza carton that contains 2 pre-filled syringes
- An alcohol swab (not included in the carton)
- Clean gauze pads or cotton balls (not included in the carton)
- A puncture resistant (sharps) disposal container (not included in the carton)

See Step 5 "DISPOSING OF ADTRALZA" at the end of the Instructions for Use.

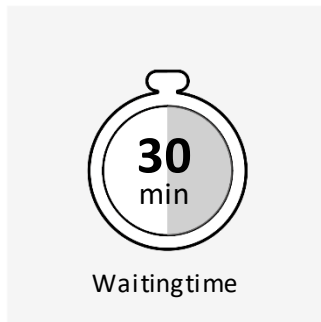
**1b: Take the Adtralza carton out of the refrigerator**



- **Check the expiry date (EXP) on the carton. Do not** use if the expiry date on the carton has passed.
- Check to make sure the seal on the Adtralza carton is intact. **Do not** use the Adtralza pre-filled syringes if the seal on the carton is broken.

**Do not** use the Adtralza pre-filled syringes if the syringes have been stored at room temperature for more than 14 days.

**1c: Let the Adtralza pre-filled syringes warm up to room temperature**

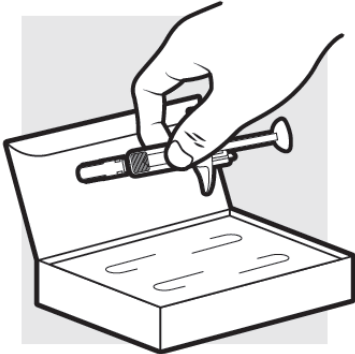


Set the Adtralza carton on a flat surface and wait 30 minutes before you inject, in order to let the pre-filled syringes warm up to room temperature (20°C to 25°C). This will help to reduce discomfort and make it easier to inject Adtralza.

- **Do not** microwave the pre-filled syringes, run hot water over them, or leave them in direct sunlight.
- **Do not** shake the syringes.
- **Do not** remove the needle cover on the pre-filled syringes until you have reached Step 3 and are ready to inject.

- **Do not** put the syringes back in the refrigerator once they have reached room temperature.

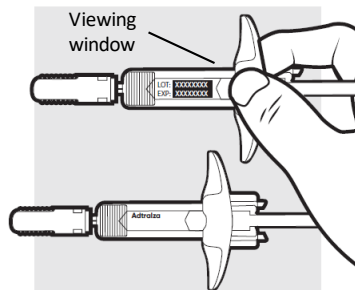
#### 1d: Remove the Adtralza pre-filled syringes from the carton



Remove the **2** Adtralza pre-filled syringes one by one from the carton by holding the body (not the plunger rod) of each pre-filled syringe.

- **Do not** touch the needle guard clips to prevent activating the safety device (needle guard) too soon.
- **Do not** remove the needle cover on the pre-filled syringes until you have reached Step 3 and are ready to inject.

#### 1e: Inspect the 2 Adtralza pre-filled syringes

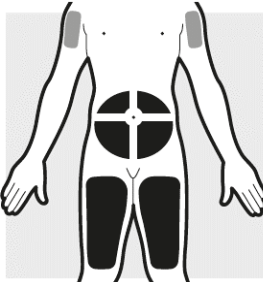


- Make sure the Adtralza name appears on the labels.
  - Check the expiry date printed on the syringes.
  - Check the medicine through the viewing window. The medicine inside should be clear to opalescent, colourless to pale yellow.
  - **Do not** use the Adtralza pre-filled syringes if:
    - the expiry date printed on the syringes has passed
    - the medicine is cloudy, discoloured, or has particles in it
    - they look damaged or have been dropped
- In these cases, dispose of the syringes in a puncture resistant (sharps) container and use new syringes.

- You may see small air bubbles in the liquid. This is normal. You do not need to do anything about it.

## STEP 2: CHOOSING AND PREPARING THE INJECTION AREA

### 2a: Choose the area for your injections



- Injection by caregiver only
- Self-injection or by caregiver

- You may inject into:
  - your stomach area (abdomen)
  - your thighs
  - your upper arm. To inject into your upper arm, you will need a caregiver to give you the injections.
- **Do not** inject where the skin is tender, bruised, scaly, scarred, damaged, hard or covered with eczema.
- **Do not** inject within 5 cm of your belly button (navel).
- **Choose a different body area with each following set of injections. Do not use the same body area 2 times in a row.**

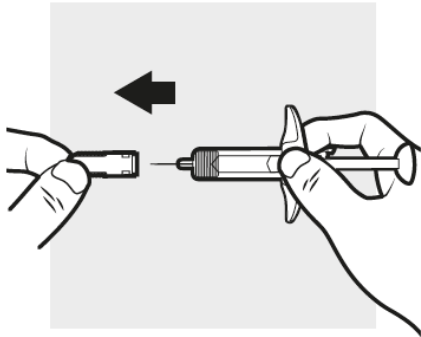
### 2b: Wash your hands and prepare your skin



- Wash your hands with soap and water.
- Clean the injection area for the 2 injections with an alcohol swab using a circular motion.
  - Let the area dry completely.
  - **Do not** blow or touch the cleaned area before injecting.

## STEP 3: INJECTING ADTRALZA

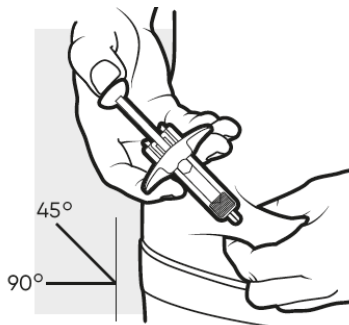
### 3a: Pull off the needle cover from the pre-filled syringe



Hold the pre-filled syringe body with one hand, pull the needle cover straight off with your other hand and throw it away in the puncture resistant (sharps) container.

- **Do not try to recap the Adtralza pre-filled syringes.**
- **Do not** hold the plunger rod or plunger head while removing the needle cover.
- You may see a drop of liquid at the end of the needle. This is normal.
- **Do not** touch the needle, or let it touch any surface. If either of these occur, throw away the syringe in a puncture resistant (sharps) container and get a new one.

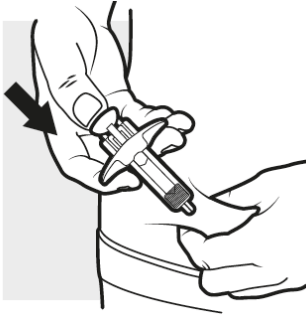
### 3b: Insert the needle



With one hand, gently pinch and hold a fold of skin where you cleaned the injection area. With the other hand, insert the needle completely into your skin at a 45 to 90 degree angle.



### 3c: Inject the medicine



Use your thumb to firmly push down the plunger head all the way down. All the medicine is injected when you cannot push the plunger head any further.

### 3d: Release and remove

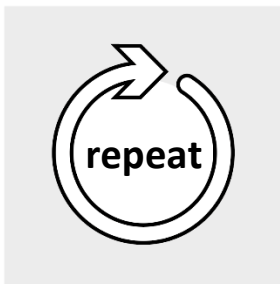


Lift your thumb off the plunger head. The needle will automatically move back inside the syringe body and lock into place.

- Place a dry cotton ball or gauze pad over the injection area for a few seconds. **Do not** rub the injection area. If needed, cover the injection area with a small bandage.
- There may be a small amount of blood or liquid where you injected. This is normal.

Throw away the used Adtralza pre-filled syringe in a puncture resistant (sharps) container. **See Step 5 “DISPOSING OF ADTRALZA”.**

## STEP 4: INJECTING THE NEXT SYRINGE



**To get your full prescribed dose, you will need to give more than 1 injection.**

- To get your full initial dose of **600 mg**, you will need to give **4** injections.
- To get your full maintenance dose of **300 mg**, you will need to give **2** injections.

**Get a new Adtralza pre-filled syringe and repeat Steps 3 and 5 for each injection you need to give for your full prescribed dose.**

**Note**

Make sure each injection is at least 3 cm from the previous injection site and within the same body area.

**STEP 5: DISPOSING OF ADTRALZA**



- Put the used Adtralza pre-filled syringes in a puncture resistant (sharps) container right away after use.
  - **Do not** throw away the Adtralza pre-filled syringes in your household trash.
  
- If you do not have a puncture resistant (sharps) container, you can use a household container that is:
  - made of heavy-duty plastic,
  - can be closed with a tight-fitting, puncture-proof lid, without sharps being able to come out,
  - upright and stable during use,
  - leak-proof, and
  - properly labeled to warn of hazardous waste inside the container.
  
- When your puncture resistant (sharps) container is almost full, you will need to follow your community guidelines for the right way to get rid of the container.
  
- **Do not** recycle your used puncture resistant (sharps) container.

Last Revised: October 13, 2021