AUSTRALIAN PRODUCT INFORMATION – XIIDRA® (Lifitegrast) eye drops

▼ 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 www.tga.gov.au/reporting-problems

1 NAME OF THE MEDICINE

Lifitegrast.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

XIIDRA eye drops contains lifitegrast in the concentration of 50 mg/mL (5%), solution. It is preservative-free.

For the full list of excipients, see Section 6.1 LIST OF EXCIPIENTS.

3 PHARMACEUTICAL FORM

Eye drops, solution.

XIIDRA is sterile, preservative-free, clear, colourless to slightly coloured solution with a pH range of 7.0 – 8.0 and an osmolality range of 200 – 330 mOsmol/kg.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

XIIDRA is indicated for the treatment of moderate to severe dry eye disease in adults for whom prior use of artificial tears has not been sufficient.

4.2 DOSE AND METHOD OF ADMINISTRATION

Adults and elderly
Instil one drop of XIIDRA in affected eye(s) using a single-use container per administration, twice a day.

Paediatric population
There is no relevant use of XIIDRA in children and adolescents aged below 18 years old in the treatment of dry eye disease.

Method of administration
For ophthalmic use only. The single-dose container should be used for one dose only and discarded immediately after use.

Contact lenses should be removed prior to the administration of XIIDRA and may be reinserted 15 minutes following administration.

4.3 CONTRAINDICATIONS

XIIDRA is contraindicated in patients with hypersensitivity to lifitegrast or any of its excipients (see Section 6.1 LIST OF EXCIPIENTS).

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

It is recommended for prescribers to perform a comprehensive eye examination to determine the aetiology of the symptoms and treat any reversible underlying conditions that are not caused by the dry eye disease condition, prior to initiating treatment with lifitegrast.

Hypersensitivity
Hypersensitivity reactions are possible with XIIDRA. Rarely, allergic-type hypersensitivity reactions, including anaphylaxis, have been reported with post marketing reports for XIIDRA. Immediately discontinue administration and initiate appropriate treatment if hypersensitivity reactions occur.

Paediatric use
The safety and efficacy of XIIDRA have not been established in paediatric patients. There have been no clinical studies in patients aged less than 18 years.

Use in the elderly
No overall differences in safety or effectiveness have been observed between elderly and younger patients.

Effects on laboratory tests
No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Due to the low systemic absorption, it is unlikely that lifitegrast contributes to systemic drug interactions. No *in vivo* interaction studies have been performed.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility
No human data on the effect of lifitegrast on fertility are available. In rats, IV administration of lifitegrast had no effect on male or female fertility at doses yielding systemic exposure (plasma AUC) thousands of times higher than in patients at the maximum recommended human dose.

Use in pregnancy
(Category B1)
There are no or limited amount of data from the use of lifitegrast in pregnant women.

Studies in rats and rabbits, involving IV administration of lifitegrast at doses yielding systemic exposures vastly in excess of that at the maximum recommended human dose, have shown no evidence of teratogenicity or other adverse effects on embryofoetal development.

The use of XIIDRA may be considered during pregnancy, if necessary.

Use in lactation
It is not known whether lifitegrast, or any of its metabolites, are excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when XIIDRA is administered to a breast-feeding woman.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

XIIDRA may cause some temporary blurring of vision after drops are administered, which could affect the ability to drive and use machines.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Clinical Trials
In clinical studies of dry eye disease, 1401 subjects received at least 1 dose of lifitegrast (1287 of which received lifitegrast 5%). The majority of subjects (84%) had ≤3 months of treatment exposure. However, 177 subjects were exposed to lifitegrast for >6 months and 170 subjects were exposed to lifitegrast for approximately 12 months (defined as ≥355 days). The lifitegrast population was predominantly female (77%) and white (84%).

The incidence rates of adverse reactions listed in Table 1 below were derived from vehicle-controlled trials of up to one year duration in subjects receiving XIIDRA 5% lifitegrast.

The most common ocular adverse reactions were eye irritation (18%), eye pain (12%) and instillation site reactions (12%); the majority of ocular adverse reactions were mild and transient in nature. The most common non-ocular adverse reaction was dysgeusia (14%).

Table 1: Adverse Reactions Reported in Clinical Trials

	XIIDRA* % (N=1287)	**Vehicle % (N=1177)**
Nervous System Disorders**		
Headache	2	1
Eye Disorders**		
Eye irritation	18	4
Eye pain	12	3
Eye pruritus	5	2
Lacrimation increased	4	1
Vision blurred	3	1
Gastrointestinal Disorders		
Dysgeusia	14.5	0.3
General Disorders and Administration Site Conditions		
Instillation site reactions	12	2

* Lifitegrast 5%.
** Some preferred terms were combined to capture similar medical concepts (i.e., eye irritation and instillation site irritation; eye pain and instillation site pain; eye pruritus and instillation site pruritus; lacrimation increased and instillation site lacrimation; and headache and tension headache).

SONATA Safety Study
The safety of lifitegrast, administered twice daily, was studied in a randomised, double-masked, vehicle-controlled study in 332 subjects with dry eye disease for one year (defined as ≥355 days). Subjects were randomised to lifitegrast 5% or vehicle in a 2:1 ratio (lifitegrast n=221; vehicle n=111). After Day 14, subjects were allowed to use artificial tears, topical ophthalmic/nasal antihistamines, steroids and mast cell stabilisers. The safety profile of lifitegrast 5% over the one year period was similar to that seen in the 12-week dry eye disease studies.

Among the subjects in the one year study who responded to a question on artificial tear use, a lower proportion of subjects in the lifitegrast group used artificial tears at any time during the study: 64 out of 195 (32.8%) lifitegrast subjects compared with 43 out of 98 (43.9%) vehicle subjects.

Post-marketing surveillance

Serious Adverse Drug Reactions from post-marketing experience for which the incidence cannot be determined:

Table 2: Hypersensitivity Adverse Reactions Reported Post-marketing

MedDRA System Organ Class Preferred Term
Eye disorders
Conjunctivitis allergic
Gastrointestinal Disorders
Swollen tongue
Immune system disorders
Anaphylactic reaction
Hypersensitivity
Type IV hypersensitivity reaction
Respiratory, thoracic and mediastinal disorders
Asthma
Dyspnoea
Pharyngeal oedema
Respiratory distress
Skin and subcutaneous tissue disorders
Angioedema
Dermatitis allergic

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 www.tga.gov.au/reporting-problems

4.9 OVERDOSE

There is no information regarding overdose in patients taking lifitegrast.

For more information on the management of overdose, contact the Poisons Information Centre telephone: 131126 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action
In vitro evaluation demonstrated that lifitegrast targets the interaction between lymphocyte function-associated antigen-1 (LFA-1), a cell surface protein found on leukocytes, and intercellular adhesion molecule-1 (ICAM-1), its cognate ligand. LFA-1 is a heterodimer integrin protein that mediates cell-to-cell interactions essential to immune and inflammatory response mechanisms. Its expression is restricted to leukocytes (neutrophil, eosinophil, basophil, monocyte, T and B lymphocyte), where it functions both as a key adhesion receptor and as a signal-transducing molecule.

ICAM-1 is a member of the immunoglobulin superfamily and is normally expressed in low levels on leukocytes, endothelium and epithelium. Its expression level can greatly increase in response to the presence of inflammatory cytokines. Notably, conjunctival biopsies from patients with dry eye disease (DED) exhibit significant expression of ICAM-1 compared with normal controls.

In vitro studies indicate that T-cells play a critical role in the development of DED. ICAM-1 has been shown to facilitate many T-cell dependent immune functions through its interaction with LFA-1, including adhesion of T-cells to endothelial and epithelial cells, T-cell recruitment and trafficking, proliferation, and the release of inflammatory cytokines. ICAM-1/LFA-1 interaction supports the formation of an immunological synapse between T-cells and antigen presenting cells (APC), such as dendritic cells; inducing T-cell activation and the release of cytokines that promote ocular inflammation, a substantial component of DED pathophysiology.

Clinical trials

The effects of lifitegrast treatment on the signs and/or symptoms of DED were assessed in a total of 2247 subjects in four 12-week, randomised, multi-centre, double-masked, vehicle-controlled studies. In all studies, subjects were randomised to XIIDRA 5% or vehicle in 1:1 ratio; Study 1: n=58, 58; Study 2: n=293, 295; Study 3: n=358, 360; and Study 4: n=355, 356. Study 1 also included 2 lower strengths of lifitegrast; subjects were randomised to the four groups in equal ratios. In these studies, the use of concomitant topical ophthalmic medicinal products including artificial tears, steroids and antihistamines were not permitted.

The majority of subjects were 55 years of age and older (68%), white (85%) and female (76%). Although the number of subjects in subgroup categories were low, there were no apparent differences in age or gender in response to treatment with XIIDRA.

Key inclusion criteria: In all studies, subjects reported a history of dry eye in both eyes at study entry. In Studies 1 and 2, subjects were selected for enrolment after exposure to a controlled adverse environment; in Studies 3 and 4 all subjects had a history of artificial tear use and met a minimum symptom threshold (EDS ≥40).
Furthermore, subjects were required to have minimum sign thresholds such as Inferior Corneal Staining Score (ICSS) with fluorescein (a score of at least 2.0 on a scale of 0-4 in one eye) and non- anaesthetised Schirmer's Tear Test, STT, (between 1 and 10 mm).

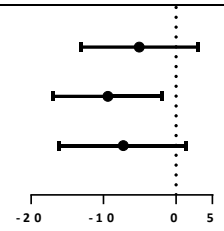
Key exclusion criteria: Patients with dry eye disease not primarily attributable to aqueous deficiency were ineligible to enroll in the lifitegrast clinical trials. For example, patients using ocular or systemic medications that cause ocular drying were excluded from

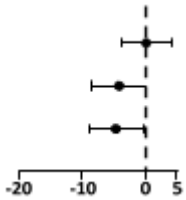
participating, as were patients with ocular conditions such as lid and lid margin disorders (e.g., blepharitis including staphylococcal, demodex, or seborrheic; meibomian gland disease, excessive lid laxity, floppy eyelid syndrome, ectropion, entropion); conjunctival pathology (scarring, xerosis, irradiation, alkali burns, manifestations of Stevens-Johnson syndrome, cicatrical pemphigoid, vitamin A deficiency, advanced conjunctivochalasis, allergic conjunctivitis); corneal disorders (Salzmann's nodular degeneration), disordered ocular sensation (post-LASIK or refractive surgery, postoperative status, advanced keratitis), asthenopia-related conditions, glaucoma, diabetic retinopathy, follicular conjunctivitis, iritis, uveitis, wet- exudative age-related macular, degeneration retinal vein occlusion, tinea versicolor, active ocular inflammation (unrelated to DED), recent ocular infection and/or ocular herpes.

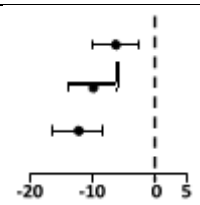
Effects on Symptoms of DED

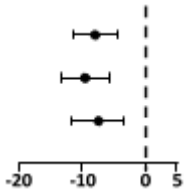
Eye dryness Score (EDS) was rated by patients using a visual analogue scale (VAS) (0 = no discomfort, 100 = maximal discomfort) at each study visit. The average baseline EDS was between 40 and 70. A larger reduction in EDS favouring XIIDRA was observed in all studies at Day 42 and Day 84, and an improvement was apparent at Day 14 in a majority of patients studied (see Figure 1).

Figure 1: Mean Change (SD) from Baseline and Treatment Difference (XIIDRA – Vehicle) in Eye Dryness Score in 12-Week Studies in Patients with Dry Eye Disease

Eye Dryness Score in Study 1				
	Vehicle	**XIIDRA**	**Difference [1]**	
Visit	**(N = 58)**	**(N = 58)**	**(95% CI)**	
Baseline	51.8 (23.55)	51.6 (24.69)		
Day 14	-3.9 (25.46)	-8.9 (21.72)	-5.1 (-13.1, 3.0)	
Day 42	-7.9 (19.60)	-17.3 (24.96)	-9.4 (-17.0, -1.9)	
Day 84	-7.2 (25.29)	-14.4 (25.36)	-7.3 (-16.1, 1.4)	
				←Favours XIIDRA

Eye Dryness Score in Study 2				
	Vehicle	**XIIDRA**	**Difference [1]**	
Visit	**(N = 295)**	**(N = 293)**	**(95% CI)**	
Baseline	41.6 (29.69)	40.2 (28.64)		
Day 14	-7.5 (29.01)	-6.7 (27.36)	0.1 (-3.9, 4.1)	
Day 42	-9.1 (30.03)	-12.6 (30.71)	-4.2 (-8.5, 0.0)	
Day 84	-11.2 (28.78)	-15.2 (31.48)	-4.7 (-8.9, -0.4)	
				←Favours XIIDRA

Eye Dryness Score in Study 3				
	Vehicle	**XIIDRA**	**Difference [1]**	
Visit	**(N = 360)**	**(N = 358)**	**(95% CI)**	
Baseline	69.2 (16.76)	69.7 (16.95)		
Day 14	-13.1 (24.04)	-19.7 (26.49)	-6.4 (-10.0, -2.8)	
Day 42	-18.2 (26.51)	-28.3 (27.69)	-9.9 (-13.8, -6.1)	
Day 84	-22.8 (28.60)	-35.3 (28.40)	-12.3 (-16.4, -8.3)	
				←Favours XIIDRA

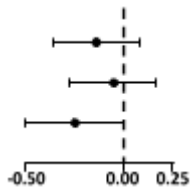
Eye Dryness Score in Study 4				
	Vehicle	**XIIDRA**	**Difference [1]**	
Visit	**(N = 356)**	**(N = 355)**	**(95% CI)**	
Baseline	69.0 (17.08)	68.3 (16.88)		
Day 14	-14.9 (22.35)	-22.7 (25.41)	-7.9 (-11.4, -4.5)	
Day 42	-23.7 (25.98)	-33.0 (27.46)	-9.6 (-13.4, -5.8)	
Day 84	-30.5 (28.03)	-37.7 (28.91)	-7.5 (-11.6, -3.5)	
				←Favours XIIDRA

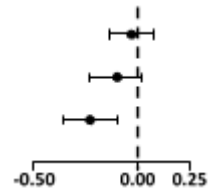
[1] Based on ANCOVA model adjusted for baseline value in Study 1, and ANCOVA model adjusted for baseline value and randomisation stratification factors in Studies 2-4. All randomised and treated patients were included in the analysis and missing data were imputed using last-available data. In Study 1, one XIIDRA treated subject who did not have a baseline value was excluded from analysis.

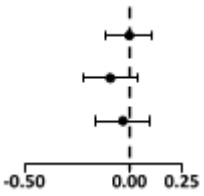
Effects on Signs of DED

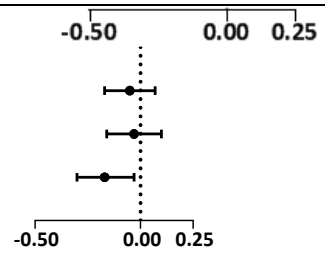
Inferior corneal staining score (ICSS) using fluorescein (0 = no staining, 1 = few/rare punctate lesions, 2 = discrete and countable lesions, 3 = lesions too numerous to count but not coalescent, 4 = coalescent) was recorded at each study visit. The average baseline ICSS was approximately 1.8 in Studies 1 and 2 and 2.4 in Studies 3 and 4. At Day 84, a larger reduction in ICSS favouring XIIDRA was observed in three of the four studies (see Figure 2).

Figure 2: Mean Change (SD) from Baseline and Treatment Difference (XIIDRA – Vehicle) in Inferior Corneal Staining Score in 12-Week Studies in Patients with Dry Eye Disease.

Inferior Corneal Staining Score in Study 1				
	Vehicle	**XIIDRA**	**Difference [1]**	
Visit	**(N = 58)**	**(N = 58)**	**(95% CI)**	
Baseline	1.65 (0.513)	1.77 (0.515)		
Day 14	0.24 (0.709)	0.06 (0.522)	-0.14 (-0.36, 0.08)	
Day 42	0.19 (0.694)	0.08 (0.591)	-0.05 (-0.28, 0.17)	
Day 84	0.38 (0.785)	0.04 (0.745)	-0.25 (-0.50, -0.00)	
				←Favours XIIDRA

Inferior Corneal Staining Score in Study 2				
	Vehicle	**XIIDRA**	**Difference [1]**	
Visit	**(N = 295)**	**(N = 293)**	**(95% CI)**	
Baseline	1.81 (0.599)	1.84 (0.597)		
Day 14	0.08 (0.771)	0.04 (0.734)	-0.03 (-0.14, 0.08)	
Day 42	-0.02 (0.893)	-0.14 (0.861)	-0.10 (-0.23, 0.02)	
Day 84	0.17 (0.819)	-0.07 (0.868)	-0.23 (-0.36, -0.10)	
				←Favours XIIDRA

Inferior Corneal Staining Score in Study 3				
	Vehicle	**XIIDRA**	**Difference [1]**	
Visit	**(N = 360)**	**(N = 358)**	**(95% CI)**	
Baseline	2.40 (0.722)	2.39 (0.763)		
Day 14	-0.48 (0.798)	-0.48 (0.802)	-0.00 (-0.11, 0.11)	
Day 42	-0.60 (0.899)	-0.69 (0.918)	-0.09 (-0.22, 0.04)	
Day 84	-0.71 (0.943)	-0.73 (0.926)	-0.03 (-0.16, 0.10)	
				←Favours XIIDRA

Inferior Corneal Staining Score in Study 4				
	Vehicle	**XIIDRA**	**Difference [1]**	
Visit	**(N = 356)**	**(N = 355)**	**(95% CI)**	
Baseline	2.46 (0.746)	2.46 (0.681)		
Day 14	-0.44 (0.775)	-0.49(0.914)	-0.05 (-0.17, 0.07)	
Day 42	-0.66 (0.927)	-0.69 (0.941)	-0.03 (-0.16, 0.1)	
Day 84	-0.63 (0.911)	-0.80 (0.939)	-0.17 (-0.30, -0.03)	
				←Favours XIIDRA

[1] Based on ANCOVA model adjusted for baseline value in Study 1, and ANCOVA model adjusted for baseline value and randomisation stratification factors in Studies 2-4. All randomised and treated patients were included in the analysis and missing data were imputed using last-available data. In Study 2, one Vehicle treated subject who did not have a study eye designated was excluded from analysis.

Subgroup analysis of patients with moderate to severe dry eye disease

Study 3 included 413 subjects (209 vehicle-treated and 204 lifitegrast-treated) with moderate to severe DED (baseline EDS ≥60 and ICSS >1.5). In this subgroup, there was a difference between lifitegrast-treated subjects and vehicle-treated subjects that achieved both

benchmarks of clinical significance (≥30% improvement in EDS and 1 point improvement in ICSS), with 40.7% vs. 25.8% for lifitegrast vs. vehicle respectively (p=0.0014).

Study 4 included 390 subjects (195 per treatment arm) with moderate to severe DED (baseline EDS ≥60 and ICSS >1.5). In this subgroup, there was a difference between lifitegrast-treated subjects and vehicle-treated subjects that achieved both benchmarks of clinical significance (≥30% improvement in EDS and 1 point improvement in ICSS), with 42.6% vs. 29.2% for lifitegrast vs. vehicle respectively (p=0.0061).

5.2 PHARMACOKINETIC PROPERTIES

Absorption

Tear

When administered twice daily for 10 days, tear pharmacokinetic parameters for lifitegrast 5% were: C_{max} = 91413 ±43308 ng/mL, AUC_{0-8} hours = 127697 ±66418 ng·h/mL and T_{max} 0.44 ±0.22 hours. There was no accumulation of lifitegrast in tears during twice daily and three times daily administration of lifitegrast.

Plasma

Lifitegrast 5% solution is rapidly absorbed into the plasma with a mean T_{max} of 0.09 ±0.01 hours (approximately 5.4 minutes) when administered twice daily for 10 days. Lifitegrast is also rapidly eliminated from plasma with lifitegrast concentrations typically being measureable for only up to 30 minutes after administration. Systemic exposure to lifitegrast is extremely low with C_{max} = 1.70 ±1.36 ng/mL and AUC_{0-8} hours = 0.69 ±0.47 ng·h/mL when administered twice daily for 10 days; therefore lifitegrast disposition half-life ($t_{½}$) cannot be determined accurately. The overall plasma pharmacokinetic profile demonstrated no systemic accumulation of lifitegrast when administered twice daily over 10 days.

Distribution

Plasma protein binding by lifitegrast is high in humans (98.9%), and chiefly albumin. Systemically absorbed lifitegrast is subject to hepatic uptake via various transporters.

Metabolism

An *in vitro* study in human hepatocytes indicated that lifitegrast is only minimally metabolised by CYP enzymes.

Excretion

Excretion in rats and dogs was shown to be mostly via the faeces (as unchanged drug) and involve biliary transport. Urinary excretion was only a minor route in laboratory animals.

5.3 PRECLINICAL SAFETY DATA

Pharmacology

Studies performed *in vitro* using a human T-cell line have demonstrated that lifitegrast inhibits T-cell adhesion to ICAM-1 with nanomolar potency, and inhibits the secretion of key inflammatory cytokines, including T-cell regulating cytokines IL-2 and IL-4 and several other cytokines associated with the clinical severity of dry eye (IL-1α, IL-1β, IL-10, IFN-γ, MIP-1α and TNF- α). Topical ocular administration of lifitegrast (≥ 0.1%) has also been shown to reduce neutrophil infiltration to the corneal stroma in a mouse model of corneal inflammation. These data suggest that by targeting the LFA-1/ICAM-1 interaction, lifitegrast reduces elevations in cytokines that have been correlated with the development and perpetuation of DED.

Ocular distribution studies in rats, rabbits and dogs showed highest levels of lifitegrast in the conjunctive and cornea following topical administration, with drug levels in posterior ocular tissues and the aqueous and vitreous humour markedly lower.

No relevant inhibition of key CYP isozymes (1A2, 2B6, 2C8, 2C9, 2C19, 2D6 or 3A4) was observed with lifitegrast at therapeutic concentrations *in vitro*. Lifitegrast was identified as a substrate for the OATP1A2 and OATP2B1 transporters, and potentially OATP1B1, but not of OATP2A1, P-glycoprotein or BCRP.

Genotoxicity
Lifitegrast was not mutagenic in bacteria in the *in vitro* Ames assay and was not clastogenic in the *in vivo* mouse micronucleus assay. An increase in chromosomal aberrations was observed with lifitegrast in an in vitro clastogenicity assay using Chinese hamster ovary cells. This occurred only at the highest concentration tested in the absence of metabolic activation, and in the context of significant cytotoxicity.

Carcinogenicity
Systemic exposure following topical ocular administration of lifitegrast is very low, therefore, long-term animal studies have not been conducted to determine the carcinogenic potential of lifitegrast.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

XIIDRA contains the following inactive ingredients:
- sodium chloride,
- dibasic sodium phosphate,
- sodium thiosulfate pentahydrate,
- sodium hydroxide and/or hydrochloric acid (for pH adjustment) and
- water for injections.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

24 months from date of manufacture.

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 below 25°C.

After opening, store single-dose containers in the original aluminium pouch in order to protect from light.

6.5 NATURE AND CONTENTS OF CONTAINER

XIIDRA is supplied in low density polyethylene (LPDE) single-use 0.2 mL ampoules, packaged in foil pouches (5 single-use ampoules per pouch). It is available in packs of 60 single-dose ampoules or 20 single-dose ampoules (Sample Pack).

Each single-use container contains 0.2 mL solution corresponding to 10 mg lifitegrast.

Pack size
Pack size: 60 single-dose containers; 20 single-dose containers (Sample Pack).

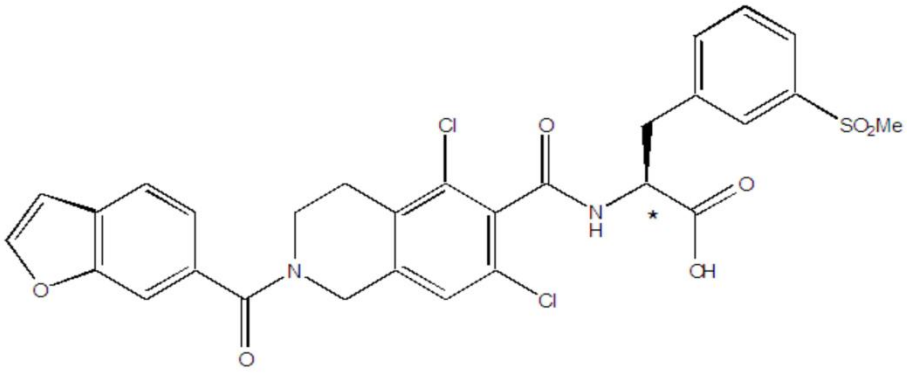
6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

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

6.7 PHYSICOCHEMICAL PROPERTIES

The active ingredient, lifitegrast, is a white to off-white powder which is soluble in water.

Chemical structure



* Chiral centre

Chemical name
The chemical name for lifitegrast is (S)-2-(2-(benzofuran-6-carbonyl)-5,7-dichloro-1,2,3,4-tetrahydroisoquinoline-6-carboxamido)-3-(3-(methylsulfonyl) phenyl)propanoic acid.

Formula
$C_{29}H_{24}Cl_2N_2O_7S$

Molecular weight
615.5

CAS number
1025967-78-5

7 MEDICINE SCHEDULE (POISONS STANDARD)

Prescription Only Medicine (S4).

8 SPONSOR

Novartis Pharmaceuticals Australia Pty Limited
ABN 18 004 244 160
54 Waterloo Road
Macquarie Park NSW 2113
®= Registered Trademark

9 DATE OF FIRST APPROVAL

21 January 2019

10 DATE OF REVISION

8 April 2020

Summary table of changes

Section Changed	Summary of new information
8	Sponsorship details for Novartis included following sponsorship transfer on 20/09/2019

Internal Document Code
Xii080420i based on PI supplied by Shire.