NOVARTIS

Regulatory Affairs

Lifitegrast

Summary of the Xiidra Safety Risk Management Plan

Active substance(s) (INN or common name):	*Lifitegrast*
Product(s) concerned (brand name(s)):	*Xiidra*
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Disclaimer:
The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimise them. The RMP summary of “Bezeichnung des Arzneimittels” is a concise document and does not claim to be exhaustive. As the RMP is an international document, the summary might differ from the “Arzneimittelinformation / Information sur le médicament” approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorization. Please note that the reference document which is valid and relevant for the effective and safe use of “Bezeichnung des Arzneimittels” in Switzerland is the “Arzneimittelinformation/ Information sur le médicament” (see www.swissmedic.ch) approved and authorized by Swissmedic. “Name of the marketing authorisation holder” is fully responsible for the accuracy and correctness of the content of the published summary RMP of “Bezeichnung des Arzneimittels”.

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SUMMARY OF ACTIVITIES IN THE RISK MANAGEMENT PLAN BY PRODUCT

VI.1 Elements of Summary Tables in the Public Assessments Reports

VI.1.1 Summary Table of Safety Concerns

Table 1: Summary of Safety Concerns	
Important identified risks	Hypersensitivity
Important potential risks	None
Missing information	Use in children Use in pregnant or breast-feeding women Off-label use

VI.1.2 Table of Ongoing and Planned Studies in the Post-authorization Pharmacovigilance Development Plan

Not applicable.

VI.1.3 Summary of Post-authorization Efficacy Development Plan

Not applicable.

VI.1.4 Summary Table of Risk Minimization Measures

Table 2: Summary of Risk Minimization Measures		
Safety Concern	**Routine Risk Minimization Measures**	**Additional Risk Minimization Measures**
Hypersensitivity	Text in CCDS Sections 4 and 7	None
Use in children	Text in CCDS Section 10.3	None
Use in pregnant or breast-feeding women	Text in CCDS Sections 10.1 and 10.2	None
Off-label use	Text in CCDS Section 2	None

CCDS=Company Core Data Sheet

VI.2 Elements for a Public Summary

VI.2.1 Overview of Disease Epidemiology

Dry eye disease is a common condition of the tears and ocular surface that results in symptoms of discomfort, disturbance in vision and tear production and possible damage to the ocular surface. Overall in the US approximately 7.8% of women and 4.3% of men aged 50 years and older have symptoms of dry eyes. In Europe, estimates range from 5.9% in Italy to 27% in the UK. Some of the key risk factors include age 50 years and older, being a woman, use of certain medications (antihistamines, diuretics), contact lens, low levels of male sex hormones, and environmental factors such as low humidity, high air speed. If not treated, the chronic nature of dry eye syndrome can lead to despair, depression, reduced productivity, and job disability.

VI.2.2 Summary of Treatment Benefits

Lifitegrast demonstrated effectiveness in reducing clinical symptoms measured by the "eye dryness score" (EDS). Improvement in EDS symptoms in patients treated with lifitegrast compared to placebo (contains no medicine) was observed as early as Day 14 in some clinical studies. In patients with moderate to severe eye dryness at baseline, lifitegrast demonstrated benefit in eye dryness and eye discomfort, which are among the most common complaints of dry eye disease patients that lead these patients to seek medical treatment.

Lifitegrast also demonstrated effectiveness in reduction of clinical signs as assessed in cornea using the "inferior corneal staining score" (ICSS). A treatment response in the change in ICSS was observed indicating a clinical benefit of lifitegrast 5% over placebo. A reduction in ICSS was also observed in patients who had previously used artificial tears.

Lifitegrast was well tolerated in both short-term and long-term studies in patients with dry eye disease.

VI.2.3 Unknowns Relating to Treatment Benefits

Little information is available on the use of lifitegrast in children and adolescents and in pregnant or breast-feeding women. Caution is recommended in these patients and lifitegrast should always be taken in accordance with the label.

VI.2.4 Summary of Safety Concerns

Table 3: Important Identified Risks

Risk	What is Known	Preventability
Allergic or hypersensitivity reactions	Patients with known allergic or hypersensitivity reactions to lifitegrast and/or its inactive ingredients are expected to be at increased risk of an allergic reaction occurring with lifitegrast treatment. Lifitegrast, and one of its inactive ingredients, contains sulfur. In patients with a history of "sulfa" or sulfur hypersensitivity (or allergy) there may be an increased risk of an allergic reaction (including strong allergic reactions) to lifitegrast and/or its inactive ingredients. Post-marketing reports of hypersensitivity reactions have been received, including anaphylaxis (allergic shock) in a patient with a history of an unspecified allergic reaction to an unspecified "sulfa" medication.	The use of lifitegrast should be avoided in patients with known hypersensitivity (allergic reactions) to lifitegrast or to any of its inactive ingredients. If a patient has had anaphylaxis or other strong hypersensitivity (allergic reactions) to lifitegrast, or to "sulfa"/sulfur containing medications it should be noted in their medical records and/or solicited by a thorough patient interview, and the use of lifitegrast should be avoided. If a patient is assessed to be at high risk, the product should be administered only when the medical need is assessed in context of the patient's risk level, and where supportive care is available for potentially life-threatening reactions.

Table 3: Important Identified Risks		
Risk	**What is Known**	**Preventability**
	It is not known what sulfur containing compound hypersensitivity medical history may be associated with increased risk of hypersensitivity reaction, if any, to lifitegrast.	

Table 4: Missing Information	
Risk	**What is Known**
Use in children and adolescents	Clinical studies have not been performed in children and adolescents. Dry eye disease mainly develops in adults over the age of 50.
Use in pregnant or breast-feeding women	There are no studies of lifitegrast use in pregnant women. It is not known whether lifitegrast is transferred into human breast milk.
Use different from that according to the indication in the package leaflet	There is a possibility that lifitegrast could be used for indications that are not approved or in unapproved age groups such as children and adolescents.

VI.2.5 Summary of Risk Minimization Measures by Safety Concern

All medicines have a label which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimizing them. An abbreviated version of this in lay language can be provided in the form of a patient information leaflet. The measures in these documents are known as routine risk minimization measures.

This medicine has no additional risk minimization measures.

VI.2.5.1 Safety Concern in Lay Terms (Medical Term)

Not applicable.

VI.2.6 Planned Post-authorization Development Plan

Not applicable.

VI.2.6.1 Studies which are a Condition of the Marketing Authorization

Not applicable.