

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Rhokiinsa 200 micrograms/ml eye drops, solution.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of solution contains 200 micrograms netarsudil (as mesylate).

Excipient(s) with known effect:

Each ml of solution contains 150 micrograms benzalkonium chloride.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Eye drops, solution (eye drops).

Clear solution, pH 5 (approximately).

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Rhokiinsa is indicated for the reduction of elevated intraocular pressure (IOP) in adult patients with primary open-angle glaucoma or ocular hypertension.

4.2 Posology and method of administration

Treatment with Rhokiinsa should only be initiated by an ophthalmologist or a healthcare professional qualified in ophthalmology.

Posology

Use in adults, including the elderly

The recommended dosage is one drop in the affected eye(s) once daily in the evening. Patients should not instill more than one drop in the affected eye(s) each day.

If one dose is missed, treatment should continue with the next dose in the evening.

Paediatric population

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

Method of administration

For ocular use.

No data on potential interactions specific to netarsudil is currently available (see section 4.5). If netarsudil is to be used concomitantly with other topical ophthalmic medicinal products, each medicinal product should be administered at least five (5) minutes apart. Due to netarsudil's vasodilating properties, other eye drops should be administered before. Eye ointments should be administered last.

Contact lenses should be removed prior to instillation of netarsudil and may be reinserted 15 minutes following its administration (see section 4.4).

The tip of the dispensing container should avoid contacting the eye, surrounding structures, fingers, or any other surface in order to avoid contamination of the solution. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions.

4.3 Contraindications

Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Ocular effects

Twice a day dosing is not well tolerated and is not recommended. Netarsudil dosed twice daily provided slightly larger IOP reductions, but had a less favorable safety profile as reflected in a higher rate and increased severity of ocular adverse reactions. Twice a day dosing was also associated with a higher discontinuation rate due to adverse reactions (53.8%) during a 12-month study. It is therefore recommended to dose netarsudil once daily.

Benzalkonium chloride content

This medicinal product contains benzalkonium chloride.

Benzalkonium chloride has been reported to cause eye irritation, symptoms of dry eyes and may affect the tear film and corneal surface and is known to discolour soft contact lenses. It should be used with caution in dry eye patients and in patients where the cornea may be compromised. Patients should be monitored in case of prolonged use.

The efficacy of netarsudil has not been studied beyond 12 months.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no or limited amount of data from the use of netarsudil in pregnant women. No effects during pregnancy are anticipated, since systemic exposure to netarsudil is negligible (see section 5.2). Animal studies with intravenous administration do not indicate direct or indirect harmful effects with respect to reproductive toxicity at clinically relevant exposures (see section 5.3). Rhokiinsa should not be used during pregnancy unless the clinical condition of the woman requires treatment with netarsudil.

Breast-feeding

It is unknown whether netarsudil/metabolites are excreted in human milk. However, while no effects on the breastfed newborn/infant are anticipated since the systemic exposure of breast-feeding women to netarsudil is expected to be negligible, no relevant clinical data are available (see section 5.2). A

decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Rhokiinsa therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

Fertility

There are no data on the effects of netarsudil on male or female fertility. However, no effects are anticipated, since systemic exposure to netarsudil is negligible (see section 5.2).

4.7 Effects on ability to drive and use machines

Rhokiinsa has negligible influence on the ability to drive and use machines.

If transient blurred vision occurs at instillation, the patient should wait until the vision clears before driving or using machines.

4.8 Undesirable effects

Summary of the safety profile

The most common ocular adverse reaction observed is conjunctival hyperemia which was reported in 51% of patients. Other ocular adverse reactions reported are: cornea verticillata (17%), instillation site pain (17%), and conjunctival haemorrhage (8%). Instillation site erythema (8%), corneal staining (7%), blurred vision (6%), increased lacrimation (6%) and erythema of eyelid (5%) were also reported.

Tabulated list of adverse reactions

The following adverse reactions have been reported with netarsudil, dosed once daily. Reactions are classified according to the convention: very common ($\geq 1/10$), common ($\geq 1/100$ to $< 1/10$), uncommon ($\geq 1/1,000$ to $< 1/100$), rare ($\geq 1/10,000$ to $< 1/1,000$), very rare ($< 1/10,000$) or not known (cannot be estimated from the available data).

| System Organ Classification | Frequency | Adverse reactions |
|------------------------------------|------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Immune system disorders | Uncommon | hypersensitivity |
| Nervous system disorders | Common | headache |
| | Uncommon | dizziness, visual field defect |
| Eye disorders | Very common | conjunctival hyperaemia ¹ , cornea verticillata ¹ , instillation site pain |
| | Common | conjunctival haemorrhage, vision blurred, lacrimation increased, erythema of eyelid, eye pruritis, eye irritation, visual acuity reduced, eyelid oedema, punctate keratitis, conjunctival oedema, foreign body sensation in eyes, conjunctivitis, conjunctivitis allergic, photophobia, eyelid pruritus, eye pain, corneal opacity, dry eye, eye discharge, |

| System Organ Classification | Frequency | Adverse reactions |
|-------------------------------------------------|-----------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| | | instillation site erythema, instillation site discomfort, instillation site pruritis, vital dye staining cornea present, intraocular pressure increased |
| | Uncommon | ocular hyperaemia, blepharitis, corneal disorder, eyelid margin crusting, eye allergy, conjunctival follicles, ocular discomfort, eye swelling, corneal deposits, eyelid disorder, meibomian gland dysfunction, corneal pigmentation, diplopia, ectropion, lenticular opacities, noninfective conjunctivitis, abnormal sensation in the eye, asthenopia, episcleral hyperaemia, halo vision, keratitis, refraction disorder, anterior chamber flare, anterior chamber inflammation, blindness, conjunctival irritation, conjunctivochalasis, diabetic retinopathy, eczema eyelids, eyelid skin dryness, glaucoma, growth of eyelashes, iris adhesions, iris bombe, iritis, ocular hypertension, visual impairment, corneal dystrophy, instillation site foreign body sensation, instillation site irritation, glassy eyes, fatigue, instillation site dryness, instillation site oedema, instillation site paraesthesia, conjunctival staining, optic nerve cup/disc ratio increased, madarosis |
| Respiratory, thoracic and mediastinal disorders | Uncommon | nasal discomfort, rhinalgia |
| Skin and subcutaneous tissue disorders | Uncommon | dermatitis allergic, dermatitis contact, lichenification, petechiae |
| Musculoskeletal and connective tissue disorders | Uncommon | polychondritis |
| Injury, poisoning and procedural complications | Uncommon | excoriation |

¹ See *Description of selected adverse reactions* for further information

Description of selected adverse reactions

Conjunctival Hyperaemia

Conjunctival hyperaemia was the most frequently reported adverse reaction associated with netarsudil treatment in clinical trials and it is attributed to the vasodilation effect of the Rho kinase inhibitor drug class. Conjunctival hyperaemia was typically mild in severity and sporadic. However, there was a relatively small proportion of subjects with moderate or severe hyperaemia who discontinued treatment because of this adverse reaction (6.0% in Phase 3 clinical studies).

Cornea Verticillata

Cornea verticillata occurred in approximately 20% of the patients in controlled Phase 3 clinical studies. The cornea verticillata seen in netarsudil-treated patients were first noted at 4 weeks of daily dosing. This reaction did not result in any apparent visual functional changes in patients. The majority of cornea verticillata resolved upon discontinuation of treatment. The incidence of cornea verticillata was higher in certain subpopulations: elderly (≥ 65 years) versus non-elderly (24.8 vs. 15.9%); males versus females (24.4 vs. 18.4%) and in white versus other races (25.6 vs. 7.0%).

Special populations

Elderly subjects

With the exception of cornea verticillata (see above), no difference in the safety profile for Rhokiinsa has been observed between subjects aged <65 or ≥ 65 years.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Systemic exposure to netarsudil following topical ocular administration has been shown to be negligible. If topical overdose of netarsudil should occur, the eye(s) may be flushed with tap water. Treatment of an overdose would include supportive and symptomatic therapy.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Ophthalmologicals, antiglaucoma preparations and miotics, ATC code: S01EX05

Mechanism of action

Netarsudil, a Rho kinase inhibitor, is believed to reduce IOP by increasing outflow of aqueous humor. Studies in animal and man suggest that the main mechanism of action is increased trabecular outflow. These studies also suggest that netarsudil lowers IOP by reducing episcleral venous pressure.

Clinical efficacy and safety

A randomised, double-blind, multicentre Phase 3 clinical trial compared the efficacy and safety of netarsudil once daily with that of timolol maleate 0.5% twice daily in reducing IOP in a total of 708 patients with open-angle glaucoma or ocular hypertension. The median age of study participants was 65.5 years (range 18 to 91 years).

The study was designed to show non-inferiority of netarsudil when dosed once daily in the evening to timolol maleate 0.5% dosed twice daily in patients with a baseline IOP of >20 mmHg and <25 mmHg. The primary efficacy outcome measure was mean IOP at each of 9 timepoints measured at 08:00, 10:00 and 16:00 on day 15, day 43 and day 90. The non-inferiority margin applied was a difference in mean IOP ≤ 1.5 mmHg for all time points over all visits through 3 months and ≤ 1.0 mmHg at a majority of these time points. The IOP reduction with netarsudil dosed once daily was non-inferior to the effect of timolol 0.5% dosed twice daily in patients with baseline IOP of <25 mmHg (Table 1). Efficacy was also investigated in patients with baseline IOP ≥ 25 mmHg and <30 mmHg. Netarsudil demonstrated clinically relevant reductions in IOP at all timepoints, however non-inferiority to timolol was not demonstrated in this population with baseline IOP ≥ 25 mmHg and <30 mmHg (Table 2).

Table 1: Mean IOP by visit: PP population with baseline IOP <25 mmHg

| Study Visit and Time Point | | Netarsudil 0.02% Once daily | | Timolol 0.5% twice daily | | <u>Difference (95% CI)</u> <u>Netarsudil – Timolol</u> |
|----------------------------|-------|--------------------------------|-------|--------------------------|-------|-----------------------------------------------------------|
| | | N | IOP | N | IOP | |
| Baseline | 08:00 | 186 | 22.40 | 186 | 22.44 | |
| | 10:00 | 186 | 21.06 | 186 | 21.27 | |
| | 16:00 | 186 | 20.69 | 186 | 20.69 | |
| Day 15 | 08:00 | 184 | 17.68 | 183 | 17.51 | 0.17 (-0.43, 0.77) |
| | 10:00 | 181 | 16.55 | 183 | 16.71 | -0.16 (-0.73, 0.41) |
| | 16:00 | 181 | 16.32 | 183 | 16.92 | -0.60 (-1.16, -0.04) |
| Day 43 | 08:00 | 177 | 17.84 | 183 | 17.60 | 0.25 (-0.34, 0.83) |
| | 10:00 | 177 | 16.75 | 182 | 16.98 | -0.22 (-0.82, 0.37) |
| | 16:00 | 176 | 16.57 | 182 | 16.67 | -0.10 (-0.66, 0.46) |
| Day 90 | 08:00 | 167 | 17.86 | 179 | 17.29 | 0.56 (-0.02, 1.15) |
| | 10:00 | 166 | 16.90 | 179 | 16.69 | 0.21 (-0.37, 0.79) |
| | 16:00 | 165 | 16.73 | 179 | 16.80 | -0.07 (-0.68, 0.55) |

Table 2: Mean IOP by visit: PP population with baseline IOP ≥ 25 and <30 mmHg

| Study Visit and Time Point | | Netarsudil 0.02% Once daily | | Timolol 0.5% twice daily | | <u>Difference (95% CI)</u> <u>Netarsudil – Timolol</u> |
|----------------------------|-------|--------------------------------|-------|--------------------------|-------|-----------------------------------------------------------|
| | | N | IOP | N | IOP | |
| Baseline | 08:00 | 120 | 26.30 | 130 | 25.96 | |
| | 10:00 | 120 | 25.18 | 130 | 24.91 | |
| | 16:00 | 120 | 24.48 | 130 | 23.99 | |
| Day 15 | 08:00 | 118 | 21.57 | 129 | 20.15 | 1.42 (0.51, 2.34) |
| | 10:00 | 116 | 20.09 | 129 | 19.34 | 0.75 (-0.15, 1.64) |
| | 16:00 | 116 | 20.01 | 129 | 19.17 | 0.83 (0.00, 1.67) |
| Day 43 | 08:00 | 112 | 21.99 | 127 | 19.84 | 2.14 (1.16, 3.13) |
| | 10:00 | 109 | 20.33 | 127 | 19.19 | 1.15 (0.30, 1.99) |
| | 16:00 | 109 | 20.03 | 127 | 19.63 | 0.41 (-0.47, 1.29) |
| Day 90 | 08:00 | 94 | 21.71 | 121 | 19.91 | 1.79 (0.74, 2.85) |
| | 10:00 | 93 | 20.80 | 120 | 18.95 | 1.85 (0.89, 2.81) |
| | 16:00 | 93 | 20.31 | 120 | 18.94 | 1.37 (0.46, 2.28) |

The safety of netarsudil has been evaluated in clinical studies, including four well-controlled Phase 3 studies.

Approximately 75% of subjects included in the netarsudil treatment groups of Phase 3 studies were Caucasian and 24% Black or African American. Over half were aged ≥ 65 years. With the exception of the incidence of cornea verticillata, no other difference in safety profile was observed between races or age groups (see section 4.8).

Completion rates in Phase 3 studies were lower in the netarsudil treatment group when compared with the timolol maleate group. Subjects with known contraindications or hypersensitivity to timolol were

excluded from the studies. Discontinuation rates due to adverse reactions were 19.3% for the netarsudil treatment group versus 1.7% for the timolol maleate group. The majority of discontinuations in the netarsudil group were associated with ocular adverse reactions, whereas the majority of discontinuations in the timolol group were associated with non-ocular adverse reactions. The most frequently reported adverse reactions associated with discontinuation in the Rhokiinsa groups were conjunctival hyperemia (5.8%), cornea verticillata (3.7%) and vision blurred (1.4%). The incidences of hyperemia and vision blurred were sporadic in nature.

The efficacy and safety of netarsudil in subjects with compromised corneal epithelium or co-existing ocular pathologies e.g. pseudoexfoliation and dispersion pigment syndrome has not been established.

Paediatric population

The European Medicines Agency has waived the obligation to submit the results of studies with Rhokiinsa in all subsets of the paediatric population for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension. (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Absorption

The systemic exposures of netarsudil and its active metabolite, AR-13503, were evaluated in 18 healthy subjects after topical ocular administration of netarsudil once daily (one drop bilaterally in the morning) for 8 days. There were no quantifiable plasma concentrations of netarsudil (lower limit of quantitation (LLOQ) 0.100 ng/ml) post dose on day 1 and day 8. Only one plasma concentration at 0.11 ng/ml for the active metabolite was observed for one subject on day 8 at 8 hours post-dose.

Biotransformation

After topical ocular dosing, netarsudil is metabolised by esterases in the eye to an active metabolite, AR-13503.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and toxicity to development. Effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use.

Intravenous administration of netarsudil mesylate to pregnant rats and rabbits during organogenesis did not produce adverse embryofetal effects at clinically relevant systemic exposures. In pregnant rats, 0.3 mg/kg/day (1000 times the recommended ophthalmic dose) and higher showed increased post-implantation loss and reduced foetal viability. In pregnant rabbits, 3 mg/kg/day (10000 times the recommended ophthalmic dose) and higher showed an increase in post-implantation loss and a decrease in foetal weight.

Long-term studies in animals have not been performed to evaluate the carcinogenic potential of netarsudil.

Netarsudil was not mutagenic in a bacterial mutation assay, in a mouse lymphoma assay, or in a rat micronucleus test.

Netarsudil and its active metabolite AR-13503 was found to have a possible phototoxic potential in a modified 3T3 NRU-PT in vitro assay, where the wavelength was extended to include UVB light.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzalkonium chloride
Mannitol
Boric acid
Sodium hydroxide (for pH-adjustment)
Water for injections

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

Opened bottle: 4 weeks after first opening the bottle. Do not store above 25°C.

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C) until opened.

For storage conditions after first opening of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Rhokiinsa is supplied sterile in opaque white low density polyethylene bottles (2.5 ml fill in a 4 ml container) and tips with white polypropylene caps and anti-tamper seals.

Carton containing 1 bottle.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Santen Oy
Niittyhaankatu 20
33720 Tampere
Finland

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/19/1400/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 19/11/2019

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency <http://www.ema.europa.eu>

ANNEX II

- A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE**
- B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**
- C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**
- D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) responsible for batch release

Aerie Pharmaceuticals Ireland, Limited
Athlone Business and Technology Park,
Dublin Road,
Garrycastle,
Athlone, Co Westmeath,
N37 DW40,
Ireland

and

Santen Oy
Kelloportinkatu 1
33100 Tampere
Finland

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

• Periodic safety update reports (PSURs)

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

• Risk management plan (RMP)

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON OUTER PACKAGING**OUTER CARTON****1. NAME OF THE MEDICINAL PRODUCT**

Rhokiinsa 200 micrograms/ml eye drops, solution
netarsudil

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 ml of solution contains 200 micrograms netarsudil (as mesylate).

3. LIST OF EXCIPIENTS

Benzalkonium chloride, boric acid, mannitol, sodium hydroxide, water for injections.
Read the package leaflet before use.

4. PHARMACEUTICAL FORM AND CONTENTS

Eye drops, solution
1 x 2.5 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Ocular use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY**8. EXPIRY DATE**

EXP
Discard 4 weeks after first opening.
Open date: _____

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator until opened.
Once opened, do not store above 25°C.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Santen Oy
Niittyhaankatu 20
33720 Tampere
Finland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/19/1400/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Rhokiinsa

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

| |
|-------------------------------------------------------------------------|
| MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS |
|-------------------------------------------------------------------------|

| |
|---------------------|
| BOTTLE LABEL |
|---------------------|

| |
|------------------------------------------------------------------------|
| 1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION |
|------------------------------------------------------------------------|

Rhokiinsa 200 micrograms/ml eye drops
netarsudil
Ocular use

| |
|------------------------------------|
| 2. METHOD OF ADMINISTRATION |
|------------------------------------|

| |
|-----------------------|
| 3. EXPIRY DATE |
|-----------------------|

EXP

| |
|------------------------|
| 4. BATCH NUMBER |
|------------------------|

Lot

| |
|----------------------------------------------------|
| 5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT |
|----------------------------------------------------|

2.5 ml

| |
|-----------------|
| 6. OTHER |
|-----------------|

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Rhokiinsa 200 micrograms/ml eye drops, solution netarsudil

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Rhokiinsa is and what it is used for
2. What you need to know before you use Rhokiinsa
3. How to use Rhokiinsa
4. Possible side effects
5. How to store Rhokiinsa
6. Contents of the pack and other information

1. What Rhokiinsa is and what it is used for

Rhokiinsa contains an active substance called netarsudil. Netarsudil belongs to a group of medicines called “Rho kinase inhibitors”, which work to reduce the amount of fluid inside the eye and so lower its pressure.

Rhokiinsa is used to lower pressure in the eyes in adults who have an eye condition known as glaucoma or who have raised pressure in their eyes. If the pressure in the eye is too high, it can damage your sight.

2. What you need to know before you use Rhokiinsa

Do not use Rhokiinsa:

- if you are allergic to netarsudil or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

- Do not use Rhokiinsa more than once a day, as you may experience more side effects.

Children and adolescents

Rhokiinsa should not be used in children and teenagers under 18 years of age as it has only been studied in adults.

Other medicines and Rhokiinsa

Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.

Pregnancy and breast-feeding

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine. Do not use Rhokiinsa if you are pregnant unless your doctor still recommends it.

Driving and using machines

You may find that your vision is blurred or abnormal just after using Rhokiinsa. Do not drive or use machines until the symptoms are cleared.

Rhokiinsa contains benzalkonium chloride

This medicine contains approximately 150 micrograms benzalkonium chloride in each ml of solution.

Benzalkonium chloride may be absorbed by soft contact lenses and may change the colour of the contact lenses. You should remove contact lenses before using this medicine and put them back 15 minutes afterwards.

Benzalkonium chloride may also cause eye irritation, especially if you have dry eyes or disorders of the cornea (the clear layer at the front of the eye). If you feel abnormal eye sensation, stinging or pain in the eye after using this medicine, talk to your doctor.

3. How to use Rhokiinsa

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Only use Rhokiinsa for your eyes (ocular use). Do not swallow or inject.

The recommended dose is one drop in the affected eye or eyes once a day in the evening. Use the medicine at around the same time each day.

How to use



- Wash your hands before you start.
- Do not touch the dropper with your fingers when opening or closing the bottle. It could infect the drops.
- Twist off the bottle cap, and lie the cap on a clean surface on its side. Continue to hold the bottle, ensuring that the tip doesn't come into contact with anything.
- Hold the bottle, pointing down, between your thumb and fingers.
- Tilt your head back.
- Pull down your lower eyelid with a clean finger to form a 'pocket' between the eyelid and your eye. The drop will go in here (Picture 1).
- Bring the bottle tip close to the eye. Do this in front of a mirror if it helps.
- Do not touch your eye, eyelid, surrounding areas or other surfaces with the dropper. It could infect the drops.
- Gently squeeze the bottle to release one drop of Rhokiinsa into your eye.
- Only put one drop into your eye each time. If a drop misses your eye, try again.

- **If you need to use the drops in both eyes**, repeat the steps for your other eye while you have the bottle open.
- Put back the bottle cap to close the bottle.

If you are using other eye drops, wait at least five minutes after using them and then use Rhokiinsa. If you are using eye ointments, these should be used last.

If you use more Rhokiinsa than you should

Rinse your eye with warm water. Do not put in any more drops until it is time for your next regular dose.

If you forget to use Rhokiinsa

Continue with the next dose as planned. Do not use a double dose to make up for a forgotten dose.

Do not use more than one drop in the affected eye(s) once a day.

If you stop using Rhokiinsa

Do not stop using Rhokiinsa without first speaking to your doctor. If you stop using Rhokiinsa the pressure in your eye will not be controlled which could lead to loss of sight.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The following side effects have been observed with Rhokiinsa:

Very common side effects (may affect more than 1 in 10 people)

- Effects in the eye: Eye redness; fine deposits on the front of the eye and pain where the drops have been put in

Common side effects (may affect up to 1 in 10 people)

- Effects in the eye: Infection or inflammation of the eye; dryness of the eye or small breaks in the film of liquid on the surface of the eye; eye discharge; itchy eyelids; clouding of the eye and vision may decrease somewhat; eye pain; feeling of grittiness or having something in the eye; general eye redness shortly after drops are put in; spots or patches of eye redness; eye inflammation caused by an allergic reaction or prominent blood vessels; eyes can become watery, sensitive to light; swelling around the eye; blurred vision
- General side effects: Headache

Uncommon side effects (may affect up to 1 in 100 people)

- Effects in the eye: Increased fluid pressure inside the eye; inflammation of the coloured part of the eye (the iris); bulging of iris; growth of eyelashes; eyelid dryness; eye disease related to diabetes; excess folds of the conjunctiva; blindness; blurred, double and halo vision; cataracts; abnormal turning outward of the lower eyelid; small colored spots on the eye surface; eye dryness caused by inflammation of the glands of the eyelids; eye allergy; eyelid crusting; glassy eyes; loss of eyelashes; tiredness
- General side effects: Increased allergic symptoms; dizziness; blurred vision; nasal discomfort and pain; redness or itching of the skin; rash on skin; inflammation of the cartilage; picking of the skin

Reporting of side effects

If you get any side effects, talk to your doctor, or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via **the national reporting system listed in Appendix V**. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Rhokiinsa

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the bottle and the carton after “EXP”. The expiry date refers to the last day of that month.

Unopened bottles: Store in a refrigerator (2°C - 8°C).

After opening the bottle: Do not store above 25°C.

Throw away the bottle 4 weeks after first opening to prevent infections and use a new bottle.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Rhokiinsa contains

- The active substance is netarsudil. Each ml of solution contains 200 micrograms netarsudil (as mesylate).
- The other excipients are benzalkonium chloride (see section 2 under ‘Rhokiinsa contains benzalkonium chloride’), mannitol, boric acid, sodium hydroxide and water for injections.

What Rhokiinsa looks like and contents of the pack

Rhokiinsa is a clear, liquid eye drop solution in a plastic bottle. Each bottle contains 2.5 ml of the medicine and each pack contains one bottle with a screw-cap.

Marketing Authorisation Holder

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Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site:
<http://www.ema.europa.eu>.