FOR THE TREATMENT OF DRY EYE

DIQUAS®-S ophthalmic solution 3%

(Diquafosol sodium 3%)

1. Product description

DIQUAS-S ophthalmic solution is a clear, colourless, sterile aqueous ophthalmic solution.
Each mL contains 30 mg of diquafosol sodium. It also contains dibasic sodium phosphate hydrate, disodium edetate hydrate, sodium chloride, potassium chloride, hydrochloric acid and sodium hydroxide as additives. The product has pH 7.2 - 7.8 and osmolar ratio 1.0 - 1.1.

2. Indication

This product should be used in patients diagnosed with dry eye, associated with keratoconjunctival epithelium disorders that accompany lacrimal fluid abnormality.

3. Recommended dosage

Instill 1 drop a time in the affected eye(s) 6 times daily.

4. Route of Administration

For ophthalmic use only

5. Pharmacological Properties

5.1. Pharmacodynamics

1) Mechanism of action

Diquafosol sodium is a mucin/aqueous secretagogue acting on the $P2Y_2$ receptors on conjunctival epithelium and goblet cell membranes. The increased intracellular calcium ions promote water and mucin secretion.

2) Stimulatory action on secretion of tear fluid including mucin

(1) A single dose administration of diquafosol sodium into the eyes of normal animals (rabbits and rats) promoted tear fluid secretion and mucin secretion from the conjunctival cells.
(2) A single dose administration of diquafosol sodium into the eyes of dry eye model rats promoted tear fluid secretion. Repeated dose administration increased mucin contents in the conjunctival tissues.

3) Stimulatory action on mucin production in corneal epithelial cells

Diquafosol sodium stimulated gene expression and protein production of membrane-associated mucin in corneal epithelial cells.

4) Improvement of corneal epithelial damage

Repeated dose administration of diquafosol sodium 6 times daily for 4 weeks improved corneal epithelial damage in rat dry eye model in a dose-dependent manner, and exhibited the maximal effect at the concentration of 1% or higher. Repeated dose of 1% diquafosol sodium for 2 weeks exhibited the maximal improvement effect when daily administration exceeded 6 times.

5.2. Pharmacokinetics

1) Plasma concentrations

After topical administration of diquafosol sodium solution either at concentrations of 0.3%, 1%, 3% or 5% to the eye of healthy adult participants one drop, once daily for one day, 6 times daily for one day or 6 times daily for 7 days, the plasma concentrations of diquafosol sodium and its metabolites were measured. Those of diquafosol sodium were below the lower limit of quantitation (2ng/mL) at every time point in all of the participants. The plasma concentration of metabolites (UTP, UDP, UMP and uridine) did not affect physiological concentrations derived from the endogenous components.
(Note: The approved concentration of this product is 3%.)

2) Ocular tissue distribution in animals

(Rabbits)
Following a single topical administration of 3% ^{14}C-diquafosol sodium ophthalmic solution to rabbit eyes, the radioactivity was distributed in the extraocular tissues including the conjunctiva and cornea, and reached the maximum radioactive concentrations in the cornea and conjunctiva at 5 minutes after administration. Thereafter, the radioactivity reduced to 4 to 30% of the maximum concentrations at 24 hours after administration.

3) Metabolism

(Human *in vitro*)
In vitro metabolism reaction using human plasma and human liver microsome demonstrated that diquafosol sodium was rapidly metabolized, and UMP, uridine and uracil were produced.

(Rabbits)
At 30 minutes after instillation of 3% ^{14}C-diquafosol sodium ophthalmic solution to rabbit eyes, diquafosol sodium was hardly detected in the ocular tissues, and instead UTP, UDP, UMP, uridine and uracil were detected.

6. Contraindications

Patients with a history of hypersensitivity to any of the ingredients of this product.

7. Warning and Precaution

1. Pediatric Use

The safety of this product to low birth weight infants, neonates, infants or children has not been established. (No clinical experience.)

2. Precautions concerning Use

1) Route of administration: For ophthalmic use only.
2) At the time of administration:
(i) Instruct the patient to be careful not to touch the tip of the bottle to the eye directly in order to avoid the contamination of the drug.
(ii) When more than one ophthalmic solution is used, at least 5 minutes of intervals should be taken.
(iii) Discard first 1~2 drops without administration (to eliminate possible foreign particle from opening the container).
(iv) After opening, use only once and discard the remaining product and the container.

3. Effects on Ability to Drive and Use Machine

As with any ocular treatment, if transient blurred vision occurs at instillation, patients should be advised not to drive or use machines until their vision has cleared.

8. Interactions with other medicaments

No interaction studies have been performed with diquafosol.

9. Pregnancy and Lactation

There are no adequate data for the use of diquafosol in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity.
It is unknown whether diquafosol and/or its metabolites are excreted in human milk.

10. Undesirable Effects

Adverse drug reactions (including abnormal changes in laboratory test values) were reported in 155 of 655 (23.7%) for diquafosol sodium ophthalmic solution 3% (multidose bottles containing preservative) conducted in Japan before approval. The major adverse reactions were eye irritation (6.7%), eye discharge (4.7%), conjunctival hyperaemia (3.7%), eye pain (2.7%), eye itching (2.4%), foreign body sensation in eyes (2.1%) and ocular discomfort (1.1%), etc.

Adverse reactions were reported in 202 of 3,196 (6.3%) in post marketing observational for diquafosol sodium ophthalmic solution 3% (multidose bottles containing preservative) in Japan. The major adverse reactions were eye irritation (0.9%), eye discharge (0.9%), eye pain (0.7%), lacrimation increased (0.6%) and blepharitis (0.6%), etc.

If adverse reactions are observed, appropriate measures including discontinuing administration should be taken.

Type \ Incidence	Incidence unknown	≥5%	0.1 - < 5%
Hypersensitivity	-	-	Blepharitis
Ophthalmic	Corneal epithelium disorder(filamentary keratitis, keratitis superficial, corneal erosion, etc.), conjunctivitis	Eye Irritation	Eye discharge, conjunctival hyperaemia, eye pain, eye itching, foreign body sensation in eyes, visual discomfort, hyposphagma, abnormal sensation in eye (eyes dry feeling of, eye strange sensation of, sticky eye sensation), vision blurred, photophobia, lacrimation
Others	-	-	Headache, increased eosinophils, elevated ALT(GPT)

Incidence was calculated based on the clinical study results up to the approval of diquafosol ophthalmic solution 3% (multi-dose bottles containing preservative).

11. Overdose and Treatment

Overdose is unlikely to occur after ocular administration. If overdose occurs, treatment should be symptomatic.

12. Storage condition

Store below 30°C.

13. Dosage forms and Packaging Available

Dosage forms: Ophthalmic solution
Packaging available: 0.4mL X 30

Manufactured by
HUONS CO., LTD.
100 Bio valley-ro, Jecheon-si, Chungcheongbuk-do, Republic of Korea

Product Registration Holder
SANTEN PHARMA MALAYSIA SDN. BHD. (1117719-T)
Unit #23A-10, Q Sentral,
No. 2A, Jalan Stesen Sentral 2, Kuala Lumpur Sentral,
50470 Kuala Lumpur, Malaysia.

Date of revision of package insert
April 2020

Bar prints 100mm @ 100%

COMMERCIAL ARTWORK	
GLAMS Part Number:	CAW-4941-02
Artwork Cycle Number:	V01
Description:	Diquas-S_Malaysia_30x0.4 ml_3%_Leaflet
Market:	Malaysia
Number of Languages:	2
Component Type:	Leaflet
SKU Code:	31027
Keyline Part Number:	N/A
Dimensions:	190 x 220 mm
Pharma/Barcode/2D:	N/A
Edge Marks:	N/A
Font Type:	Helvetica Neue, Helvetica Neue LT Std, Myriad Pro
Font Size:	6.5 pt Body text, 5 pt Minimum font size
Braille:	N/A
Printed Packaging Material Code:	01
Variable Data Info:	N/A
Serialization (Y/N):	N
Tamper Evident/Resistant (Y/N):	N
CMO:	Huons
Site Item Number:	NA
Old Item Code:	N/A
Site SPEC Number:	N/A
SGK Job Number:	123018530_404579987
Date:	19 MAY 2026

Printable Colours:

Black

Non Print:

Diecut, Technical Info

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