

1 NAME OF THE MEDICINAL PRODUCT

Bentifen 0.25 mg/ml, eye drops, solution in single-dose containers.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

0.4 ml contains 0.138 mg ketotifen fumarate corresponding to 0.1 mg ketotifen.

Each drop contains 9.5 microgram ketotifen fumarate.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Eye drops, solution in single-dose containers.

Clear, colourless to faintly yellow solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Symptomatic treatment of seasonal allergic conjunctivitis.

4.2 Posology and method of administration

Adults, elderly and children (age 3 and older): one drop of Bentifen into the conjunctival sac twice a day. The contents of a single-dose container are sufficient for one administration into both eyes.

The contents remain sterile until the original closure is broken. To avoid contamination do not touch any surface with the tip of the container.

The safety and efficacy of Bentifen in children aged from birth to 3 years have not yet been established

4.3 Contraindications

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

4.4 Special warnings and special precautions for use

No special warning.

4.5 Interaction with other medicinal products and other forms of interaction

If Bentifen is used concomitantly with other eye medications there must be an interval of at least 5 minutes between the medications.

The use of oral dosage forms of ketotifen may potentiate the effects of CNS depressants, antihistamines and alcohol. Although this has not been observed with Bentifen eye drops, the possibility of such effects cannot be excluded.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no adequate data from the use of ketotifen eye drops in pregnant women. Animal studies using maternally toxic oral doses showed increased pre- and postnatal mortality, but no teratogenicity. Systemic levels after ocular administration are much lower than after oral use. Caution should be exercised when prescribing to pregnant women.

Breast-feeding

Although animal data following oral administration show excretion into breast milk, topical administration to human is unlikely to produce detectable quantities in breast milk. Ketotifen eye drops can be used during lactation.

Fertility

There is no data available on the effect of ketotifen hydrogen fumarate on fertility in humans.

4.7 Effects on ability to drive and use machines

Any patient who experiences blurred vision, somnolence or dizziness should not drive or operate machines.

4.8 Undesirable effects

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 ($< 1/10,000$), not known (cannot be estimated from the available data).

Immune system disorders

Uncommon: Hypersensitivity

Nervous system disorders

Uncommon: Headache

Eye disorders

Common: Eye irritation, eye pain, punctate keratitis, punctate corneal epithelial erosion

Uncommon: Vision blurred (during instillation), dry eye, eyelid disorder, conjunctivitis, photophobia, conjunctival haemorrhage.

Gastrointestinal disorders

Uncommon: Dry mouth

Skin and subcutaneous tissue disorders

Uncommon: Rash, eczema, urticaria

General disorders and administration site conditions

Uncommon: Somnolence

Adverse drug reactions from post marketing experience (Frequency not known):

The following post marketing events have also been observed:

- hypersensitivity reactions including local allergic reaction (mostly contact dermatitis, eye swelling, eyelid pruritis and oedema), systemic allergic reactions including facial swelling/oedema (in some cases associated with contact dermatitis) and exacerbation of pre-existing allergic conditions such as asthma and eczema.
- dizziness

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

No case of overdose has been reported.

Oral ingestion of the contents of a single-dose container would be equivalent to 0.1 mg of ketotifen which is 5% of a recommended oral daily dose for a 3 year old child. Clinical results have shown no serious signs or symptoms after oral ingestion of up to 20 mg of ketotifen.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Ophthalmologicals, other antiallergics
ATC code: S01GX08

Ketotifen is a histamine H₁-receptor antagonist. *In vivo* animal studies and *in vitro* studies suggest the additional activities of mast cell stabilisation and inhibition of infiltration, activation and degranulation of eosinophils.

5.2 Pharmacokinetic properties

In a pharmacokinetic study conducted in 18 healthy volunteers with Bentifen eye drops, plasma levels of ketotifen after repeated ocular administration for 14 days were in most cases below the limit of quantitation (20 pg/ml).

After oral administration, ketotifen is eliminated biphasically, with an initial half life of 3 to 5 hours and a terminal half life of 21 hours. About 1% of the substance is excreted unchanged in the urine within 48 hours and 60 to 70% as metabolites. The main metabolite is a practically inactive ketotifen-N-glucuronide.

5.3 Preclinical safety data

Preclinical data reveal no special hazard which is considered relevant in connection with use of Zaditen eye drops in humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential and toxicity to reproduction.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycerol (E422)
Sodium hydroxide (E524)
Water for injections

6.2 Incompatibilities

Not applicable.

6.3 Shelf-life

In unopened blister/pouch: 2 years.

Opened blister/pouch: 28 days.

Single-dose containers stored without blister/pouch in the outer carton: 3 months.

After opening, the contents of a single-dose container should be used immediately.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

The container is a transparent LDPE single-dose container. Blocks of 5 single-dose containers are each packed in a blister made of PVC, aluminium, polyamide tray sealed with an aluminium foil cover and paper layer, or in a pouch made of polyethylene, aluminium and polyester. Carton boxes of 5, 20, 30, 50 and 60 single-dose containers.

Not all pack sizes may be marketed

6.6 Special precautions for disposal and other handling

Single-dose containers must be discarded after use.

7 MARKETING AUTHORISATION HOLDER

<[To be completed nationally]>

8 MARKETING AUTHORISATION NUMBER(S)

<[To be completed nationally]>

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

2000-06-30/2010-06-30

10 DATE OF REVISION OF THE TEXT

2025-09-11