

# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Ketofall 0.25 mg/ml eye drops, solution in single-dose container

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One ml solution contains 0.25 mg ketotifen (as hydrogen fumarate).

Each single-dose container of 0.4 ml solution contains 0.1 mg ketotifen (as hydrogen fumarate).

Each drop contains approximately 6.95 microgram ketotifen (as hydrogen fumarate).

For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Eye drops, solution in single-dose container.

Clear, colourless solution, with a pH of 5.0 – 6.0 and an osmolality of 230 – 300 mOsm/kg.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

Symptomatic treatment of seasonal allergic conjunctivitis.

### 4.2 Posology and method of administration

#### Posology

Adults, elderly and children (age 3 and older): one drop of Ketofall 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 the eye or any other surface with the tip of the container.

#### *Paediatric population*

The safety and efficacy of Ketofall in children below the age of 3 years have not been established.

#### Method of administration

Ocular use.

### 4.3 Contraindications

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

### 4.4 Special warnings and precautions for use

No special warning.

### 4.5 Interaction with other medicinal products and other forms of interaction

If Ketofall 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 ketotifen 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.

Breastfeeding

Although animal data following oral administration show excretion into breast milk, topical administration to human is unlikely to produce detectable quantities in breast milk. Ketofall 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 or somnolence should not drive or operate machines.

4.8 Undesirable effects

Adverse drug reactions from clinical trials (table 1) are listed by MedDRA system organ class.

Within each system organ class, the adverse drug reactions are ranked by frequency, with the most frequent reactions first. Within each frequency grouping, adverse drug reactions are presented in order of decreasing seriousness. In addition, the corresponding frequency category for each adverse drug reaction is based on the following convention (MedDRA): *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*).

Table 1 Adverse reactions

System Organ Class	Frequency	Adverse Reaction
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 reactions from post marketing experience (frequency not known).

The following post marketing events have also been observed with ketotifen eye drops: hypersensitivity reactions including local allergic reaction (mostly contact dermatitis, eye swelling, eyelid pruritus 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.

#### 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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: [www.hpra.ie](http://www.hpra.ie); e-mail: [medsafety@hpra.ie](mailto:medsafety@hpra.ie)

## 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 of overdose 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

#### Mechanism of action

Ketotifen is a histamine H<sub>1</sub>-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 ketotifen-containing 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

Non-clinical data reveal no special hazard which is considered relevant in connection with use of ketotifen-containing 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) (for pH-adjustment)  
Water for injections

## 6.2 Incompatibilities

Not applicable.

## 6.3 Shelf life

In unopened aluminium pouch: 2 years.

In opened aluminium pouch: 28 days (4 weeks).

Ketofall contains no preservative. After opening, the contents of a single-dose container should be used immediately. The solution remaining in the single-dose container after the application has to be discarded.

## 6.4 Special precautions for storage

Do not store above 25°C.

Do not refrigerate or freeze.

Keep the container in the aluminium pouch.

## 6.5 Nature and contents of container

The container is a transparent low-density polyethylene (LDPE) single-dose container. One single-dose container contains 0.4 ml. Either one, or two blocks of 5 single-dose containers each are packed in an aluminium laminated pouch.

Packages with 5, 10, 20, 30, 50 and 60 single-dose containers.

Not all pack sizes may be marketed.

## 6.6 Special precautions for disposal and other handling

No special requirements for disposal.

## 7 MARKETING AUTHORISATION HOLDER

Pharma Stulln GmbH  
Werksstrasse 3  
92551 Stulln  
Germany

## 8 MARKETING AUTHORISATION NUMBER

PA1815/002/001

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 14<sup>th</sup> October 2016

Date of last renewal: 4<sup>th</sup> October 2017

## 10 DATE OF REVISION OF THE TEXT

April 2017