SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Ofloxacin mibe, 3 mg/ml eye drops, solution.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml eye drops solution contains 3 mg ofloxacin.
One single dose (1 drop) contains 0.1 mg ofloxacin.

Excipient with known effect:
1 ml eye drops solution contains 0.025 mg benzalkonium chloride.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Eye drops, solution.
Clear yellowish solution (pH 6.2 to 6.7, 280 to 340 mOsmol/kg).

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

<product name> is used for infections of the anterior eye segment in adults and children caused by ofloxacin-susceptible pathogens.
Consideration should be given to official guidance on the appropriate use of antibacterial agents (see section 5.1).

4.2 Posology and method of administration

Posology

Instillation of one drop of <product name> in the conjunctival sac of the affected eye(s) every two to four hours for the first two days, followed by four times daily.
The product should not be used for more than 14 days.

Specific populations

Elderly
No dosage adjustment is necessary for elderly patients (see section 4.4).

Paediatric population
Safety and effectiveness in infants below the age of one year have not been established.
The dosage for children does not differ from the one for adults. However, experience in children is limited. Dose-finding-studies are not available.

Method of administration

Ocular use.

If other eye drops/eye ointments are used concomitantly, an interval of about 15 minutes should be kept between the applications and an eye ointment should always be applied last.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

<product name> is not for injection.

Serious and occasionally fatal hypersensitivity (anaphylactic/anaphylactoid) reactions, some following the first dose, have been reported in patients receiving systemic quinolones, including ofloxacin. Some reactions were accompanied by cardiovascular collapse, loss of consciousness, angioedema (including laryngeal, pharyngeal or facial edema), airway obstruction, dyspnea, urticaria, and itching.

If an allergic reaction to <product name> occurs, discontinue the drug. Use <product name> with caution in patients who have exhibited sensitivities to other quinolone antibacterial agents.

When using <product name> the risk of rhinopharyngeal passage, which can contribute to the occurrence and the diffusion of bacterial resistance, should be considered. As with other anti-infectives, prolonged use may result in overgrowth of non-susceptible organisms.

If worsening infection occurs or if clinical improvement is not noted within a reasonable period, discontinue use and institute alternative therapy.

The use of <product name> in neonates with ophthalmia neonatorum caused by *Neisseria gonorrhoeae* or *Chlamydia trachomatis* is not recommended as it has not been evaluated in such patients.
Neonates with ophthalmia neonatorum should receive appropriate treatment for their condition.

Use in elderly: No comparative data are available with topical dosing in elderly versus other age groups, but considering the minimal systemic absorption the same posology can be applied.

Clinical and non-clinical publications have reported the occurrence of corneal perforation in patients with pre-existing corneal epithelial defect or corneal ulcer when treated with topical fluoroquinolone antibiotics. However, significant confounding factors were involved in many of these reports including advanced age, presence of large ulcers, concomitant ocular conditions (e.g. severe dry eye), systemic inflammatory diseases (e.g. rheumatoid arthritis), and concomitant use of ocular steroids or non-steroidal anti-inflammatory drugs. Nevertheless, it is necessary to advise caution regarding the risk of corneal perforation when using product to treat patients with corneal epithelial defects or corneal ulcers.

Corneal precipitates have been reported during treatment with topical ophthalmic ofloxacin. However, a causal relationship has not been established.
Sun or UV-exposition should be avoided during use of ofloxacin due to the potential for photosensitivity.

Tendon inflammation and rupture may occur with systemic fluoroquinolone therapy including ofloxacin, particularly in older patients and those treated concurrently with corticosteroids. Therefore, caution should be exercised and treatment with <product name> should be discontinued at the first sign of tendon inflammation (see section 4.8).

<Product name> contains the preservative benzalkonium chloride

Benzalkonium chloride has been reported to cause eye irritation, symptoms of dry eyes and may affect the tear film and corneal surface. 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.

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.

4.5 Interaction with other medicinal products and other forms of interactions

It has been shown that the systemic administration of some quinolones inhibits the metabolic clearance of caffeine and theophylline. Drug interaction studies conducted with systemic ofloxacin have demonstrated that metabolic clearance of caffeine and theophylline are not significantly affected by ofloxacin.

Although there have been reports of an increased prevalence of CNS toxicity with systemic dosing of fluoroquinolones when used concomitantly with systemic nonsteroidal anti-inflammatory drugs (NSAIDs), this has not been reported with the concomitant systemic use of NSAIDs and ofloxacin.

Since the systemic exposure of ofloxacin is anticipated to be very low after use of <product name>, no relevant interactions are however expected.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no adequate data on the use of ofloxacin eye drops in pregnant women. Animal studies have not shown teratogenic effects (section 5.3). Serum concentrations after ophthalmic doses are at least 1000x lower than after standard oral doses.
Ofloxacin eye drops 0.3 % should only be used during pregnancy if clearly needed.

Breast-feeding
It is not known if ofloxacin is excreted in human milk after ophthalmic administration. Maximum serum concentrations after ophthalmic doses are x1000 lower than after standard oral doses. Caution should be applied when administered during breast-feeding.

Fertility
Ofloxacin had no influence on fertility in rats (see section 5.3).

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

Transient blurring of vision may occur on instillation of eye drops. Do not drive, operate hazardous machinery or work without a secure hold unless vision is clear.

4.8 Undesirable effects

General
Serious reactions after the systemic use of Ofloxacin are rare and most of the symptoms are reversible. Since a small amount of ofloxacin is systemically absorbed after topical administration, side-effects reported with systemic use could possibly occur.

Frequency categories: Very common (≥1/10); Common (≥1/100 to <1/10); Uncommon (≥1/1,000 to <1/100); Rare (≥1/10,000 to <1/1,000); Very rare (<1/10,000) and not known (cannot be estimated from the available data).

Immune system disorders
Very rare: Hypersensitivity (including angioedema, dyspnea, anaphylactic reaction/shock, oropharyngeal swelling and tongue swollen).

Nervous system disorders
Not known: Dizziness.

Eye disorders
Common: Eye irritation; Ocular discomfort.
Rare: Corneal deposits, especially in pre-existing corneal diseases.
Not known: Keratitis; Conjunctivitis; Vision blurred; Photophobia; Eye oedema; Periorbital oedema (including eyelid oedema); Foreign body sensation in eyes; Lacrimation increased; Dry eye; Eye pain; Ocular hyperaemia; Hypersensitivity (including eye pruritus and eyelid pruritus).
Hypersensitivity reactions in the form of conjunctival redness and/or mild burning in the treated eye, are possible. However, these symptoms are usually short term.

Gastrointestinal disorders
Not known: Nausea.

Skin and subcutaneous tissue disorders
Not known: Periorbital oedema, Facial oedema; Stevens-Johnson syndrome, Toxic epidermal necrolysis

Musculoskeletal and connective tissue disorders:
Not known: Ruptures of the shoulder, hand, Achilles, or other tendons that required surgical repair or resulted in prolonged disability have been reported in patients receiving systemic fluoroquinolones. Studies and post marketing experience with systemic quinolones indicate that a risk of these ruptures may be increased in patients receiving corticosteroids, especially geriatric patients and in tendons under high stress including Achilles tendon (see section 4.4).

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:

<to be completed nationally>

4.9 Overdose

No case of overdose has been reported.
In the event of a topical overdosage, flush the eye with water.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: ophthalmologicals, antiinfectives, fluoroquinolones.

ATC code: S01AE01

Mechanism of action
The mechanism of action of ofloxacin is based on disruption of DNA synthesis through inhibition of bacterial topoisomerase II (gyrase) and topoisomerase IV. This results in a bactericidal effect.

Pharmacokinetic/pharmacodynamic relationship

Efficacy primarily depends on the ratio between the peak serum level (C_{max}) and minimum inhibitory concentration (MIC) of the pathogen concerned, or the ratio between AUC (area under the curve, area under the concentration-time curve) and the MIC of the pathogen.

Resistance mechanisms

Resistance to ofloxacin may be based on the following mechanisms:

- Change in target structures: The most common mechanism of resistance to ofloxacin and other fluoroquinolones consists of changes in topoisomerase II or IV as a result of a mutation.
- Other mechanisms of resistance lead to a reduction in fluoroquinolone concentrations at the target site. This is due to reduced cell penetration as a result of decreased porin formation or increased efflux from the cell by efflux pumps.
- Transferable, plasmid-encoded resistance has been observed with *Escherichia coli*, *Klebsiella* spp. and other *Enterobacterales*.

There is partial or complete cross-resistance between ofloxacin and other fluoroquinolones.

Susceptibility testing breakpoints:

MIC (minimum inhibitory concentration) interpretive criteria for susceptibility testing have been established by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) for ofloxacin and are listed here: https://www.ema.europa.eu/documents/other/minimum-inhibitory-concentration-mic-breakpoints_en.xlsx.

Prevalence of acquired resistance

The prevalence of acquired resistance for individual species can vary geographically and over time. Therefore, local information on the resistance status is desirable, especially for the adequate treatment of severe infections. If, based on the local resistance status, the efficacy of ofloxacin is questionable, expert therapeutic advice should be sought. Particularly in the case of serious infections or treatment failure, a microbiological diagnosis should be sought, with identification of the pathogen and its susceptibility to ofloxacin.

The information on antibiotics resistance is **mainly** based on data from national (German) resistance monitoring projects. Hence, the aerobic bacteria mentioned constitute mostly a representative image of the germs to be considered in eye infections in Germany. It is to be assumed that the frequency distribution of ophthalmologically relevant bacteria is not identical in other countries, but will be similar, so that the germs listed below will be the predominant cause of bacterial infections of the outer eye there as well.

Prevalence of acquired resistance in Germany based on data from the last 5 years from national resistance monitoring projects and studies (as at: May 2025):

Commonly susceptible species
Aerobic gram-positive micro-organisms
Staphylococcus saprophyticus [1] °
Streptococcus pyogenes
Aerobic gram-negative micro-organisms
Acinetobacter pittii [$]
Citrobacter koseri
Enterobacter cloacae
Haemophilus influenzae
Klebsiella aerogenes
Klebsiella oxytoca
Legionella pneumophila °
Moraxella catarrhalis
Proteus vulgaris °
Salmonella enterica (only *Salmonella* Enteritidis)
Serratia marcescens
Other micro-organisms
Chlamydia pneumoniae ° [$]
Chlamydia trachomatis ° [$]

Mycoplasma hominis ° $
Mycoplasma pneumoniae ° $
Ureaplasma urealyticum ° $
Species in which acquired resistance may pose a problem during use
Aerobic gram-positive micro-organisms
Enterococcus faecalis $
Streptococcus pneumoniae $
Aerobic gram-negative micro-organisms
Acinetobacter baumannii $
Citrobacter freundii
Escherichia coli
Klebsiella pneumoniae
Morganella morganii
Neisseria gonorrhoeae
Proteus mirabilis
Pseudomonas aeruginosa $
Naturally resistant species
Aerobic gram-positive micro-organisms
Enterococcus faecium
Anaerobic micro-organisms
Bacteroides spp.
Clostridioides difficile
Stenotrophomonas maltophilia

The categorisations given are based almost exclusively on data on ciprofloxacin.

° No current data were available when the tables were published. Susceptibility is assumed in the primary literature, standard works and therapy recommendations.

$ The natural susceptibility of most isolates is in category I (susceptible at increased exposure).

1 Applies only to uncomplicated cystitis isolates

5.2 Pharmacokinetic properties

In a healthy volunteer study, mean tear film concentrations of ofloxacin measured four hours after topical dosing (9.2 µg/g) were higher than the 2 µg/ml minimum concentration of ofloxacin necessary to inhibit 90 % of most ocular bacterial strains (MIC90) *in-vitro*.
Maximum serum ofloxacin concentrations after ten days of topical dosing were about 1000 times lower than those reported after standard oral doses of ofloxacin, and no systemic side-effects attributable to topical ofloxacin were observed.

5.3 Preclinical safety data

No toxicologic effects were observed following local application of ofloxacin at clinically relevant doses.
Several *in-vitro*- and *in-vivo*-tests for induction of gene- and chromosome mutations were negative. Long-term animal studies for carcinogenicity have not been performed. There are no signs for a cataractogenic or co-cataractogenic effect. Ofloxacin has no influence on fertility, peri- and post-natal development and is non-teratogenic. Following systemic administration of ofloxacin to test animals, degenerative changes to the articular cartilage have been observed. The articular cartilage damages that occurred were dose-dependent and age-related. (The younger the animal, the more pronounced the damages were.)

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Benzalkonium chloride
Hydrochloric acid and sodium hydroxide solution (for pH adjustment)

Water for injections.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

After opening, use within 4 weeks.

6.4 Special precautions for storage

Do not store above 25 °C.

Keep bottle in the outer carton in order to protect from light.

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

6.5 Nature and contents of container

LDPE bottle with LDPE dropper applicator and HDPE tamper-proof screw cap.
Each bottle contains 5 ml eye drops solution.

Pack sizes:

1 x 5 ml
2 x 5 ml
3 x 5 ml and
6 x 5 ml

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

<to be completed nationally>

8. MARKETING AUTHORISATION NUMBER(S)

<to be completed nationally>

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

2014-04-23

10. DATE OF REVISION OF THE TEXT

24 Oct 2025