



# GPs guide to some topical eye medications

## KEY POINTS

- **Specialist prescribing restrictions have been removed from some topical eye treatments**
- **Although general practitioners can now initiate some topical eye treatments, it does not mean they should**
- **Significant corneal disease, intraocular inflammation and glaucoma still require specialist diagnosis and management**
- **Primary care will still be involved in the ongoing support and education of people with these conditions and the continuation of the medications used to treat them**

## EYE MEDICATIONS ARE OFTEN USED IN HIGH RISK SITUATIONS REQUIRING SPECIALIST SKILLS

Some eye medications are used when there is high risk of visual loss and their misuse can increase this risk. Initiation and monitoring often require specialist expertise as well as the availability and ability to use specialist equipment. For example:

- Slit-lamp examination is needed for accurate diagnosis and monitoring of intraocular inflammation, such as iritis and keratitis and ulceration of the cornea.
- Accurate diagnosis and monitoring for adequacy of treatment of glaucoma requires accurate detailed assessment of intraocular pressure, the optic disk and visual fields.
- Accurate distinction between infective and non-infective inflammatory conditions is essential because medications, such as steroid drops, used for some conditions, will make others much worse.
- Use of steroid drops for more than ten days requires, monitoring for steroid-induced glaucoma.

## PRIMARY CARE ROLE STILL IMPORTANT

Although primary care is not equipped to initiate and monitor treatment for these conditions, it still plays a valuable role. People will still look to primary care for support, education and continuation of treatment. Clinicians, particularly prescribers, need to understand the actions of these medications and how to avoid and identify possible adverse effects. For example:

- Some topical preparations, e.g. beta blockers, if sufficiently absorbed, may cause systemic effects.
- Unless medically indicated, soft contact lenses should not be used for the duration of treatment with eye drops and ointments.<sup>1</sup>
- However, it is safe to replace contact lenses 15 minutes after use of some drops.
- Application of gentle pressure to the tear duct after instilling drops increases exposure of the anterior eye tissues to the treatment and reduces systemic absorption. This is especially advisable in children.<sup>2</sup>

# eye medications

## ANTIVIRAL

### Acyclovir 3% ointment [Zovirax]

Acyclovir eye ointment is indicated for treatment of herpes simplex (HSV) keratitis and dendritic ulceration of the corneal epithelium.

Viruses other than HSV may cause dendritic ulceration and slit lamp microscopy and laboratory examination of a corneal scrape is recommended for accurate diagnosis.

Recommended dose is a 1cm ribbon of ointment, applied five times daily inside the lower eyelid and continued for at least three days after apparent healing. Contact lenses should not be used during this time.

Stinging is common after application but is usually transient. Occurrence of superficial punctate keratopathy is also quite common but treatment can be continued and the keratopathy expected to heal.

## ANTIBACTERIALS

Ciprofloxacin, gentamicin and tobramycin eye drops are not first line treatments for common conjunctival or adnexal eye infections and their use should be strictly guided by laboratory identification and determination of the antibiotic sensitivities of pathogens.

### Ciprofloxacin 0.3% drops [Ciloxan]

Indicated for bacterial keratitis (infected corneal ulcers), severe bacterial conjunctivitis and blepharitis due to susceptible bacteria. Ciprofloxacin is active against a wide range of gram-positive and gram-negative bacteria. Laboratory identification and sensitivity testing is advised. Superinfection with resistant bacteria can occur.

The recommended dose for treating corneal lesions with ciprofloxacin eye drops is 1–2 drops, used at 15 minute intervals for the first six hours.<sup>3</sup> Local burning discomfort, white precipitate and foreign body sensation may occur.

Ciprofloxacin is not recommended for use in children under one-year-old and contraindicated in case of hypersensitivity to other quinolones.

### Gentamicin 0.3% drops [Genoptic]

Indicated for bacterial keratitis, conjunctivitis and blepharitis, meibomian gland and lacrimal/tear duct infections (dacryocystitis).

Gentamicin is effective against a wide range of gram-negative and gram-positive bacteria. There is increasing *Strep. pneumoniae* resistance.

Caution applies to use in pregnancy due to risk of foetal nephrotoxicity and ototoxicity.

Recommended dose is 1–2 drops four hourly. Transient irritation may occur.

### Tobramycin 0.3% drops and ointment [Tobrex]

Indications are as for gentamicin and the antibacterial activity is similar. Resistance to one may confer resistance to the other.

Adverse events include local ocular toxicity and delayed corneal wound healing. Tobramycin eye drops may be inactivated by systemic beta-lactam antibiotics. Antiemetics can mask ototoxic effects of tobramycin.

Caution applies to use in pregnancy due to the possibility of foetal nephrotoxicity and ototoxicity.

Recommended dose is 1–2 drops four hourly for 7–10 days.

## CORTICOSTEROID DROPS & OINTMENTS

Corticosteroid eye treatments pose four main dangers:<sup>4</sup>

- Undiagnosed red eye and risk of uncontrolled infection
- Steroid-induced glaucoma in susceptible individuals
- Steroid-induced cataract and atrophy of the cornea and sclera from prolonged use
- Steroid and antibiotic combinations should not be prescribed as empiric treatments for an undiagnosed red eye, which may be caused by HSV and may be difficult to diagnose.<sup>5</sup> Their use for any reason requires close supervision.

In general, the cautions outlined below apply to all corticosteroid eye drops.

**Steroid use is contraindicated in Herpes simplex keratitis** and in untreated other viral and bacterial eye infections – there is risk for progressive corneal injury and globe perforation.

Steroid use may cause recrudescence of quiescent herpes simplex virus and access to frequent slit lamp examination is mandatory.

Intensive and prolonged use of topical steroids should be avoided but some chronic recurrent inflammatory conditions such as iritis or iridocyclitis may necessitate such use - obtain specialist advice.

Topical steroids are not effective in Sjogren's keratoconjunctivitis.

If used for more than ten days, intraocular pressure needs to be monitored in case of steroid glaucoma in susceptible individuals – this can be difficult in children.

Persistent corneal ulceration as a result of fungal keratopathy may be associated with long-term topical steroid use.

Topical steroids are also used in selected infective conditions, including herpes zoster keratitis and after trauma including thermal, chemical or radiation injury, after weighing the risk against the benefit of reduction of inflammation. In these situations, specialist involvement is strongly advised.<sup>6</sup>

In the general practice setting, topical steroids are best avoided after removal of a foreign body – a simple ocular lubricant or antibiotic ointment is useful and mostly sufficient in this context.

### **Dexamethasone 0.1% drops and ointment [Maxidex]**

Dexamethasone is a potent corticosteroid used for non-infective inflammatory and allergic conditions affecting the anterior eye.

Recommended treatment is to instil drops four to six times daily (soft contact lenses can be replaced 15 minutes after use of drops) or a ribbon of ointment four times daily.

Safety and effectiveness in children has not been established.<sup>7</sup>

### **Fluoromethalone 0.1% drops [Flucon]**

Fluoromethalone is indicated for inflammation of anterior eye tissues. It is contraindicated in Herpes simplex keratitis and untreated other infections of the eye.

Safety in pregnancy and safety and efficacy in children under two-years-old has not been established.<sup>8</sup>

Recommended dose is 1–2 drops two to four times daily.

### **Prednisolone drops [Pred Forte, Pred Mild, Minims Prednisolone]**

Preparations available are prednisolone acetate in Pred Forte 1.0% or Pred Mild 0.12% and prednisolone sodium phosphate in Minims Prednisolone 0.5%.

Prednisolone is indicated for non-infective inflammatory anterior eye conditions.

Safe use in pregnancy, breast feeding and children is not established.<sup>9</sup>

Recommended dose is 1 drop two to four times daily. Brief burning or stinging may occur.

## **NON-STEROIDAL ANTIINFLAMMATORY DROPS**

### **Diclofenac sodium eye drops 0.1% [Voltaren]<sup>10</sup>**

Diclofenac drops are used to reduce inflammatory response to cataract, squint and trabecular surgeries, and to relieve pain and photophobia after corneal surgery or accidental corneal trauma.

Diclofenac drops are contraindicated in people with Aspirin/NSAID sensitive asthma, urticaria or acute rhinitis.

Do not use in the third trimester of pregnancy – there is risk of premature closure of the ductus arteriosus. Paediatric experience is limited, so caution applies to use in children.

Transient burning, itching, blurring of vision and punctate keratopathy can occur. As with steroid drops, non-steroidal antiinflammatory drops can mask infection.

Recommended dose is 1 drop four to six hourly. Contact lenses can be replaced 15 minutes after use.

## INTRAOCULAR PRESSURE REDUCTION WITH TOPICAL EYE TREATMENTS

Specialist prescribing authority has been removed from several topical agents used in the treatment of ocular hypertension and chronic open-angle glaucoma. However we recommend that they continue to be used under specialist supervision. Initiation and monitoring often require specialist expertise as well as the availability and ability to use specialist equipment. Prescribing eye drops for glaucoma treatment in between specialist reviews continues to be an appropriate role for GPs.

Glaucoma affects 1% of people over 40 years of age and open-angle glaucoma is the most common form (80%). Gradual obstruction occurs in the trabecular meshwork so that the rise of intraocular pressure (IOP) is often slow and asymptomatic despite significant loss of visual field. Viewed through an ophthalmoscope the optic disc is depressed or cupped because of loss of nerve fibres.

Note: the topical eye drugs mentioned here are discussed in relation to ocular hypertension and chronic open-angle glaucoma and not in relation to acute angle-closure glaucoma. Acute angle-closure glaucoma is a medical emergency. A shallow anterior chamber creates an abnormally narrow angle between the cornea and the base of the iris. The iris seals off the trabecular meshwork and blocks the outflow of aqueous from the anterior chamber.<sup>11</sup> IOP is usually > 40mm Hg.<sup>12</sup> An urgent specialist opinion is essential.

### Topical beta blockers

These are first-line agents for lowering IOP in ocular hypertension and chronic open-angle glaucoma. They probably lower IOP by reducing the rate of production of the aqueous.<sup>13</sup> They are used alongside miotic agents, sympathomimetic agents and carbonic anhydrase inhibitors to get full control of IOP in chronic open-angle ocular hypertension and glaucoma.

Because topical beta blockers, such as betaxolol, levobunolol and timolol, do not have miotic action, they have the advantage of not causing the blurred vision and poor night vision associated with miosis.<sup>14</sup>

They can cause problems related to systemic absorption, which can be reduced by applying gentle pressure on the nasolacrimal duct for two minutes after use.

Betaxolol is cardio-selective (blocks only beta-1 receptors) and in clinical studies the eye drops have minimal effect on pulmonary and cardiovascular parameters. However, some patients may be affected.<sup>15</sup>

Levobunolol and timolol are not cardio-selective (they block both beta-1 and beta-2 receptors) so their systemic absorption poses more potential risk to pulmonary and cardiovascular function.

A strong caution or contraindication applies to use of these three drugs in people with bradycardia, heart block, cardiac failure, airways disease or history of anaphylaxis.<sup>16</sup>

General management of severe adverse systemic effects is adrenaline.

Ophthalmic beta-blockers can mask hypoglycaemia in diabetes and also some clinical signs of thyrotoxicosis.<sup>17</sup>

Gradual withdrawal should be considered prior to general anaesthesia to protect sympathetic/adrenergic cardiac responses.<sup>18</sup>

Avoid use in pregnancy near parturition – foetal and neonatal bradycardia can occur.<sup>19</sup>

Note that beta-blockers are prohibited in some sports by the world anti-doping agency (WADA).<sup>20</sup>

**Betaxolol eye drops** [Betoptic 0.5% and Betoptic S 0.25%] Betaxolol lowers intraocular pressure within 30 minutes of use. Twice daily use keeps the IOP below 22mm Hg in most patients.<sup>21</sup>

**Levobunolol eye drops** [Levobunolol 0.5%<sup>22</sup>, Betagan 0.25%<sup>23</sup>] IOP falls within an hour of use and by 6-8 mm Hg over several weeks. Twice daily use effects long-term control in most cases.

**Timolol eye drops** [Apo-Timopt 0.25%, Timoptol 0.25%, Timoptol-XE 0.25%, Nyogel 0.1%]

Recommended treatment starts with one drop of 0.25% solution twice daily. IOP reduction occurs after 20 minutes. Viscous drops or gel enable once daily treatment.

Local reactions may occur with any one of these agents.

**Carbonic anhydrase inhibitors** reduce IOP by reducing aqueous production in the ciliary body.<sup>24</sup>

**Dorzolamide eye drops 2%**<sup>25</sup> [Trusopt]

Dorzolamide is a carbonic anhydrase inhibitor that can be used as monotherapy (one drop three times daily) or as adjunctive therapy with an ophthalmic beta-blocker (one drop twice daily).

Dorzolamide has a structure similar to sulphonamide and therefore has potential for sulphonamide-like adverse effects.

Its use is contra-indicated in pregnancy, lactation and in renal impairment. Local eye reactions and a bitter taste may be experienced. Headache, dizziness and nausea may also occur.

Separate administration from other eye drops by at least ten minutes.

**Dorzolamide combined with Timolol**

Dorzolamide is combined with timolol in Cosopt eye drops.<sup>26</sup>

This may be used when monotherapy is not sufficient to lower IOP below 22mm Hg.

Contraindications and cautions are similar to those for individual components.

**Alpha-2 agonists** reduce the rate of production of aqueous in the ciliary body by alpha-mediated vasoconstriction of afferent ciliary blood vessels. However, they are also mydriatic and are not recommended for use in patients with risk of angle-closure, unless an iridectomy has been done.

**Brimonidine eye drops 0.2%**<sup>27</sup> [Alphagan]

Brimonidine is a selective alpha-2 agonist that can be used to reduce IOP in patients for whom beta-blockers are not appropriate. It can also be used as adjunctive therapy when IOP is poorly controlled.

Caution is necessary in severe cardiovascular or cerebrovascular disease, pregnancy and breast feeding.

Drowsiness may occur and pose a risk to driving.

Local ocular reactions may occur.

Brimonidine is combined with timolol in Combigan, which may be considered when monotherapy fails to lower IOP below 22mm Hg. Contraindications and cautions are those that apply to the individual components.

**Direct-acting parasympathomimetic drops**

These have cholinergic effects i.e. they constrict the pupil and cause contraction of the ciliary muscle. Contraction of the ciliary muscle stretches the trabecular meshwork and improves the outflow of aqueous.

**Pilocarpine eye drops 2%**<sup>28</sup> [Minims Pilocarpine Nitrate]<sup>29</sup>

Pilocarpine is a tertiary amine and can diffuse through the cornea into the aqueous. There is dimming of vision and poor night vision because of pupillary constriction.

Pupillary constriction is contraindicated in acute iritis and in case of risk for retinal detachment.

Caution applies to use in asthma, pregnancy and lactation.

The contraction of ciliary muscle causes myopia in young

patients. Irritant eye reactions occur and frontal headache can be problematic if there is ciliary muscle spasm.

Recommended dose is 1–2 drops two to four times daily.

### Changing drops being used to treat ocular hypertension

If changing from one beta blocker to another, use the final daily dose of the old agent and start the new agent the very next day. If a beta blocker is being substituted for a non-betablocker, the beta blocker is added to the non-beta blocker for one day and the non-beta blocker stopped the next day.<sup>30</sup>

### Prostaglandin analogues

Prostaglandin analogues are believed to reduce IOP by increasing the outflow of aqueous humor.

#### **Travaprost** eye drops 0.004% [Travatan]

The reduction in IOP starts after approximately two hours and is maintained for at least 24 hours.

Recommended dose is one drop instilled in the affected eye(s) daily with optimal effect if this is administered in the evening.

Travaprost is contraindicated for pregnant women and those attempting to become pregnant.

Travatan eye drops may gradually change the eye colour by increasing the number of pigment granules. The changes may be permanent and the long term consequences of this are not yet known. Darkening of the skin around the eye has also been reported.

### Reference Notes

1. BNF 53, Mar 2007, 11.9, p568
2. Medsafe data sheet: Prednisolone sodium phosphate, Oct 2006
3. see Medsafe dose data or BNF or MIMS
4. BNF 53, March 2007, 11.4.1, p555
5. BNF 53, Mar 2007, 11.3.1, p553
6. Medsafe data sheet: Maxidex, Jul 1999
7. Medsafe data sheet: Maxidex, Jul 1999
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19. Medsafe data sheet: Apo-Betaxolol Oct 2001; Betoptic Mar 1999
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