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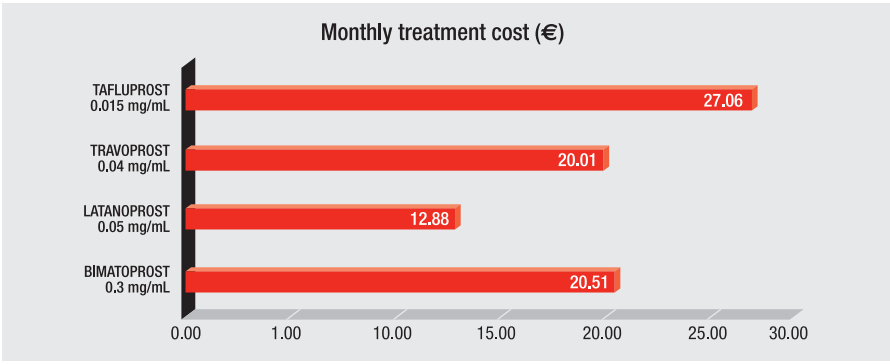
Tafluprost▲ (Saflutan®) for elevated intraocular pressure in open-angle glaucoma and ocular hypertension

A new prostaglandin analogue with no advantages

If a prostaglandin analogue is indicated then latanoprost is the elective option



Therapeutic indications[1]

It is indicated for the reduction of elevated intraocular pressure in open-angle glaucoma and ocular hypertension. It may be used as monotherapy in patients who would benefit from preservative-free eyedrops, are insufficiently responsive to first-line therapy, or are intolerant or contraindicated to first-line therapy. It may be used as adjunctive therapy to beta-blockers.

Mechanism of action[1]

Tafluprost is a fluorinated analogue of prostaglandin $F_{2\alpha}$. Tafluprost acid, the active metabolite, is a very potent and selective agonist of the human prostanoid receptor FP. Tafluprost reduces intraocular pressure by increasing the uveoscleral outflow of aqueous humour.

Posology and form of administration[1]

The recommended dose is one eye drop in the conjunctival sac of the affected eye, once a day in the evening. More frequent administrations can reduce its efficacy. One container for a single dose is sufficient to treat both eyes. Any unused solution should be discarded after use.

Any excess solution on the skin should be wiped off in order to reduce the risk of darkening of the eyelids. As in the case of other eye drops, nasolacrimal occlusion or gently closing the eyelid with caution is recommended after applying the eye drops. Any systemic absorption can be reduced this way. If any other topical eye solution is to be applied then it should be done after an interval of at least five minutes.

- Tafluprost is indicated in the reduction of elevated intraocular pressure in patients with open-angle glaucoma and ocular hypertension, both in monotherapy in cases of intolerance to preservatives, or as adjunctive therapy with beta-blockers.
- Data on the efficacy of tafluprost compared to other prostaglandin analogues originate from a single clinical trial in which non-inferiority was not shown when compared to latanoprost.
- It presents a similar profile to other prostaglandin analogues regarding adverse reactions. The most frequent adverse effect is ocular and conjunctival hyperaemia.
- Despite being the first prostaglandin analogue free of preservatives, it has not shown better tolerance compared to the other analogues containing preservatives.

The qualification assigned to the drug was agreed by the Drug Assessment Committees of Andalusia, Basque Country, Catalonia Institute of Health, Aragon and Navarre. The current report is based on the available information and is susceptible to be updated according to the latest evidence. Let us remind the reader about the importance of notifying the Pharmacovigilance Centre when there are suspicions of adverse reactions to drugs.

Clinical efficacy

There are three randomised, double blind and multicenter clinical trials available that have evaluated the efficacy of tafluprost in the reduction of elevated intraocular pressure in patients with open-angle glaucoma.

In two of the trials[1,2] a direct comparison of the efficacy was made with an active comparator. In the first[1] which lasted 6 months, the results have not been published, but it was observed that tafluprost reduced the intraocular pressure (IOP) by 5-7 mmHg compared to a reduction of 4-6 mmHg with timolol.

In the second study[2] which lasted 24 months (n=533), 0.0015% tafluprost was compared to 0.005% latanoprost in a non-inferiority trial. Both eye drops contained the preservative benzalkonium chloride. The established limit for non-inferiority was a difference in the reduction of IOP of 1.5 mmHg. Tafluprost presented a lower reduction of IOP than latanprost (average of 1.2 mmHg), with an upper limit of the confidence interval of 1.52, and so, non-inferiority could not be shown when compared to latanoprost.

Another 6-week study[3] (n=185) was carried out in patients with inadequate control with a single active agent. The IOP-lowering effect of tafluprost was compared with its vehicle when used adjunctively with timolol. Timolol included an adjuntive agent. After six weeks, the reduction of IOP in the tafluprost + timolol combination oscillated between -5.49 and -5.82 mmHg, while in the vehicle+timolol, the reduction varied between -3.99 and -4.15 mmHg with an average difference between both groups of -1.49 (upper limit, -0.66; 95%CI, p<0.001).

Safety

Adverse effects

The most frequent notified adverse effect in clinical studies was ocular hyperaemia, which occured in approximately 13% of the patients. In the majority of the cases the effect was mild, and treatment was discontinued in an average of 0.4% of the patients participating in these trials[1].

Amongst the most frequent eye disorders, other effects have been described (1-10%): pruritus, pain and eye irritation, changes in eye lashes (increase in length, thickness and quantity of lashes), eyelash decolouration, dry eyes, foreign body sensation in the eyes, eyelid erythema, blurred vision, increased lacrimation, blepharal pigmentation, eye discharge, reduction in visual acuity, photophobia, blepharal oedema and increase in iris pigmentation.

Other less common eyelid side effects have been described (0.1-1%): superficial punctate keratitis, asthenopia, conjunctival oedema, blepharitis, ocular discomfort, anterior chamber flare, conjunctival follicles, allergic conjunctivitis, anterior chamber cell, conjunctival pigmentation and abnormal sensation in eye.

Among the side effects not affecting the eye, cefalea, is frequent (1-10%), while hypertrichosis of the eyelid appears less frequently (0.1-1%).

The safety profile of tafluprost is similar to the other prostaglandin analogues already approved. In the comparative study with latanoprost, when aggregating the cases of ocular and conjuntival hyperaemia, the total incidence was 9.1% in the case of tafluprost and 7.5% with latanoprost (p=0.033)[2].

The effect on tolerance of the preservative was evaluated in a single comparative study (n=43) between both preserved (with benzalkonium chloride) and non-preserved formulations of tafluprost. There were more cases of conjunctival hyperaemia in the group without the preservative (six cases versus 2 cases)[4].

Precautions and contraindications[1]

This agent is contraindicated in cases of hypersensitivity to tafluprost or to any of its excipients.

Tafluprost can produce eyelash growth, darkening of eyelid skin and an increase in pigmentation of the iris. Some of these changes can be permanent and can cause differences in the appearance of the eyes when only one eye is treated.

Caution is required in aphakic patients, pseudophakic patients with torn posterior lens capsule or anterior chamber lenses, or in patients with known risk factors for cystoid macular oedema or iritis/uveitis.

There is only very limited experience in aphakic patients and in pigmentary and pseudoexfoliative glaucoma. There is no experience available in patients with neovascular, angle-closure, narrow angle or congenital glaucoma. Nor is there experience in patients with severe asthma.

Use in special situations[1]

Pregnancy: there is no sufficient data regarding its use. It should not be employed unless when strictly necessary or no other therapeutic options are available. **Lactation:** it is unknown whether tafluprost is excreted in human breastmilk. It should not be employed during the lactation period. **Elderly:** no dose adjustments are necessary. **Children and adolescents under 18 years of age:** it is not recommended given the lack of data on safety and efficacy in this group. **Renal and liver impairment:** no studies are available in these patients and therefore caution should be taken when employed.

Place in therapeutics

There are already different drugs employed in the treatment of open-angle glaucoma, which are administered topically, in either monotherapy or combined treatment. They reduce elevated intraocular pressure and therefore progression of the disease. Beta-blockers and prostaglandin analogues are the elective management options[7].

Tafluprost is a new prostaglandin analogue indicated in the reduction of elevated IOP in patients with glaucoma and ocular hypertension. In the only clinical trial directly comparing tafluprost with latanoprost, another prostaglandin analogue, non-inferiority was not established. The efficacy of tafluprost in combined treatment with betablockers has been studied in a clinical trial which showed additive effects when combined with timolol.

As a prostaglandin analogue, tafluprost has a similar safety profile to the rest of the group. The most frequent side effect is ocular hyperaemia, and other frequent effects include cefalea, pruritus, and eye irritation, eye pain, changes in eyelashes, pigmentation and eyelid oedema.

The non-preservative formulation of tafluprost differentiates it from the rest of the prostaglandin analogues. For this reason it may be useful in patients with allergies or who present intolerance to presevatives. However in the only clinical trial carried out with both formulations (with and without preservatives), no better tolerance was shown with the non-preservative formulation.

Presentation

Saflutan 15 mcg/mL eyedrops 30 single dose containers with 0.3 mL solution each (28.99 €). Store in refrigerator (between 2°C and 8°C). Prescription medicine only.

References

A complete report can be found at: www.dtb.navarra.es

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