



Generic Latanoprost Prescribing

The patent for Xalatan® expired on 17 January 2012. The MHRA has granted Pfizer and twenty other companies licences for generic latanoprost production. At least ten of these companies, including Pfizer, are now distributing generic latanoprost eye drops in the UK.

The European Agency for the Evaluation of Medicinal Products' document 'Note for guidance on the Clinical requirements for locally applied, locally acting products containing known constituents' (CPMP/EWP/239/95) recognises that changes in formulation can affect the bioavailability and therefore efficacy of these products. Thus, bioavailability and efficacy studies are only required if there are changes in formulation or presentation such as:

- change in active ingredient(s) \with regard to specification of the physical properties
- change in inactive ingredient(s)
- change in application with regard to application device (e.g. inhalation chamber)

Product Characteristics

Examination of the Summaries of Product Characteristics of nine versions of generic latanoprost shows that the formulation of these generic products is **very similar or identical to that of the original formulation of Xalatan®** i.e.:

- Latanoprost 50 micrograms/ml (0.005%)
- Benzalkonium chloride 200 micrograms/ml (0.02%)
- Sodium chloride
- Sodium dihydrogen phosphate monohydrate or sodium dihydrogen phosphate dehydrate or monobasic sodium phosphate
- Anhydrous disodium phosphate or disodium phosphate dodecahydrate
- Water for Injections or Purified Water

One generic may also contain sodium hydroxide or hydrochloric acid to adjust the pH.

The pH (ranges 6.2 – 7.2) is similar to that of the Xalatan® formulation available until March 2013 (6.5-6.9) as is the osmolality (ranges 240-330 mOsm/Kg), that of Xalatan® having been 250-300 mOsm/Kg.

Studies on Efficacy and Tolerability of Generics

There are a number of studies comparing the efficacy and tolerability of generic versions of latanoprost with Xalatan®.

A study from Slovakia (N=77) showed the equivalence of Unilat®, a generic version of latanoprost, to Xalatan® in terms of efficacy and tolerability².

A smaller study from India (N=29) was not sufficiently powered to detect a significant difference in safety, showed a significant difference in intraocular pressure between the two treatments at week 12 (Xalatan® more efficacious) but there was no significant difference at week 24³. The authors of the latter study suggest that the higher pH (value not stated) of the generic version may explain the higher (but non-significant) incidence of ocular irritation in the group receiving generic latanoprost.

A larger European multicentre, investigator-masked study (N=257) compared the efficacy and safety of Xalatan® and the Bausch and Lomb formulation of latanoprost packed in identical containers over a 6 week period. Both treatment groups showed sustained and comparable decreases in IOP at all assessed time points. The mean decrease in IOP with the Bausch & Lomb latanoprost was statistically noninferior to that seen with Xalatan® and there was no significant difference in adverse events⁴.

A fourth study (N=184) conducted over 12 weeks compared Xalatan® and an Italian generic latanoprost (Mipharm SpA, Milan, Italy) with exactly the same qualitative and quantitative composition. There was no significant difference in IOP at 9am, 1pm or 5pm at 12 weeks between patients using Xalatan® and those using the generic version⁵.

None of the generic versions of latanoprost used in these studies is available in the UK.

The general guidance is that prescribers can be confident that the contents of the bottle will be similar so bioavailability should be similar.

Licence for Paediatric use

Prescribers and pharmacists should be aware that the Actavis, Beacon and Tubilux generics are not licensed for paediatric use

Storage requirements

From 1st March 2013, Pfizer have been distributing a new formulation of Xalatan® with a higher phosphate content and lower pH than that of the original formulation. This change has reduced the shelf life from 3 years to 2 years but allows storage at room temperature throughout the 2 year shelf life⁶. The other generics must be stored in a refrigerator until opened but may be stored at room temperature for the four weeks that the bottle is in use.

Variation in appearance of bottle (See Photo)

It is also important to note that the bottle could be quite different and patients who have been able to manage a bottle of Xalatan® may well not be able to manage a different bottle. The patient should be offered alternative generic equivalents and/or a compliance aid to help with administration of the eye drops.



Adverse reaction

Suspected side effects (also known as adverse drug reactions) to a medicine, vaccine, herbal or complementary remedy should be reported to the Medicines and Healthcare Products Regulatory Agency via its Yellow Card Reporting website <http://yellowcard.mhra.gov.uk/>

The Yellow Card Scheme, run by the MHRA and the Commission on Human Medicines, is used to collect information from both health professionals and the general public on suspected side effects.

References

1. European Agency for the Evaluation of Medicinal Products Note for guidance on the Clinical requirements for locally applied, locally acting products containing known constituents (CPMP/EWP/239/95) 1995 available at http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003687.pdf (accessed 4.4.12)
2. Strmen P et al Clinical trial of the generic product UNILAT following its efficiency and safety in glaucoma and intraocular hypertension Cesk Slov Oftalmol. 2010 Dec;66(6):258-61
3. Narayanaswamy A. et al. Indian J Ophthalmol. A randomized, crossover, open label pilot study to evaluate the efficacy and safety of Xalatan in comparison with generic Latanoprost (Latanoprost) in subjects with primary open angle glaucoma or ocular hypertension. 2007;55:2:127-131
4. Allaire C et al. Latanoprost 0.005% test formulation is as effective as Xalatan in patients with ocular hypertension and primary open angle glaucoma Eur J Ophthalmol. 2012 Jan-Feb; 22(1): 19-27
5. Diguini M et Al An evaluation of therapeutic noninferiority of 0.005% latanoprost ophthalmic solution and Xalatan in patients with glaucoma or ocular hypertension J Glaucoma 2012 (e published ahead of print)
6. Xalatan® Summary of Product Characteristics available at <http://www.medicines.org.uk/emc/medicine/9043/SPC/>

The Royal College of Ophthalmologists
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