1.5. SPECIFIC REQUIREMENTS FOR DIFFERENT TYPES OF APPLICATIONS

1.5.2. Information for generic, "hybrid" or bio-similar applications

Introduction

The present marketing authorisation application is related to a medicinal product claiming essential similarity to Xalatan® (latanoprost) eye drops solution 50 µg/mL (Pfizer) and authorized pursuant to Article 10(3) hybrid application of Directive 2001/83/EC, as it has:

- the same qualitative and quantitative composition in active substances as the reference medicinal product,
- the same pharmaceutical form as the reference medicinal product (eye drops solution)
- the bioavailability studies cannot be used to demonstrate bioequivalence for locally acting products subsequent to the CPMP/EWP/239/95 final 'Note for Guidance on clinical requirements for locally applied, locally acting products containing known constituents'

The reference medicinal product is Xalatan® (latanoprost) eye drops solution 50 µg/mL (Pfizer), which has been authorized in the European community for more than ten years.

Compositions of Latanoprost/Pharmathen and Xalatan

The qualitative and quantitative composition of Latanoprost/Pharmathen 0.005% eye drops solution is presented in the following table.

Table 1. Composition of Latanoprost/Pharmathen 0.005% eye drops solution

Ingredients	**% w/v**	**mg per ml solution**	**Function for excipients**
Latanoprost	0.005	0.05	Drug substance
Macrogolglycerol hydroxystearate (nominal value:40)			Solubilizing/stabilizing agent
Sodium Chloride			Tonicity agent
Disodium Edetate			Chelating agent
Sodium dihydrogen phosphate dihydrate			Buffering agent
Anhydrous disodium phosphate			Buffering agent
Hydrochloric acid or Sodium hydroxide*			pH-adjustment agent
Water for Injections			vehicle
Total solution volume	**100.000**	**1ml**	

*Sodium hydroxide solution or/and Hydrochloric Acid solution is used for pH adjustment.

The reference product Xalatan also contains 0.05 mg of latanoprost. The other excipients are BAK, sodium chloride, sodium dihydrogen phosphate monohydrate, anhydrous disodium phosphate and water for injections.

Comparison of physicochemical properties of Latanoprost/Pharmathen 0.005% and Xalatan 0.005%

The comparative presentation of the impurities and the physicochemical properties of Latanoprost/Pharmathen 0.005% and Xalatan 0.005% are depicted in the following table.

Table 2. *Comparative presentation of physicochemical properties of Latanoprost/Pharmathen 0.005% and Xalatan 0.005%*

Tests/ Specifications	**LATANOPROST 0.05mg/mL preservative free eye drops solution**			**XALATAN 0.005% eye drops solution**		
	Lot.	**Lot.**	**Lot.**	**B/N:**	**B/N:**	**B/N:**
Appearance	Clear, colourless aqueous solution in white plastic bottle with ophthalmic dispenser	Clear, colourless aqueous solution in white plastic bottle with ophthalmic dispenser	Clear, colourless aqueous solution in white plastic bottle with ophthalmic dispenser	Clear, colourless solution	Clear, colourless solution	Clear, colourless solution
pH 5.5-6.5						
Osmolality 234-286 mOsm/Kg						
Extractable volume NLT 3.0mL						
Drop Volume (μL) *(for information only)*						
Viscosity (cP) Speed: 100rpm *(for information only)*						
Buffering capacity (mmol/Lt)/ΔpH *(for information only)*						
Assay Latanoprost *95.0-105.0% of the stated amount of Latanoprost*						
Related Substances of LATANOPROST						
Acid Latanoprost NMT 1.0%	ND	ND	ND			
5,6-trans Latanoprost	ND	ND	ND			

Tests/ Specifications	LATANOPROST 0.05mg/mL preservative free eye drops solution			XALATAN 0.005% eye drops solution		
	Lot. ND0140	**Lot. NE0067**	**Lot. NE0107**	**B/N: M55622 (DE)**	**B/N: M80108_ M65670 (BEL)**	**B/N: N31182_ N23345 (AUT)**
NMT 1.0%						
Enantiomer Latanoprost NMT 1.0%	ND	ND	ND	ND	ND	ND
15S-Latanoprost NMT 1.0%	ND	ND	ND	ND	ND	ND
Any unknown NMT 1.0%	ND	ND	ND			
	ND	ND	ND			
	ND	ND	ND			
	ND	ND	ND			
	ND	ND	ND			
Total: NMT 6.0%		ND	ND			

The profile comparison between Latanoprost preservative free eye drops solution (Pharmathen) and Xalatan eye drops solution reference products (Pfizer) reveals similarity between the products. The results for the physicochemical properties are almost essentially similar.

Conclusion

In conclusion, Latanoprost/Pharmathen and Xalatan/Pfizer:

- are both aqueous ophthalmic solutions,
- contain the same concentration of the active substance latanoprost,
- have some differences in excipients (absence of BAK, presence of macrogolglycerol hydroxystearate 40, and disodium edetate dehydrate in Latanoprost/Pharmathen) that are not expected to exert any influence on efficacy, and may lead to less adverse effects on the ocular surface in the case of Latanoprost/Pharmathen compared to Xalatan/Pfizer,
- are similar as per their physicochemical characteristics,
- display comparable absorption and distribution of latanoprost within the eye in a rabbit model.
- according to the relevant guidelines a waiver of the need to provide equivalence data via an *in vivo* study can be granted.

Therefore abridged applications for this product should be regarded as “hybrid applications” in compliance with Article 10(3) of Directive 2001/83/EC as amended.