NEW DRUG SUBMISSION / NOTICE OF COMPLIANCE: DEC 2022

Aequus PHARMACEUTICALS

Zimed® PF

Bimatoprost 0.03%
Preservative Free
Multi-Dose

ZIMED® PF (bimatoprost ophthalmic solution 0.03% w/v) preservative free in multi-dose container, is indicated for the reduction of elevated intraocular pressure in patients with open angle glaucoma or ocular hypertension.

Zimed® PF

Introducing: Zimed® PF

Reduction of elevated intraocular pressure in open-angle glaucoma and ocular hypertension	Indication
The recommended dose is one drop in the affected eye(s) once daily, in the evening	Dosage
If more than one topical ophthalmic drug is being used, the drugs should be administered at least five (5) minutes apart. Contact lenses should be removed prior to instillation of ZIMED® PF and may be reinserted 15 minutes following administration	Method of Administration

Canada's first & only preservative free and multi-dose ophthalmic PGA

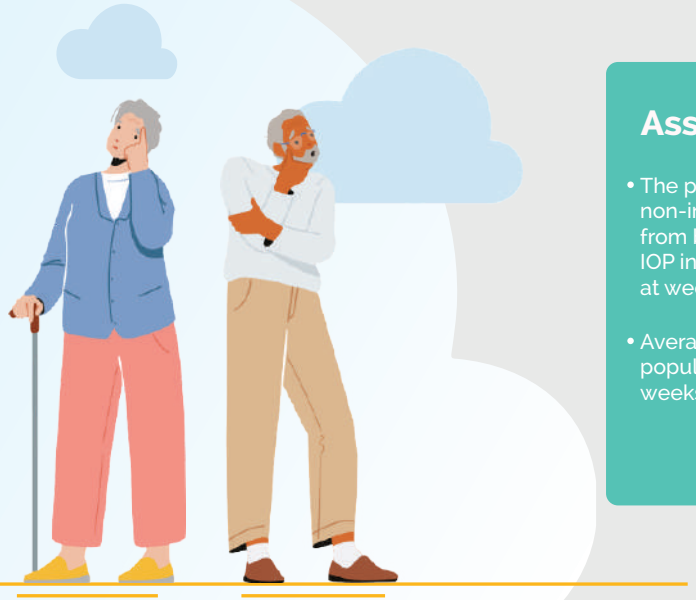
Zimed® PF

Zimed® PF vs Lumigan® for glaucoma or ocular hypertension

A prospective, multicentre (36 sites in the USA), double-masked, randomised, parallel-group,12-week study. 597 patients were randomised (preservative free bimatoprost, n=302 and preserved bimatoprost, n=295)[1]

Inclusion Criteria

- At least 18 years old with OHT and various types of glaucoma
- 4 days to 4 weeks washout period
- IOP 22-30 mmHg in each eye
- Assymetry between the eyes of no more than 3mmHg
- Snellen score of 20/100.



Assessment

- The primary analysis for non-inferiority was change from baseline in worse eye IOP in the PP population at week 12
- Average eye IOP in the ITT population at each time point at weeks 2, 6 and 12

Treatment

- Stratified by baseline mean diurnal IOP (≤24 mm Hg or >24 mm Hg)
- Randomly assigned to receive PF bimatoprost or preserved bimatoprost in a 1:1 ratio.

Result:
Preservative free bimtoprost 0.03% is non-inferior (IOP-lowering) and equivalent (safety) to preserved bimatoprost 0.03%

1 Day DG, et al. (2013). Bimatoprost 0.03% preservative-free ophthalmic solution versus bimatoprost 0.03% ophthalmic solution (Lumigan) for glaucoma or ocular hypertension: a 12-week, randomised, double-masked trial. Br J Ophthalmol. 97(8):989-93. doi: 10.1136/bjophthalmol-2012-303040.

Zimed® PF

Zimed® PF is an alternative to Lumigan with no BAK*[1]

WORSE EYE ANALYSIS:

For the change from baseline in worse eye IOP at each hour at week 2,6 and 12 in the pre-protocol population, the 95% CI upper limit of the between-group difference did not exceed 0.78 mm Hg at any hour. Both treatments showed statistically and clinically significant decreases in IOP from baseline at all time points (p<0.001)

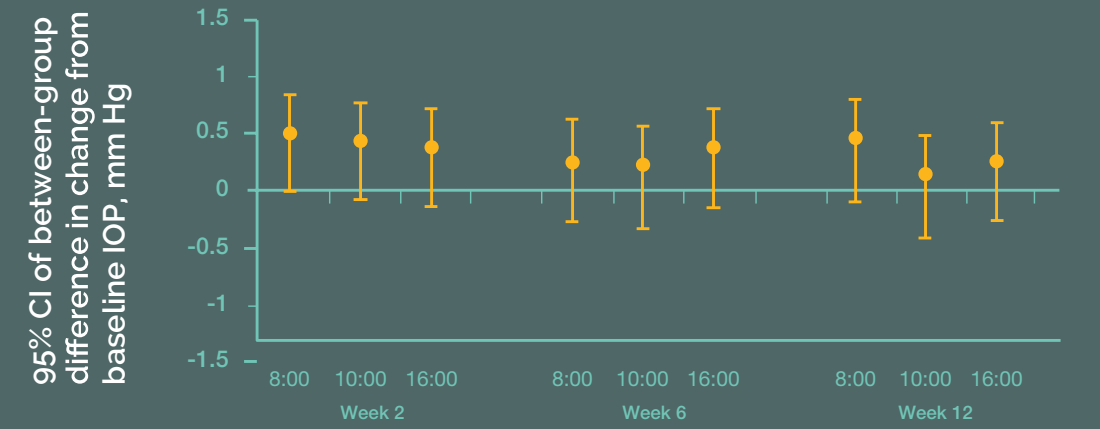


Figure 1 Between-group differences at each time point in change from baseline in worse eye intraocular pressure (IOP), per-protocol population. Upper limit of 95% CI of between-group difference=0.75 mm Hg at week 12.

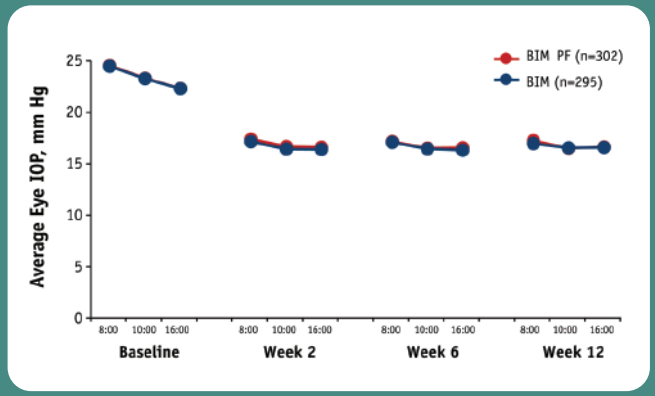


Figure 2 Mean average IOP at each time point, intent-to-treat population. Difference between groups <0.3 mm Hg.

AVERAGE EYE ANALYSIS:

For mean change from baseline in average eye IOP at week 2, 6 and 12 in the ITT population, the upper and lower 95% CI limits were within a 1.0 mmHg margin at each hour. Both treatments showed statistically and clinically significant mean decreases from baseline at all time points (p<z.001).

* At hours 0, 2 and 8, at week 12 visit for worse eye IOP change from baseline. Upper limit of the 95% CI for between-treatment difference did not exceed 1.0 mmHg

1. Day DG, et al. (2013). Bimatoprost 0.03% preservative-free ophthalmic solution versus bimatoprost 0.03% ophthalmic solution (Lumigan) for glaucoma or ocular hypertension: a 12-week, randomised, double-masked trial. Br J Ophthalmol. 97(8):989-93. doi: 10.1136/bjophthalmol-2012-303040.

IOP= Intraocular Pressure

Zimed® PF

Zimed® PF has a similar safety profile to Lumigan®

Zimed® PF provides a well-tolerated and efficacious treatment alternative for patients with sensitivity to preservatives[1]

- **Ocular adverse events:**
  - Preserved bimatoprost - 34.9% (102/295)
  - PF bimatoprost - 31.9% (96/301)
- The most frequent ocular AE was conjunctival hyperaemia

- **AEs other than ocular:**
  - Preserved bimatoporst - 14.2% (42/295)
  - PF bimatoprsot - 13.6% (41/301)
- Nasopharyngitis was the most common

- Conjunctival hyperaemia AEs were reported as mild or moderate for the majority of patients
- Six patients (PF bimatoprost, n=2 and preserved bimatoprost, n=4) reported serious AEs

- Five patients (PF bimatoprost, n=2 and preserved bimatoprost, n=3) discontinued due to AEs

1. Day DG, et al. (2013). Bimatoprost 0.03% preservative-free ophthalmic solution versus bimatoprost 0.03% ophthalmic solution (Lumigan) for glaucoma or ocular hypertension: a 12-week, randomised, double-masked trial. Br J Ophthalmol. 97(8):989-93. doi: 10.1136/bjophthalmol-2012-303040.

AE = Adverse Events; PF = Preservative free

Zimed® PF

Zimed® PF Benefits

Manage glaucoma without worrying about preservative load

- Preservative free formula
- Non-inferior efficacy[1]
- Equivalent safety[1]

Zimed® PF was developed for patients with sensitivity to preservatives[1].

- Similar to the eye, Zimed® PF has a pH of 7.3[2]
- Zimed® PF stores at room temperature (15-25°C)
- Discontinuation rate - 0.7% (2/301)[1]

1. Day DG, et al. (2013). Bimatoprost 0.03% preservative-free ophthalmic solution versus bimatoprost 0.03% ophthalmic solution (Lumigan) for glaucoma or ocular hypertension: a 12-week, randomised, double-masked trial. Br J Ophthalmol. 97(8):989-93. doi: 10.1136/bjophthalmol-2012-303040.

2. EMC, 2022. Zimed Preservative Free 0.3mg/ml, eye drops solution. https://www.medicines.org.uk/emc/product/13887

Sustainability with Zimed®PF

Single-dose unit (SDU) vs Zimed® PF in a multi-dose use (MDU) bottle[3]

Is sustainability important to you and your patients?

RAW MATERIALS:

SDU uses 4.6x more plastic than Zimed® PF multi-dose.

DRUG WASTE:

SDU uses 8.5x higher drug waste than Zimed® PF multi-dose.

TRANSPORTATION:

SDU need 9 trucks for transport to dispensaries versus only 1 truck for Zimed® PF multi-dose.

3. Nemera data on file. Sustainability analysis Novelia vs monodoses. October 17, 2022.

Zimed® PF

Zimed® PF bottle convenience

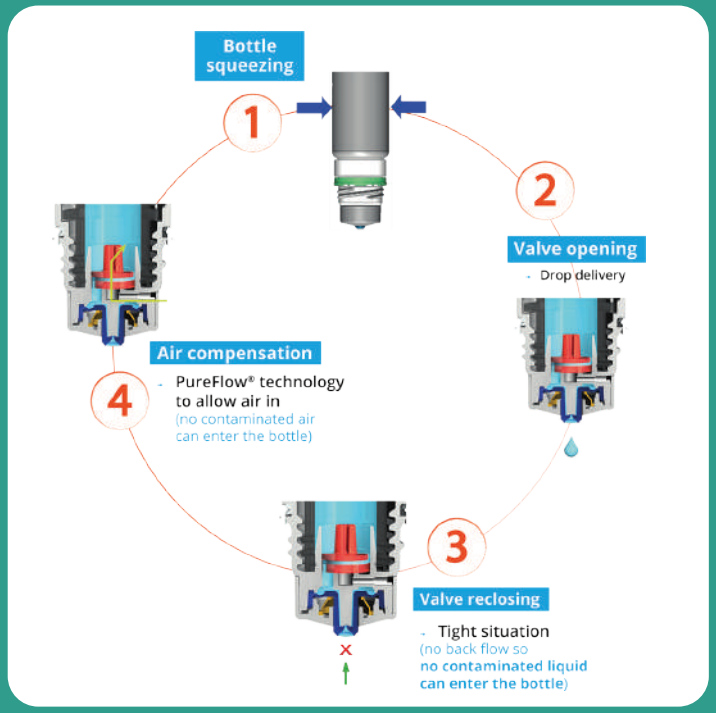
Zimed®PF is equipped with the Novelia® one-way valve & PureFlow® technology

Addressing patient challenge[4]

- Easy to use ergonomic design
- 28-32 microlitre calibrated drops
- Full flow control
- Blue tip for targeting
- Portability with screw-on cap

Zimed® PF is manufactured in Spain.
Nemera bottle is made in France.

How the PureFlow® technology works:



Novelia® and PureFlow™ are trademarks of Nemera La Verpillière SAS. The shape and color of the nozzle of Novelia dispenser and the shape of Novelia Vented Cap are protected by trademarks of Nemera La Verpillière SAS.

4. Nemera. Ophthalmic drug delivery (2021). Available at: https://www.nemera.net/wp-content/uploads/2021/05/ODD-Ophthalmic-drug-delivery-Nemera_2021-04.pd

Zimed® PF - Canada's first & only PF, multi-dose PGA

INSTILLATION:
Neutral pH 7.3
Storage: Room temperature

FORMULATION:
Bimatoprost 0.03%
100% preservative free

ADMINISTRATION:
Multi-dose bottle
Secure twist recappable
Portable

Efficacy

Benefit

Convenience

Zimed® PF - as eZ as EBC

Zimed® PF

Date of Preparation:
November 2023

Scan for product monograph

eZ on the eyes

Indication

ZIMED® PF (bimatoprost ophthalmic solution 0.03% w/v) is indicated for: the reduction of elevated intraocular pressure in patients with open angle glaucoma or ocular hypertension.

Contraindication

ZIMED® PF is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container.

Most Serious Warnings and precautions

Ocular inflammation: use with caution.

Macular edema: use with caution in patients with macular edema risk factors.

Other relevant warnings and precautions

Increased Pigmentation: of iris, periorbital tissue or eyelashes.

Silver: avoid if history of contact sensitivity to silver.

Pregnant women: should be administered during pregnancy only if the potential benefit justifies the potential risk to the fetus.

For more information:

Consult the **Product Monograph** for important information relating to adverse reactions, drug interactions, and dosing information which have not been discussed in this piece.

The Product Monograph is also available by calling 1-833-542-2633.

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