Attachment 1: Product information for AusPAR Saflutan Tafluprost Merck Sharpe & Dohme PM-2009-3896-5 Final 3 May 2012. This Product Information was approved at the time this AusPAR was published.

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PRODUCT INFORMATION

SAFLUTAN™

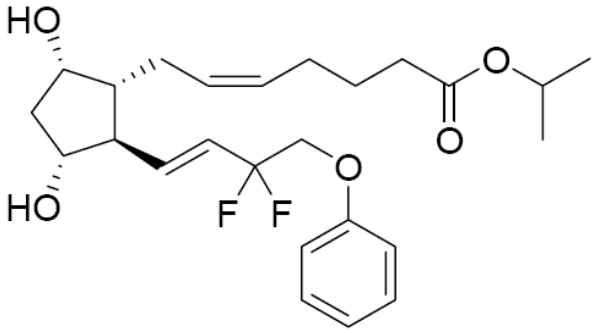
(tafluprost, MSD)

DESCRIPTION

The active ingredient in SAFLUTAN is tafluprost, a prostaglandin analogue.

The chemical name for tafluprost is 2-Propyl (5Z)-7-[(1R, 2R, 3R, 5S)-2-[(1E)-3,3-difluoro-4-phenoxybut-1-enyl]-3,5-dihydroxycyclopentyl]hept-5-enoate. The empirical formula of tafluprost is $C_{25}H_{34}F_2O_5$ and its molecular weight is 452.53.

Tafluprost is a colourless to light yellow viscous liquid that is practically insoluble in water. Its structural formula is:



CAS Registry Number: 209860-87-7

SAFLUTAN is available as an ophthalmic solution containing 15 micrograms of tafluprost per mL. SAFLUTAN does not contain preservatives such as benzalkonium chloride.

One single-dose container (0.3 mL) contains 4.5 micrograms of tafluprost.

SAFLUTAN contains the following inactive ingredients: glycerol, sodium phosphate – dibasic dihydrate, disodium edetate, polysorbate 80, sodium hydroxide and/or hydrochloric acid, and water for injections.

PHARMACOLOGY

Mechanism of Action

Tafluprost is a fluorinated analogue of prostaglandin $F_{2\alpha}$. Tafluprost acid, the biologically active metabolite of tafluprost, is a highly potent and selective agonist of the human prostanoid FP receptor. Tafluprost acid has sub-nanomolar affinity for the FP receptor (K_i, 0.4 nM), 12-times higher than that of latanoprost acid.

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Reduction of the intraocular pressure in humans starts about 2 to 4 hours after administration and maximum effect is reached 12 hours after instillation. The effect is maintained for at least 24 hours.

Pharmacodynamic studies in monkeys indicate that tafluprost reduces intraocular pressure by increasing the uveoscleral outflow of aqueous humour.

Pharmacokinetics

Absorption

Tafluprost is absorbed through the cornea where the isopropyl ester is hydrolysed to the biologically active acid metabolite. Pharmacokinetics of tafluprost acid were obtained from a study comparing preservative-containing and preservative-free ophthalmic solutions. The preservative-free formulation showed similar pharmacokinetic properties to the preservative-containing formulation. Mean plasma C_{max} for the preservative-containing and preservative-free formulations were 24 pg/mL and 26 pg/mL, respectively on Day 1, and 31 pg/mL and 27 pg/mL, respectively on Day 8. Mean plasma $AUC_{0\text{-last}}$ for the preservative-containing and preservative-free formulations were 406 pg*min/mL and 394 pg*min/mL, respectively on Day 1, and 581 pg*min/mL and 432 pg*min/mL, respectively on Day 8. Mean plasma concentrations were below the limit of quantification at 30 minutes for both formulations.

In a rabbit study, the absorption of tafluprost into the aqueous humour was comparable after a single ocular instillation of preservative-free or preservative-containing tafluprost 0.0015% ophthalmic solution.

Distribution

After topical administration of 1µg ^{3}H-tafluprost on the monkey eye, the maximum radioactivity in the aqueous humour was detected at 2 hours (30-40 ng equivalents/mL) and declined to 0.3-0.4 ng equivalents/mL at 24 hours. Lower levels of drug related radioactivity were observed in tissues outside the eye and also declined over 24 hours.

The binding of tafluprost acid to human serum albumin was >99%. It is anticipated that tafluprost acid will be highly protein bound in human plasma.

Metabolism

Tafluprost, an ester prodrug, is hydrolysed to its biologically active acid metabolite in the eye. The acid metabolite is further metabolised via fatty acid β-oxidation and phase II conjugation.

Cytochrome P450 (CYP) enzyme system is not involved in the metabolism of tafluprost acid.

Elimination

In two clinical studies, mean tafluprost acid metabolite concentrations fell below the limit of quantification in plasma (10 pg/mL) 30 minutes after administration, indicating rapid elimination.

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Characteristics in patients:

Renal Insufficiency
Tafluprost has not been studied in patients with renal insufficiency and should therefore be used with caution in such patients.

Hepatic Insufficiency

Tafluprost has not been studied in patients with hepatic insufficiency and should therefore be used with caution in such patients.

Pharmacodynamics

Tafluprost in clinical doses has not been found to have any significant pharmacological effects on the cardiovascular system.

CLINICAL TRIALS

Clinical Effects on Intraocular Pressure

The efficacy of tafluprost as monotherapy, or as adjunctive therapy to timolol, was investigated in clinical studies of up to two-years duration in patients with primary open-angle glaucoma or ocular hypertension.

Reduction of intraocular pressure (IOP) starts between 2 and 4 hours after the first administration and maximum effect is reached at around 12 hours after instillation. The duration of effect is maintained for at least 24 hours. Pivotal studies with a tafluprost formulation containing the preservative benzalkonium chloride have demonstrated that tafluprost is effective as monotherapy and has an additive effect when administered as adjunctive therapy to timolol.

Monotherapy Versus Active Comparator

The efficacy of tafluprost as monotherapy in patients with primary open-angle glaucoma or ocular hypertension (baseline IOP $\geq$22 mmHg) was demonstrated in two large clinical studies of up to two-years duration. The IOP-lowering effect of tafluprost was demonstrated throughout the day and this effect was maintained during long-term administration.

A randomised, double-masked, active controlled, parallel group, multicentre Phase III study compared the efficacy and safety of tafluprost 0.0015% q.d. (N=269) eye drops with that of latanoprost 0.005% q.d. (N=264) eye drops in patients with open-angle glaucoma or ocular hypertension. The protocol-specified primary outcome measure was the difference in diurnal IOP reduction at 6 months from baseline. The primary efficacy endpoint was the change from baseline in the overall diurnal IOP at month 6 and the non-inferiority was determined if the 95% CI of the treatment difference did not exceed 1.5mm Hg. The primary efficacy analysis, change from baseline to 6 months in the diurnal IOP, used a repeated measurements analysis of covariance (RM ANCOVA) model which included fixed effects for baseline, pooled centre, treatment visit and time, and all interactions among treatment, visit

and time. A sensitivity analysis without baseline IOP as a covariate (RM ANOVA) was also performed. The study was continued for up to 24 months. The IOP lowering effects over 24 months and the treatment difference based ITT (Intent to Treat) dataset are presented in Tables 1 and 2 below. ITT dataset included all randomised patients who had received at least one dose of study treatment and had at least one efficacy measurement available.

Table 1: IOP (in worse eye) and Reduction Compared to Baseline Over 24 Months

		Tafluprost			Latanoprost		
Visit	Time Point	N	Mean (SD) mmHg	Change (% Change)	N	Mean (SD) mmHg	Change (% Change)
Baseline	8:00	264	25.84 (2.94)	---	264	25.26 (2.86)	---
	12:00	264	24.48 (3.41)	---	264	24.17 (3.02)	---
	16:00	263	23.60 (3.67)	---	264	23.11 (3.45)	---
	20:00	264	23.16 (3.66)	---	264	22.82 (3.63)	---
Week 2	8:00	264	17.72 (3.32)	-8.12 (-31.4%)	264	16.70 (3.20)	-8.56 (-33.7%)
Week 6	8:00	263	17.83 (3.43)	-8.01 (-30.8%)	260	16.59 (3.02)	-8.69 (-34.0%)
Month 3	8:00	254	17.55 (3.25)	-8.29 (-31.8%)	256	16.16 (2.87)	-9.10 (-35.7%)
	12:00	252	17.07 (3.10)	-7.34 (-29.5%)	256	15.80 (2.89)	-8.39 (-34.3%)
	16:00	250	16.72 (3.02)	-6.93 (-28.4%)	254	15.85 (2.83)	-7.18 (-30.5%)
	20:00	252	16.84 (2.94)	-6.29 (-26.3%)	255	15.84 (2.83)	-6.95 (-29.8%)
Month 6	8:00	244	17.77 (3.48)	-8.05 (-31.0%)	251	16.10 (2.95)	-9.16 (-35.9%)
	12:00	242	17.28 (3.22)	-7.09 (-28.6%)	251	15.67 (2.93)	-8.48 (-34.3%)
	16:00	243	16.96 (3.10)	-6.72 (-27.5%)	248	15.55 (2.87)	-7.51 (-31.8%)
	20:00	243	16.82 (3.14)	-6.30 (-26.5%)	248	15.75 (2.67)	-7.05 (-30.0%)
Month 9	8:00	242	18.02 (3.61)	-7.80 (-30.0%)	250	16.36 (2.90)	-8.90 (-34.8%)
Month 12	8:00	227	18.13 (3.66)	-7.63 (-29.4%)	247	16.31 (2.99)	-8.98 (-35.1%)
	12:00	224	17.26 (3.43)	-7.00 (-28.3%)	246	15.91 (2.97)	-8.28 (-33.7%)
	16:00	222	17.23 (3.40)	-6.24 (-25.7%)	244	15.74 (2.95)	-7.29 (-30.8%)
	20:00	220	17.23 (3.44)	-5.77 (-24.2%)	243	16.01 (3.30)	-6.71 (-28.5%)
Month 15	8:00	192	17.38 (3.48)	-8.22 (-31.8%)	224	15.79 (2.73)	-9.41 (-36.9%)
Month 18	8:00	188	17.19 (3.35)	-8.43 (-32.7%)	220	15.87 (3.16)	-9.31 (-36.4%)
	12:00	186	16.59 (3.09)	-7.49 (-30.5%)	218	15.85 (3.02)	-8.18 (-33.4%)
	16:00	185	16.46 (3.08)	-6.89 (-28.8%)	219	15.55 (2.99)	-7.32 (-31.0%)
	20:00	184	16.49 (3.08)	-6.40 (-27.0%)	218	15.68 (3.09)	-6.78 (-29.2%)
Month 24	8:00	185	17.56 (4.00)	-8.01 (-31.3%)	217	16.13 (2.85)	-9.01 (-35.4%)
	12:00	186	16.87 (3.68)	-7.23 (-29.4%)	216	15.82 (2.93)	-8.20 (-33.6%)
	16:00	183	16.79 (3.43)	-6.63 (-27.4%)	216	15.86 (2.87)	-7.03 (-29.7%)
	20:00	181	16.69 (3.44)	-6.32 (-26.5%)	212	15.82 (2.91)	-6.59 (-28.5%)

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Table 2: The Estimated treatment differences (tafluprost – latanoprost)

ITT Efficacy	RM ANCOVA		RM ANOVA	
Visit	Difference	Upper 95% CI	Difference	Upper 95% CI
Month 3	1.05	1.46*	0.79	1.28*
Month 6	1.32	1.73	1.05	1.54
Month 12	1.44	1.86	1.2	1.7
Month 18	1.05	1.49*	0.81	1.33*
Month 24	1.15	1.6	0.91	1.44*
Overall	1.2	1.52	0.95	1.38*

* Non-inferiority demonstrated

Tafluprost 0.0015% once daily showed a significant IOP-lowering effect from baseline of 6 to 8 mmHg as compared to 7 to 9 mmHg with latanoprost 0.005%. At the primary endpoint following 6 months treatment, non-inferiority was not demonstrated. However, at the 3-month, 18-month and 24-month (RM ANOVA; unadjusted for baseline IOP) time points and the 3-month and 18-month (RM ANCOVA; adjusted for baseline IOP) time points, non-inferiority was demonstrated. The IOP-lowering effect of tafluprost was sustained throughout this study up to 24 months.

A randomised, double-masked, active controlled, parallel group, multicenter Phase III clinical study compared the efficacy and safety of tafluprost 0.0015% with timolol 0.5% in patients with open-angle glaucoma or ocular hypertension. The primary efficacy endpoint was the change from baseline in the overall diurnal IOP at month 6 and the non-inferiority was determined if the 95% CI did not exceed 1.5mmHg. At the 6 month timepoint, there was a mean change of 5 to 7 mmHg in the tafluprost 0.0015% q.d. group (N=267) and 4 to 6 mmHg in the 0.5% timolol b.i.d. group (N=191). Non-inferiority to timolol was demonstrated. The IOP-lowering effect of tafluprost was sustained in the extension of this study up to 12 months.

The treatment difference based on ITT (Intent to Treat) dataset are presented in Tables 3 and 4 below. ITT dataset included all randomised patients who had received at least one dose of study treatment and had at least one efficacy measurement available.

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Table 3: IOP (in worse eye) and Reduction Compared to Baseline Over 12 Months

		Tafluprost			Timolol		
Visit	Time Point	N	Mean (SD) mmHg	Change (% Change)	N	Mean (SD) mmHg	Change (% Change)
Baseline	8:00	265	25.61 (3.06)	---	187	25.63 (3.18)	---
	10:00	265	23.52 (3.61)	---	187	23.80 (3.84)	---
	16:00	265	22.57 (3.70)	---	187	22.66 (4.03)	---
Week 2	8:00	265	18.64 (3.32)	-6.96 (-26.8%)	187	19.14 (3.37)	-6.49 (-25.0%)
	10:00	77	17.44 (2.95)	-6.12 (-24.8%)	62	17.65 (2.91)	-5.94 (-23.9%)
	16:00	77	17.45 (2.88)	-5.44 (-22.3%)	62	17.76 (2.99)	-5.03 (-20.4%)
Week 6	8:00	260	18.56 (3.23)	-7.07 (-27.2%)	185	18.64 (3.50)	-6.94 (-26.8%)
	10:00	141	17.29 (3.18)	-5.73 (-24.0%)	105	17.49 (3.07)	-5.95 (-24.5%)
	16:00	140	16.95 (3.09)	-5.13 (-21.8%)	105	17.69 (3.33)	-5.00 (-21.1%)
Month 3	8:00	257	18.96 (3.44)	-6.67 (-25.8%)	180	19.32 (3.93)	-6.28 (-24.4%)
	10:00	257	17.75 (3.23)	-5.74 (-23.7%)	179	17.87 (3.46)	-5.87 (-24.1%)
	16:00	257	17.32 (2.94)	-5.21 (-21.9%)	180	17.71 (3.40)	-4.84 (-20.5%)
Month 6	8:00	251	19.02 (3.42)	-6.58 (-25.4%)	171	19.03 (3.72)	-6.45 (-25.2%)
	10:00	251	17.90 (3.32)	-5.54 (-22.9%)	172	17.97 (3.43)	-5.64 (-23.1%)
	16:00	249	17.22 (2.83)	-5.27 (-22.4%)	171	18.06 (3.14)	-4.38 (-18.2%)
Month 9	8:00	247	18.42 (3.32)	-7.20 (-27.8%)	165	18.88 (3.27)	-6.50 (-25.3%)
	10:00	246	17.65 (3.22)	-5.80 (-24.0%)	165	17.96 (3.30)	-5.46 (-22.6%)
Month 12	8:00	240	18.92 (3.49)	-6.67 (-25.7%)	162	18.49 (3.07)	-6.81 (-26.7%)
	10:00	239	17.82 (3.42)	-5.55 (-23.0%)	159	17.83 (3.26)	-5.49 (-22.7%)
	16:00	239	17.65 (3.21)	-4.74 (-20.0%)	159	18.15 (2.94)	-3.94 (-16.7%)

Table 4: The Estimated Treatment Difference (tafluprost-timolol)

ITT Efficacy	RM ANCOVA		RM ANOVA	
Visit	Difference	Upper 95% CI	Difference	Upper 95% CI
Month 6	-0.28	0.21*	-0.27	0.29*
Month 12	-0.09	0.43*	-0.26	0.32*

* Non-inferiority demonstrated

Adjunctive therapy to Beta-Blocker

The efficacy of tafluprost as adjunctive therapy to timolol in patients with primary open-angle glaucoma or ocular hypertension (baseline IOP ≥23 mmHg) was demonstrated in a 6-week randomised, double-masked, placebo controlled, parallel group, multinational study. The diurnal IOP-lowering effect of tafluprost 0.0015% q.d. (N=96) was compared to vehicle q.d. (N=89) when used adjunctively with timolol 0.5% administered b.i.d. Compared to baseline values (measured after a 4-week run in on timolol), the additional IOP-lowering effects were 5 to 6 mmHg in the timolol-tafluprost group and 3 to 4 mmHg in the timolol-vehicle group.

Preservative-Free Versus Preservative-Containing

In a small 4-week randomised, investigator-masked, multinational cross-over study, the diurnal IOP-lowering effect of preservative-free tafluprost 0.0015% q.d. was compared with the preservative-containing formulation (N=43). Patients were dosed for 4-weeks with the preservative-free and for 4-weeks with the preservative-containing formulation in cross-over

fashion, with an intervening wash-out period. Compared to baseline values, the preservative-containing and the preservative-free formulations of tafluprost showed a similar IOP-lowering effect of approximately 5 mmHg. Both the preservative-free and preservative-containing formulations were generally well tolerated.

Open-Label Preservative-Free Cross-Over

The tolerability and IOP reducing effect of preservative-free tafluprost was investigated in an open-label, phase IIIb study of 158 patients exhibiting ocular surface signs or symptoms during latanoprost 0.005% treatment. Preservative-free tafluprost 0.0015% maintained IOP at the same level after 12 weeks treatment as latanoprost at baseline. After switching to tafluprost, the number of patients with abnormal Schirmer´s test was significantly reduced, and, tear break-up time improved significantly. A reduction in the number of patients with abnormal conjunctival cells based on HLA-DR and MUC5AC was also detected. Patients had fewer ocular signs or symptoms while taking preservative-free tafluprost than while taking latanoprost.

INDICATIONS

SAFLUTAN is indicated for the reduction of elevated intraocular pressure in open-angle glaucoma or ocular hypertension, as monotherapy or as adjunctive therapy to beta blockers.

CONTRAINDICATIONS

Hypersensitivity to tafluprost or to any of the excipients.

PRECAUTIONS

Before treatment is initiated, patients should be informed of the possibility of eyelash growth, darkening of the eyelid skin and increased iris pigmentation. Some of these changes may be permanent, and may lead to differences in appearance between the eyes when only one eye is treated.

The change in iris pigmentation occurs slowly and may not be noticeable for several months. The change in eye colour has predominantly been seen in patients with mixed coloured irises, e.g. blue-brown, grey-brown, yellow-brown and green-brown. Unilateral treatment can result in permanent heterochromia.

There is no experience with tafluprost in neovascular, angle-closure, narrow-angle or congenital glaucoma. There is only limited experience with tafluprost in aphakic patients and in pigmentary or pseudoexfoliative glaucoma.

Macular oedema, including cystoid macular oedema, has been reported during treatment with prostaglandin F2α analogues. These reports have mainly occurred in aphakic patients, pseudophakic patients with a torn posterior lens capsule or anterior chamber lenses, or in patients with known risk factors for macular oedema. Therefore, caution is recommended when using tafluprost in these patients. Caution is also recommended in patients with known risk factors for iritis/uveitis.

Tafluprost has not been studied in patients with compromised lung function and should therefore be used with caution in these patients.

Effects on Fertility

In male and female rats, no adverse effects on mating performance, fertility or early embryonic development were observed with intravenous dosing of tafluprost at up to 100 µg/kg/day, yielding systemic exposure to tafluprost acid over 14000-times the maximum clinical exposure based on C_{max} or greater than 3600-times based on AUC.

Use in Pregnancy (Category B3)

There are no adequate and well-controlled studies with SAFLUTAN in pregnant women.

In embryofetal development studies, tafluprost administered intravenously caused increases in post-implantation losses in rats and rabbits and reductions in fetal body weights in rats. Tafluprost also increased the incidence of spine malformations and vertebral skeletal variations in rats and the incidence of skull, brain and spine malformations in rabbits. In the rats, there were no adverse effects on embryofetal development at 3 µg/kg/day, yielding maternal plasma levels of tafluprost acid that were 343-times the maximum clinical exposure based on C_{max}. In rabbits, effects were seen at doses ≥0.03 µg/kg/day, producing maternal plasma levels of tafluprost acid during the critical period of development that were 5.3-times higher than the clinical exposure based on C_{max}. At the no effect dose in rabbits, maternal plasma levels of tafluprost acid were below the lower limit of quantification (20 pg/mL) and less than the clinical C_{max}.

In a pre- and postnatal development study in rats, increased mortality of newborns were observed with tafluprost at ≥1 µg/kg/day by intravenous administration (yielding 114-times the clinical C_{max}) and decreased birth weights and delayed development (pinna unfolding) were observed at 10 µg/kg/day.

Although animal reproduction studies are not always predictive of human response, SAFLUTAN should not be used during pregnancy unless the potential benefit justifies the potential risk to the fetus.

Women of childbearing age/potential should have adequate contraceptive measures in place.

Use in Lactation

A study in lactating rats demonstrated that radiolabeled tafluprost and/or its metabolites (0.1% of the dose) were excreted in milk. It is not known whether this drug or its metabolites are excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when SAFLUTAN is administered to a nursing woman.

Use in Children

Safety and effectiveness of SAFLUTAN in paediatric patients have not been established. Therefore, treatment with SAFLUTAN is not recommended.

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Use in the Elderly

No differences in efficacy or adverse events profile have been observed between elderly (> 65 years) and non-elderly (≤ 65 years) patients. Therefore, no dosage adjustment is required for elderly patients.

Carcinogenicity

Tafluprost was not carcinogenic when administered subcutaneously daily for 24 months at doses up to 30 µg/kg/day in rats and for 18 months at doses up to 100 µg/kg/day in mice (over 1600- and 1300-times, respectively, the maximum clinical exposure based on plasma AUC).

Genotoxicity

Tafluprost was not mutagenic or clastogenic in a battery of genetic toxicology studies, including an *in vitro* microbial mutagenesis assay, an *in vitro* chromosomal aberration assay in Chinese hamster lung cells, and an *in vivo* mouse micronucleus assay in bone marrow.

Interactions with Other Medicines

No interactions are anticipated in humans, since systemic concentrations of tafluprost are extremely low following ocular dosing. Therefore, specific drug interaction studies have not been performed with tafluprost.

In clinical studies tafluprost was used concomitantly with timolol without evidence of an increase in incidence of adverse events.

Effects on laboratory tests

SAFLUTAN was not associated with clinically meaningful electrolyte disturbances. Clinical laboratory investigations were performed in pivotal phase-III clinical trials. No clear-cut trends of shifts in the clinical laboratory variables, or obvious pathological values linked to the treatment could be observed during 6 months of treatment.

Other

As with any ocular treatment, if transient blurred vision occurs at instillation, the patient should wait until the vision clears before driving or using machinery.

ADVERSE EFFECTS

Multiple dose strengths of tafluprost have been studied in over 1110 patients in U.S. and multinational phase II and phase III studies either as monotherapy or as adjunctive therapy to timolol 0.5%, primarily using preservative-containing formulations. The clinical dose strength of tafluprost 0.0015% has been studied in 724 patients in U.S. and multinational masked phase II and phase III trials. The most common drug-related adverse reaction in these patients treated with tafluprost 0.0015% was ocular hyperaemia, which was reported

in 14.2% of patients. Most adverse reactions in this population were mild and led to discontinuation in 2.1% of patients participating in these studies.

The following additional drug-related adverse reactions were reported during treatment up to 24 months (within each frequency grouping, adverse reactions are presented in order of decreasing frequency):

Eye disorders

Common (≥ 1%, < 10%): Eye pruritus, eye irritation, eye pain, growth of eyelashes, dry eye, eyelash discolouration, lacrimation increased, erythema of eyelid, foreign body sensation in eyes, vision blurred, photophobia, visual acuity reduced, eyelash thickening, punctate keratitis, eye discharge, eyelid oedema and iris hyperpigmentation.

Uncommon (≥ 0.1%, < 1%): Blepharal pigmentation

Nervous System Disorders

Common (≥ 1%, < 10%): Headache

DOSAGE AND ADMINISTRATION

The recommended dose is one drop of SAFLUTAN in the conjunctival sac of the affected eye(s) once daily in the evening.

The dose should not exceed once daily as more frequent administration may lessen the intraocular pressure lowering effect.

SAFLUTAN is a sterile solution that does not contain a preservative. For single use only, one container is sufficient to treat both eyes. Any unused solution should be discarded immediately after use.

If more than one topical ophthalmic product is being used, each one should be administered at least 5 minutes apart.

To reduce the risk of darkening of the eyelid skin the patients should wipe off any excess solution from the skin. As with any other eye drops, nasolacrimal occlusion or gently closing the eyelid after administration is recommended. This may reduce the systemic absorption of products administered via the ocular route.

Use in Elderly Patients
No dosage adjustment is required for elderly patients.

Use in Paediatric Patients
Safety and effectiveness of SAFLUTAN in paediatric patients have not been established. Therefore, treatment with SAFLUTAN is not recommended.

Use in Patients with Renal Insufficiency
SAFLUTAN has not been studied in patients with renal insufficiency and should therefore be used with caution in such patients.

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Use in Patients with Hepatic Insufficiency
SAFLUTAN has not been studied in patients with hepatic insufficiency and should therefore be used with caution in such patients.

OVERDOSAGE

No case of overdose has been reported. Overdose is unlikely to occur after ocular administration. If overdose occurs, treatment should be symptomatic.

Contact the Poisons Information Centre on 131126 for advice on management.

PRESENTATION AND STORAGE CONDITIONS

SAFLUTAN Eye Drops are supplied in low density polyethylene (without additives) unit dose containers packed in a foil pouch. Each single dose container has a fill volume of 0.3 mL and there are 10 individual containers in each foil pouch.

The following pack sizes are available: 30 x 0.3 mL single dose containers and 10 x 0.3 mL single dose containers (Starter pack).

Shelf life
Unopened foil pouch: 36 months.
Opened foil pouch: 28 days.

Storage
Store the unopened foil pouches at 2°C – 8°C. Refrigerate. Do not freeze.

After opening the foil pouch:
• Keep the single-dose containers in the original foil pouch.
• Store below 25°C.
• Discard unused single-dose containers after 28 days from date of first opening of the foil pouch.
• Discard an opened single-dose container with any remaining solution immediately after use.

NAME AND ADDRESS OF SPONSOR

Merck Sharp & Dohme (Australia) Pty Limited
54 - 68 Ferndell Street
South Granville, NSW 2142

POISON SCHEDULE OF THE MEDICINE

Prescription only medicine (S4)

DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS (ARTG)