002560

OPHTHALMIC SOLUTION FOR THE TREATMENT OF GLAUCOMA AND OCULAR HYPERTENSION

TAFLOTAN® Ophthalmic Solution 0.0015%

(Tafluprost 0.0015%)

Santen

Composition

TAFLOTAN® ophthalmic solution 0.0015% is a clear, colorless, sterile aqueous ophthalmic solution. Each mL contains 15 μg of Tafluprost. It also contains Polysorbate 80, concentrated glycerin, disodium edetate hydrate, sodium dihydrogen phosphate dihydrate and pH adjuster as additives. Its pH is 5.7 – 6.3 and its osmolar ratio is 0.9 – 1.1.

Indications

Reduction of elevated intraocular pressure in open angle glaucoma and ocular hypertension.

Dosage and Administration

Instill 1 drop in the affected eye(s) once daily.

< Precautions >

Do not use more than once daily because more frequent administration may lessen the IOP-lowering effect.

Pharmacology

1. Intraocular pressure (IOP) lowering effect

Ocular administration of Tafluprost ophthalmic solutions ranged from 0.00002% to 0.005% in a single dose to monkeys showed the IOP lowering effect in a concentration-dependent manner. The effect was statistically significant in the groups of the concentration of 0.0005% and higher, compared with the vehicle group. In a repeated dose study in monkeys of Tafluprost ophthalmic solutions ranged from 0.001% to 0.005% once daily for 5 days, IOP lowering effect at every concentration was stable and did not attenuate during the administration period.

2. Mechanism of action

Tafluprost acid form, an active metabolite, showed high affinity for the prostanoid FP receptor (Ki=0.40 nM). Aqueous humor dynamics in monkeys was evaluated using fluorophotometry, two-level constant pressure perfusion and ^{125}I-^{131}I labeled albumin perfusion methods following the repeated administration of 0.005% Tafluprost ophthalmic solution once daily for 3 to 5 days. Uveoscleral outflow significantly increased without any change in aqueous production.

3. Effect on ocular blood flow

1) A repeated instillation of 0.0015% Tafluprost ophthalmic solution into rabbit eyes once daily for 28 days significantly increased the blood flow in the optic nerve head, measured with laser speckle method.
2) A single dose instillation of 0.0015% Tafluprost ophthalmic solution into eyes of healthy adults significantly increased the blood flow rate in the paraoptic nerve head retinal artery and the blood flow at the paraoptic nerve head retina.

Contraindications (This product is contraindicated in the following patients.)

Patients with a history of hypersensitivity to any of the ingredients of this product.

Precautions

1. Careful administration (This product should be administered with care to the following patients.)

1) Patients with aphakia or pseudophakia [this product may induce macular oedema including cystoid macular oedema, and the associated visual acuity reduced.]
2) Patients with bronchial asthma or a history of bronchial asthma [this product may aggravate or induce asthmatic attack.]
3) Patients with endophthalmitis (iritis, uveitis) [other drugs in this category have been reported to cause elevation of intraocular pressure.]
4) Pregnant, parturient and lactating women [see "Use during Pregnancy, Delivery or Lactation".]

2. Important precautions

1) Pigmentation in iris and eyelid (increased melanin content), or hypertrichosis around the eyes may occur. These symptoms gradually progress with continued administration, and stop when the treatment is discontinued. The symptoms like blepharal pigmentation and hypertrichosis around the eyes can gradually disappear or diminish after the administration is discontinued, however, there are reports of the cases that the symptom of iris pigmentation persists even after the administration was discontinued. In such cases, iris color change can be detected clearly in patients with mixed-colored irises and even in patients with single-color dark brown irises (seen among most Japanese) as well. The difference in iris color between right and left eyes could be noted particularly in the case of unilateral administration. As long-term observation data about these symptoms are not yet available, doctors are required to closely observe patients through periodic checkups. Patients should be well informed of the possibility of these symptoms and instructed to wipe off any excess solution from the skin around the eye or to wash the face in order to prevent blepharal pigmentation or hypertrichosis around the eyes.
2) Corneal epithelium disorder (superficial punctate keratitis, filamentary keratitis or corneal erosion) may occur during the treatment. Instruct patients to consult a doctor immediately if subjective symptoms including smarting pain, itching and eye pain, continue.
3) This product should be administered with care because there is no clinical experience in patients with closed angle glaucoma.
4) Temporary blurred vision may develop after administration of this product. Patients should be instructed to refrain from activities like driving or operating machines until such symptoms disappears.

3. Adverse Reactions

The following safety data were based on the clinical study result of Tafluprost ophthalmic solution 0.0015% containing benzalkonium chloride.

Upon Approval

Adverse drug reactions (including abnormal change in laboratory test values) were reported in 326 of 483 patients (67.5%) in clinical studies in Japan. The major adverse drug reactions were conjunctival hyperaemia in 151 patients (31.3%), abnormality in eyelashes in 93 patients (19.3%), itching in 85 patients (17.6%), eye irritation in 65 patients (13.5%), iris pigmentation in 39 patients (8.1%), etc.

Post-marketing surveilance

Adverse drug reactions were reported in 396 of 3,260 patients (12.1%) in post-marketing surveilance in Japan. The major adverse drug reactions were blepharal pigmentation in 93 patients (2.9%), conjunctival hyperaemia in 74 patients (2.3%), corneal epithelium disorder including corneal erosion in 58 patients (1.8%), hypertrichosis of eyelids in 40 patients (1.2%), abnormality in eyelashes in 39 patients (1.2%), etc.

1) Clinically significant adverse drug reactions

Iris pigmentation (8.1%): Since iris pigmentation may occur, patients should be examined periodically, and administration should be discontinued depending on the clinical status when iris pigmentation is observed.

2) Other adverse drug reactions

If an adverse drug reaction is observed, appropriate measures including discontinuing administration should be taken.

Type \ Incidence	Incidence unknown	≥ 5%	5%> ≥ 1%	1%> ≥ 0.1%
Ophthalmic	Conjunctivitis, iritis, keratoconjunctivitis sicca, deepening of upper eyelid sulcus, macular oedema	Conjunctival hyperaemia, abnormality in eyelashes (increased length, thickness and number of lashes, etc.), itching, irritation, foreign body sensation, blepharal pigmentation, corneal epithelium disorder including superficial punctate keratitis, abnormal sensation in the eye (discomfort, sticky sensation, dry sensation, etc.)	Eye pain, hypertrichosis of eyelid, eye discharge, photophobia, heavy feeling of eye, lacrimation, blurred vision, conjunctival oedema, blepharitis (redness of eyelid, oedema, etc.)	Subconjunctival hemorrhage
Neuropsychiatric	–	–	Headache	Dizziness
Hypersensitivity	Eyelid dermatitis, rashes	–	Erythema	–
Others	–	–	Elevated AST(GOT), positive urine protein, elevated serum potassium	Elevated ALT(GPT), elevated γ-GTP, positive urine sugar, increased eosinophils, decreased leukocyte count, increased uric acid

Incidence was calculated based on the clinical study results up to the approval of Tafluprost ophthalmic solution 0.0015% containing benzalkonium chloride.

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Approved 20-May-2021 05-01 UTC

4. Use in the elderly

Because physiological function is generally reduced in the elderly, caution should be exercised.

5. Use during Pregnancy, Delivery or Lactation

1) This product should be used in pregnant women or women who may possibly be pregnant only if the expected therapeutic benefits are judged to outweigh the possible risks associated with the treatment. [The safety of this product for use during pregnancy has not been established. In animal studies, when Tafluprost solution was administered intravenously to pregnant rats at a dose of 30 μg/kg/day (2000 times the clinical dose*), teratogenicity and post-implantation embryonic mortality rate increased; at 10 μg/kg/day (about 670 times the clinical dose*) adverse effect on fetal development (low body weight and unossification of breast bone in fetuses) was observed. In an intravenous administration in pregnant rabbits at 0.1 μg/kg/day (about 6.7 times the clinical dose*), miscarriage and mortality rate after implantation increased, and luteal body and implantation decreased ; at 0.03 μg/kg/day (2 times the clinical dose*) teratogenicity was observed. In an intravenous administration study in pregnant and lactating rats at a dose level of 1 μg/kg/day (about 67 times the clinical dose*), mal -nursing of dams was observed and 4-day survival rate of new born baby decreased. On the other hand, in the study using uteri isolated from rats, uterine contraction was observed at about 3.3 times the plasma concentration of Tafluprost (less than 30 pg/mL), or about 420 times the plasma concentration of unbound Tafluprost (less than 0.24 pg/mL), calculated based on protein binding ratio, estimated after ocular administration of the clinical dose.]

* Dosage (0.015 μg/kg/day) when one drop (30 μL) of this product is instilled into both eyes at a time for a 60 kg patient.

2) Avoid administration to nursing mothers. If administration is judged to be essential, the patients should be instructed to stop breastfeeding during the treatment. [A study in rats has shown excretion of Tafluprost in breast milk after ocular instillation.]

6. Pediatric Use

The safety of this product to low birth weight infants, neonates, infants or children has not been established. (No clinical experience.)

7. Precautions concerning Use

1) Route of administration: For ophthalmic use only.

2) At the time of administration:

Followings should be instructed to patients.

(1) Be careful not to touch the tip of the container to the eye directly in order to avoid the contamination of the drug.

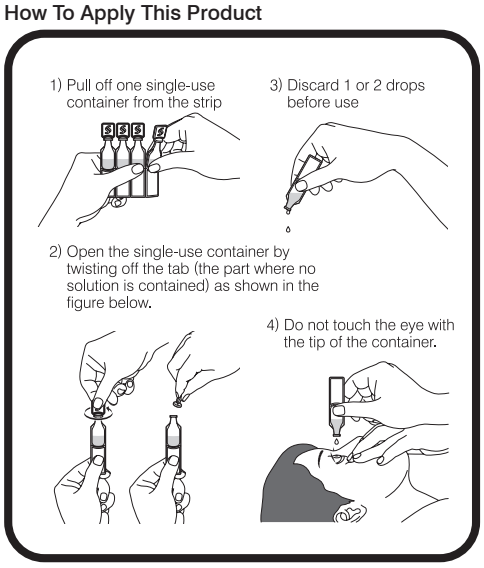
(2) Wipe off or wash the face immediately when any excess solution touches the skin around the eye.

(3) When more than one ophthalmic drug is used, at least 5 minutes of intervals should be taken.

(4) Discard 1 or 2 drops before use (in order to eliminate fragments of container possibly contaminated at opening).

(5) Discard any remaining solution immediately after use. This product is a sterilized single use disposable medical product which does not contain any preservative agents for prevention of cross contamination.

How To Apply This Product



Clinical Studies

1. In a randomized blind comparative study in 109 patients with primary open angle glaucoma or ocular hypertension using Latanoprost ophthalmic solution as a comparator, the decrease in intraocular pressure (IOP) for 0.0015% Tafluprost ophthalmic solution was 6.6 mmHg (95% confidence interval: 5.8 -7.3 mmHg), which demonstrated non inferiority to the comparator.

Comparison of IOP (mmHg)

	Tafluprost (n=46)	Latanoprost (n=51)
Baseline IOP	23.8 ± 2.3	23.7 ± 2.3
Endpoint IOP (at 4-week discontinued point)	17.2 ± 2.8	17.5 ± 2.7
Change in IOP	-6.6 ± 2.5	-6.2 ± 2.5
Difference of IOP change (Tafluprost minus comparator)	-0.41	
95% confidence interval of difference of IOP change	-1.42 to 0.60	

(mean ± standard deviation), Non inferiority margin: 2 mmHg

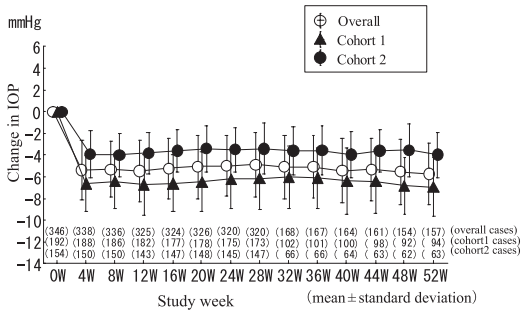
2. In a randomized blind comparative study in 94 patients with normal tension glaucoma using placebo ophthalmic solution as a comparator, the decrease in IOP for 0.0015% Tafluprost ophthalmic solution was 4.0 mmHg (95% confidence interval: 3.5-4.5 mmHg), which showed significant IOP lowering effect compared with placebo.

Comparison of IOP (mmHg)

	Tafluprost (n=48)	Placebo (n=42)
Baseline IOP	17.7 ± 1.3	17.8 ± 1.5
Endpoint IOP (at 4-week discontinued point)	13.8 ± 2.1	16.4 ± 2.2
Change in IOP	-4.0 ± 1.7	-1.4 ± 1.8
Difference of IOP change (Tafluprost minus placebo)	-2.60	
95% confidence interval of difference of IOP change	-3.35 to -1.85	
P Value (t-test)	<0.001	

(mean ± standard deviation)

3. In a long term administration study in 351 patients with open angle glaucoma including normal tension glaucoma, or patients with ocular hypertension, the decrease in IOP for 0.0015% Tafluprost ophthalmic solution remained between 4.9 and 5.7 mmHg for 52 weeks, which demonstrated stable IOP lowering effect in long term administration.
IOP decrease was 6.0-6.9 mmHg in cohort 1* and 3.4-4.0 mmHg in cohort 2 over 52 weeks.
*Cohort 1: 22-34 mmHg at baseline
Cohort 2: 16-21 mmHg at baseline



Storage

Store in a refrigerator (2-8°C) and protect from light.
After opening the aluminum foil pouch.
Store in a refrigerator (2-8°C) and protect from light. Use within 6 months.
If the product is stored at 1-25°C, it should be used within one month. Use the product in the pouch which has been opened first.

How Supplied

30 plastic containers in a box
(Plastic container of 0.3 mL, 10 containers per aluminum foil pouch x 3 pouches)
Box, 3 pouch @ 10 single-dose containers @ 0.3 mL

HARUS DENGAN RESEP DOKTER

On Medical Prescription Only

No. Reg:

Manufactured by:

SANTEN PHARMACEUTICAL CO., LTD.

Noto Plant: 2-14, Shikinami, Hodatsushimizu-cho, Hakui-gun, Ishikawa, Japan

Imported and Marketed by:

meiji PT MEIJI INDONESIAN PHARMACEUTICAL INDUSTRIES

Bangil-Pasuruan, Jawa Timur-Indonesia

Informasi Obat untuk Pasien

TAFLOTAN® Ophthalmic Solution 0.0015%

(Tafluprost 0.0015%)

Santen

Baca semua informasi dalam leaflet ini sebelum Anda mulai menggunakan obat ini, karena leaflet ini mengandung informasi penting untuk Anda.

- Simpan leaflet ini. Anda mungkin perlu membacanya lagi.
- Jika Anda memiliki pertanyaan, tanyakan kepada dokter, apoteker atau perawat Anda.
- Obat ini hanya diresepkan untuk Anda. Jangan berikan obat ini kepada orang lain.
  Itu dapat membahayakan mereka, bahkan jika tanda-tanda penyakit mereka sama dengan Anda.
- Jika Anda mengalami efek samping, bicarakan kepada dokter, apoteker, atau perawat Anda. Termasuk efek samping yang tidak tercantum dalam leaflet ini.

Apa yang terdapat dalam leaflet ini?

1. Apakah TAFLOTAN® dan apa kegunaannya

Jenis obat apakah itu dan bagaimana cara kerjanya?

TAFLOTAN® mengandung Tafluprost, merupakan golongan zat yang dikenal sebagai analog prostaglandin. TAFLOTAN® menurunkan tekanan pada mata. Itu digunakan ketika tekanan pada mata terlalu tinggi.

Apa Kegunaan TAFLOTAN®?

TAFLOTAN® digunakan untuk mengurangi peningkatan tekanan bola mata pada tipe glukoma yang dikenal sebagai *glaukoma sudut terbuka* dan hipertensi okular.

2. Apa yang perlu Anda ketahui sebelum menggunakan TAFLOTAN®

Jangan gunakan TAFLOTAN®

Jika Anda memiliki riwayat hipersensitif terhadap salah satu bahan dari produk ini (tercantum pada bagian 6).

Peringatan dan Perhatian

Konsultasikan dengan dokter, apoteker, atau perawat Anda sebelum menggunakan TAFLOTAN®.

1) Pemberian dengan hati-hati (Produk ini harus diberikan dengan hati-hati):
   - Jika Anda menderita kehilangan lensa mata/mendapatkan lensa mata palsu.
   - Jika Anda menderita asma atau riwayat asma.
   - Jika Anda menderita peradangan bola mata akibat infeksi (mata merah dan nyeri).
2) Perhatian Khusus
   - TAFLOTAN® dapat menyebabkan warna kulit di sekitar mata menjadi lebih gelap. Bersihkan larutan yang berlebih pada kulit. Ini akan mengurangi risiko penggelapan kulit.
   - TAFLOTAN® dapat menambah panjang, ketebalan, warna dan/atau jumlah bulu mata dan menyebabkan pertumbuhan rambut yang tidak biasa pada kelopak mata Anda.
   - Gangguan epitel kornea (keratitis punctata superficialis, filamentary keratitis atau erosi kornea) dapat terjadi selama perawatan.
   - Produk ini harus diberikan dengan hati-hati karena tidak tersedia data klinis pada glukoma tipe *closed angle glaucoma*.
   - Penglihatan kabur sementara dapat terjadi setelah pemberian produk ini.

Penggunaan pada lansia

Karena fungsi fisiologis lansia pada umumnya berkurang, harus digunakan secara hati-hati.

Penggunaan selama kehamilan, persalinan atau laktasi

Produk ini sebaiknya hanya digunakan pada wanita hamil atau wanita yang mungkin hamil jika manfaat terapetik dinilai lebih besar dibandingkan risiko yang mungkin terjadi selama pengobatan. Hindari penggunaan pada ibu menyusui. Jika pemberian dinilai sangat perlu, pasien harus diinstruksikan untuk berhenti menyusui selama pengobatan.

Penggunaan untuk pediatrik

Keamanan produk ini untuk bayi dengan berat lahir rendah, neonates, bayi atau anak-anak belum ditetapkan.

Obat-obatan lainnya

Beri tahu dokter atau apoteker Anda jika Anda sedang meminum, baru saja meminum, atau mungkin berencana akan meminum obat lainnya.

Mengemudi dan mengoperasikan mesin

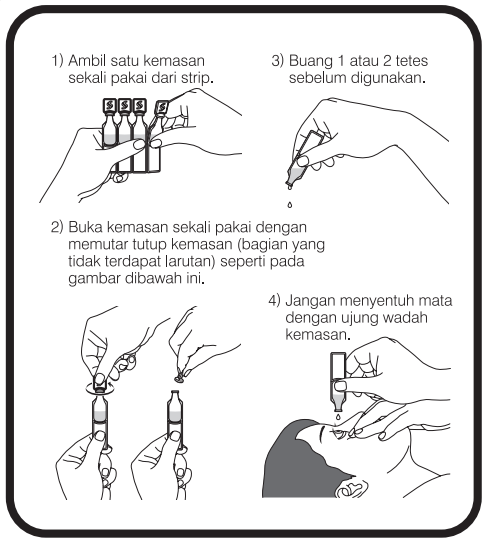
TAFLOTAN® tidak memiliki pengaruh pada kemampuan mengemudi dan mengoperasikan mesin. Anda mungkin akan merasakan penglihatan Anda kabur sesaat setelah Anda menggunakan TAFLOTAN® pada mata Anda. Jangan mengemudi atau mengoperasikan alat atau mesin sampai penglihatan Anda jelas.

3. Bagaimana menggunakan TAFLOTAN®

a. Selalu gunakan obat ini sesuai anjuran dokter atau apoteker Anda. Tanyakan kepada dokter atau apoteker Anda jika Anda tidak yakin.
b. Dosis yang dianjurkan adalah 1 tetes TAFLOTAN® pada salah satu mata atau kedua mata, sekali sehari.
c. Jangan meneteskan lebih banyak tetes atau lebih sering dari anjuran dokter Anda.
d. Hanya gunakan TAFLOTAN® pada kedua mata jika dokter Anda menganjurkan demikian.
e. Untuk digunakan sebagai tetes mata. Jangan ditelan.

Petunjuk Penggunaan:

1) Ketika Anda mulai menggunakan kemasan baru: Jangan gunakan produk jika wadah rusak.
2) Setiap Anda menggunakan TAFLOTAN® :
   - Cuci tangan Anda
   - Bersihkan dan cuci wajah Anda segera ketika larutan berlebih mengenai sekitar mata Anda.
   - Buang larutan yang tersisa segera setelah produk digunakan.
3) Aturan Pakai :



- Jika tetesan tidak mengenai mata, ulangi tetesan pada mata.
- Jika Anda menggunakan obat-obatan lain pada mata, setidaknya jeda selama 5 menit antara pemberian TAFLOTAN dengan obat lainnya.
- Jika obat ini tertelan secara tidak sengaja, hubungi dokter untuk meminta saran.
- Jika Anda lupa menggunakan TAFLOTAN®, gunakan satu tetes setelah Anda ingat. Jangan gunakan dosis ganda untuk mengganti dosis yang terlupakan.
- Jangan berhenti menggunakan TAFLOTAN® tanpa bertanya kepada dokter Anda.
- Jika Anda memiliki pertanyaan lebih lanjut tentang penggunaan obat ini, tanyakan kepada dokter, apoteker atau perawat Anda.

4. Kemungkinan efek samping

Seperti semua obat-obatan, obat ini dapat menyebabkan efek samping walaupun tidak semua orang mengalaminya. Sebagian besar efek samping tidak serius. Efek samping berikut dapat timbul:

a. Efek samping yang signifikan terjadi secara klinis
   Pigmentasi iris. Jika hal ini terjadi, Anda harus diperiksa secara berkala dan pemberian harus dihentikan tergantung pada status klinis ketika pigmentasi iris diamati.

b. Efek samping lain

Tipe \ Kejadian	Tidak diketahui	≥ 5%	≥ 1% sampai > 5%	≥ 0.1% sampai > 1%
Oftalmik	Peradangan selaput mata, mata merah dan nyeri, penurunan produksi air mata/sindrom mata kering, pendalaman lipatan kelopak mata atas, pembengkakan di daerah dekat retina	Kemerahan konjungtiva (selaput mata), kelainan pada bulu mata (peningkatan panjang, ketebalan, dan jumlah bulu mata, dan lain-lain), rasa gatal, iritasi, sensasi adanya benda asing, pigmentasi kelopak mata, gangguan epitel kornea termasuk adanya bintik-bintik putih pada permukaan mata. sensasi abnormal pada mata, (rasa tidak nyaman, sensasi lengket, sensasi kering, dan lain-lain)	Nyeri pada mata, pertumbuhan rambut berlebihan pada kelopak mata, kotoran pada mata berlebih/ eye discharge, kondisi tidak nyaman ketika melihat cahaya terang, rasa berat pada mata, mata berair, penglihatan kabur, pembengkakan selaput mata, peradangan pada kelopak mata (kemerahan pada kelopak mata, bengkak, dan lain-lain)	Perdarahan di dalam selaput mata
Neuropsikiatri	–	–	Sakit Kepala	Pusing
Hipersensitifitas	Kelopak mata kering, gatal dan teriritasi pada kelopak mata, ruam	–	Adanya bercak merah	–
Lainnya	–	–	Peningkatan enzim Aspartat Aminotransferase (Glutamic Oxaloacetic Transaminase), positif protein pada urin, peningkatan kalium pada serum	Peningkatan enzim Alanine Aminotransferase (Glutamate Pyruvate Transaminase), peningkatan enzim γ-Gamma-Glutamyl Transferase, positif gula pada urin, peningkatan eosinofil, penurunan jumlah leukosit, peningkatan asam urat

c. Pelaporan efek samping
Jika Anda mendapat efek samping, sampaikan kepada dokter, apoteker, atau perawat Anda.
Laporkan juga bila Anda mengalami efek samping yang tidak tercantum dalam leaflet ini.

5. Cara menyimpan TAFLOTAN®

a. Jauhkan obat ini dari pandangan dan jangkauan anak-anak.
b. Jangan gunakan obat ini setelah tanggal kedaluwarsa.
c. Simpan dalam lemari es (2-8°C) dan lindungi dari cahaya.
d. Jangan membuka kemasan sampai Anda mulai menggunakan obat tetes mata.
e. Setelah membuka kemasan aluminium foil
1) Simpan di lemari es (2-8°C) dan lindungi dari cahaya. Gunakan dalam 6 bulan.
2) Jika produk disimpan pada suhu 1-25°C, produk tersebut harus digunakan dalam waktu satu bulan. Gunakan produk dalam kemasan yang telah terbuka terlebih dahulu.
3) Simpan wadah dosis tunggal dalam kemasan foil aslinya.
4) Jangan simpan di atas suhu 25°C.
5) Buang wadah dosis tunggal yang telah terbuka dengan sisa larutan segera setelah digunakan.
6) Jangan buang obat apa pun melalui limbah atau limbah rumah tangga. Tanyakan kepada apoteker Anda cara membuang obat yang tidak lagi Anda gunakan. Hal ini akan membantu melindungi lingkungan.

6. Isi kemasan dan informasi lainnya

Apa kandungan TAFLOTAN®

Bahan aktif TAFLOTAN® adalah Tafluprost. 1 ml larutan mengandung 15 mikrogram Tafluprost. TAFLOTAN® juga mengandung *Polysorbate 80, Concentrate Glycerin, Disodium Edetate Hydrate, Sodium Dihydrogen Phosphate Dihydrate*, dan pengatur pH sebagai bahan tambahan.
Rentang pH sekitar 5,7 – 6,3 dan rentang osmolaritas sekitar 0,9 – 1,1.

Bagaimana bentuk dan isi kemasan TAFLOTAN®

TAFLOTAN® merupakan larutan mata steril, jernih, tidak berwarna, yang dikemas dalam wadah dosis tunggal, masing-masing mengandung 0.3 ml larutan. Sepuluh wadah dosis tunggal dikemas dalam satu kemasan. TAFLOTAN® tersedia dalam kemasan berisi 30 wadah dosis tunggal.

HARUS DENGAN RESEP DOKTER

No. Reg:

Diproduksi oleh:
SANTEN PHARMACEUTICAL CO., LTD.
Noto Plant: 2-14, Shikinami, Hodatsushimizu-cho, Hakui-gun, Ishikawa, Japan

Diimpor dan dipasarkan oleh:
meiji **PT MEIJI INDONESIAN PHARMACEUTICAL INDUSTRIES**
Bangil-Pasuruan, Jawa Timur-Indonesia