Prescription drug

COSOPT®
Dorzolamide HCl / Timolol Maleate
Ophthalmic Solution

COMPOSITION

Each ml contains 22.26 mg of dorzolamide hydrochloride corresponding to 20 mg dorzolamide and 6.83 mg of timolol maleate corresponding to 5 mg timolol.

DESCRIPTION

Ophthalmic solution, single dose container

Clear, colourless to nearly colourless, slightly viscous solution, with a pH between 5.5 and 5.8, and an osmolality of 242-323 mOsm/kg.

INDICATION

Indicated in the treatment of elevated intraocular pressure (IOP) in patients with open angle glaucoma when topical beta blocker monotherapy is not sufficient

POSOLOGY AND ADMINISTRATION

Posology

The dose is one drop of COSOPT in the (conjunctival sac of the) affected eye(s) two times daily.

If another topical ophthalmic agent is being used, COSOPT and the other agent should be administered at least ten minutes apart.

This medicinal product is a sterile solution that does not contain a preservative. The solution from one individual single dose container is to be used immediately after opening for administration to the affected eye(s). Since sterility cannot be maintained after the individual single dose container is opened, any remaining contents must be discarded immediately after administration.

Patients should be instructed to wash their hands before use and avoid allowing the container to come into contact with the eye or surrounding structures as this could cause injury to the eye (see instructions for use).

Patients should also be instructed that ocular solutions, if handled improperly, can become contaminated by common bacteria known to cause ocular infections. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions.

When using nasolacrimal occlusion or closing the eyelids for 2 minutes, the systemic absorption is reduced. This may result in a decrease in systemic side effects and an increase in local activity.

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Instructions for use

Since different shapes of the single-dose containers are available, patients should be informed of the correct handling of the single-dose container. Please see SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING for shape-specific diagrams and instructions for use.

Use in children and adolescents

Safely and effectiveness in children and adolescents has not been established.

CONTRAINDICATION

COSOPT is contraindicated in patients with:

- reactive airway disease, including bronchial asthma or a history of bronchial asthma, or severe chronic obstructive pulmonary disease
- sinus bradycardia, sick sinus syndrome, sino-atrial block, second or third degree atrioventricular block not controlled with pacemaker, overt cardiac failure, cardiogenic shock
- severe renal impairment (CrCl < 30 ml/min) or hyperchloraemic acidosis
- hypersensitivity to one or both active substances or to any of the excipients.

The above are based on the components and are not unique to the combination

SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Cardiovascular/Respiratory Reactions

Like other topically applied ophthalmic agents timolol is absorbed systemically. Due to beta-adrenergic component, timolol, the same types of cardiovascular, pulmonary and other adverse reactions seen with systemic beta-adrenergic blocking agents may occur. Incidence of systemic ADRs after topical ophthalmic administration is lower than for systemic administration. To reduce the systemic absorption, see POSOLOGY AND ADMINISTRATION.

Cardiac disorders:
In patients with cardiovascular diseases (e.g. coronary heart disease, Prinzmetal's angina and cardiac failure) and hypotension therapy with beta-blockers should be critically assessed and the therapy with other active substances should be considered. Patients with cardiovascular diseases should be watched for signs of deterioration of these diseases and of adverse reactions.

Due to its negative effect on conduction time, beta-blockers should only be given with caution to patients with first degree heart block.

Vascular disorders:
Patients with severe peripheral circulatory disturbance/disorders (i.e. severe forms of Raynaud's disease or Raynaud's syndrome) should be treated with caution.

Respiratory disorders:
Respiratory reactions, including death due to bronchospasm in patients with asthma have been reported following administration of some ophthalmic beta-blockers.

COSOPT should be used with caution, in patients with mild/moderate chronic obstructive pulmonary disease (COPD) and only if the potential benefit outweighs the potential risk.

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Hepatic Impairment

This medicinal product has not been studied in patients with hepatic impairment and should therefore be used with caution in such patients.

Immunology and Hypersensitivity

As with other topically-applied ophthalmic agents, this medicinal product may be absorbed systemically. Dorzolamide contains a sulfonamido group, which also occurs in sulfonamides. Therefore, the same types of adverse reactions found with systemic administration of sulfonamides may occur with topical administration, including severe reactions such as Stevens-Johnson syndrome and toxic epidermal necrolysis. If signs of serious reactions or hypersensitivity occur, discontinue use of this preparation.

Local ocular adverse effects, similar to those observed with dorzolamide hydrochloride eye drops, have been seen with this medicinal product. If such reactions occur, discontinuation of COSOPT should be considered.

While taking beta-blockers, patients with a history of atopy or a history of severe anaphylactic reaction to a variety of allergens may be more reactive to repeated challenge with such allergens and may be unresponsive to the usual doses of adrenaline used to treat anaphylactic reactions.

Concomitant Therapy

The effect on intra-ocular pressure or the known effects of systemic beta-blockade may be potentiated when timolol is given to the patients already receiving a systemic beta-blocking agent. The response of these patients should be closely observed. The use of two topical beta-adrenergic blocking agents is not recommended (see DRUG INTERACTIONS).

The use of dorzolamide and oral carbonic anhydrase inhibitors is not recommended.

Withdrawal of Therapy

As with systemic beta-blockers, if discontinuation of ophthalmic timolol is needed in patients with coronary heart disease, therapy should be withdrawn gradually.

Additional Effects of Beta-Blockade

Hypoglycaemia/diabetes:
Beta-blockers should be administered with caution in patients subject to spontaneous hypoglycaemia or to patients with labile diabetes, as beta-blockers may mask the signs and symptoms of acute hypoglycaemia.

Beta-blockers may also mask the signs of hyperthyroidism. Abrupt withdrawal of beta-blocker therapy may precipitate a worsening of symptoms.

Corneal diseases
Ophthalmic beta-blockers may induce dryness of eyes. Patients with corneal diseases should be treated with caution.

Surgical anaesthesia
Beta-blocking ophthalmological preparations may block systemic beta-agonist effects e.g. of adrenaline. The anaesthesiologist should be informed when the patient is receiving timolol.

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Therapy with beta-blockers may aggravate symptoms of myasthenia gravis.

Additional Effects of Carbonic Anhydrase Inhibition

Therapy with oral carbonic anhydrase inhibitors has been associated with urolithiasis as a result of acid-base disturbances, especially in patients with a prior history of renal calculi. Although no acid-base disturbances have been observed with COSOPT, urolithiasis has been reported infrequently. Because COSOPT contains a topical carbonic anhydrase inhibitor that is absorbed systemically, patients with a prior history of renal calculi may be at increased risk of urolithiasis while using this medicinal product.

Other

The management of patients with acute angle-closure glaucoma requires therapeutic interventions in addition to ocular hypotensive agents. This medicinal product has not been studied in patients with acute angle-closure glaucoma.

Corneal oedema and irreversible corneal decompensation have been reported in patients with pre-existing chronic corneal defects and/or a history of intraocular surgery while using dorzolamide. There is an increased potential for developing corneal oedema in patients with low endothelial cell counts. Precautions should be used when prescribing COSOPT to these groups of patients.

Choroidal detachment has been reported with administration of aqueous suppressant therapies (e.g. timolol, acetazolamide) after filtration procedures.

As with the use of other antiglaucoma medicines, diminished responsiveness to ophthalmic timolol maleate after prolonged therapy has been reported in some patients. However, in clinical studies in which 164 patients have been followed for at least three years, no significant difference in mean intraocular pressure has been observed after initial stabilization.

Contact Lens Use

This medicinal product has not been studied in patients wearing contact lenses.

Paediatric population

See PHARMACODYNAMIC PROPERTIES.

DRUG INTERACTIONS

Specific medicine interaction studies have not been performed with COSOPT.

In a clinical study, this medicinal product was used concomitantly with the following systemic medications without evidence of adverse interactions: ACE-inhibitors, calcium channel blockers, diuretics, non-steroidal anti-inflammatory medicines including aspirin, and hormones (e.g., estrogen, insulin, thyroxine).

There is a potential for additive effects resulting in hypotension and/or marked bradycardia when ophthalmic beta-blockers solution is administered concomitantly with oral calcium channel blockers, catecholamine-depleting medicines or beta-adrenergic blocking agents, antiarrhythmics (including amiodarone), digitalis glycosides, parasympathomimetics, quanethidine, narcotics, and monoamine oxidase (MAO) inhibitors.

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Potentiated systemic beta-blockade (e.g., decreased heart rate, depression) has been reported during combined treatment with CYP2D6 inhibitors (e.g. quinidine, fluoxetine, paroxetine) and timolol.

Although COSOPT alone has little or no effect on pupil size, mydriasis resulting from concomitant use of ophthalmic beta-blockers and adrenaline (epinephrine) has been reported occasionally.

Beta-blockers may increase the hypoglycaemic effect of antidiabetic agents.

Oral beta-adrenergic blocking agents may exacerbate the rebound hypertension which can follow the withdrawal of clonidine.

FERTILITY, PREGNANCY AND LACTATION

Pregnancy

COSOPT should not be used during pregnancy.

Dorzolamide
No adequate clinical data in exposed pregnancies are available. In rabbits, dorzolamide produced teratogenic effect at maternotoxic doses (see PRECLINICAL SAFETY DATA).

Timolol
There are no adequate data for the use of timolol in pregnant women. Timolol should not be used during pregnancy unless clearly necessary. To reduce the systemic absorption, see POSOLOGY AND ADMINISTRATION.

Epidemiological studies have not revealed malformative effects but show a risk for intra uterine growth retardation when beta-blockers are administered by the oral route. In addition, signs and symptoms of beta-blockade (e.g. bradycardia, hypotension, respiratory distress and hypoglycaemia) have been observed in the neonate when beta-blockers have been administered until delivery. If this medicinal product is administered until delivery, the neonate should be carefully monitored during the first days of life.

Breast-feeding

It is not known whether dorzolamide is excreted in human milk. In lactating rats receiving dorzolamide, decreases in the body weight gain of offspring were observed.
Beta-blockers are excreted in breast milk. However, at therapeutic doses of timolol in eye drops it is not likely that sufficient amounts would be present in breast milk to produce clinical symptoms of beta-blockade in the infant. To reduce systemic absorption, see POSOLOGY AND ADMINISTRATION. If treatment with COSOPT is required, then lactation is not recommended.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

No studies on the effects on the ability to drive and use machines have been performed. Possible side effects such as blurred vision may affect some patients' ability to drive and/or operate machinery.

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UNDESIRABLE EFFECTS

Like other topically applied ophthalmic medicines, timolol is absorbed into the systemic circulation. This may cause similar undesirable effects as seen with systemic beta-blocking agents. Incidence of systemic ADRs after topical ophthalmic administration is lower than for systemic administration.

The following adverse reactions have been reported with COSOPT or one of its components either during clinical trials or during post-marketing experience:

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[Very Common: (≥1/10), Common: (≥1/100, <1/10), Uncommon: (≥1/1000, <1/100), and Rare: (≥1/10,000, <1/1000), Not known (cannot be estimated from the available data)]

System Organ Class (MedDRA)	Very Common	Common	Uncommon	Rare	Not Known**
Immune system disorders				signs and symptoms of systemic allergic reactions, including angioedema, urticaria, pruritus, rash, anaphylaxis	pruritus
Metabolism and nutrition disorders					hypoglycaemia
Psychiatric disorders					insomnia*, nightmares*, memory loss, depression*
Nervous system disorders					dizziness*, paraesthesia*, headache*, syncope*, paraesthesia*, increase in signs and symptoms of myasthenia gravis, decreased libido*, cerebrovascular accident*, cerebral ischaemia

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Eye disorders	burning and stinging	conjunctival injection, blurred vision, corneal erosion, ocular itching, tearing			signs and symptoms of ocular irritation including redness*, pain*, eyelid crusting*, blepharitis*, keratitis*, decreased corneal sensitivity, dry eyes*, visual disturbances including refractive changes (due to withdrawal of miotic therapy in some cases)*, ptosis, diplopia, choroidal detachment following filtration surgery* (see Special warning and precautions for use), itching, tearing, corneal oedema*, ocular hypotony*, transient myopia (which resolved upon discontinuation of therapy), iridocyclitis* eyelid inflammation*, eyelid irritation*

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Ear and labyrinth disorders					tinnitus*
Cardiac disorders					atrioventricular block, cardiac failure, bradycardia*, chest pain*, palpitation*, oedema*, arrhythmia*,
Vascular disorders					hypotension*, claudication, Raynaud's phenomenon*, cold hands and feet*
Respiratory, thoracic, and mediastinal disorders		sinusitis		shortness of breath, respiratory failure, rhinitis, rarely bronchospasm	epistaxis*, dyspnoea*, bronchospasm (predominantly in patients with pre-existing bronchospastic disease)*, respiratory failure, cough*

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Gastrointestinal disorders	dysgeusia				nausea*, throat irritation, dry mouth*, dyspepsia*, diarrhoea, dysgeusia, abdominal pain, vomiting
Skin and subcutaneous tissue disorders				contact dermatitis, Stevens-Johnson syndrome, toxic epidermal necrolysis	rash*, alopecia*, psoriasiform rash or exacerbation of psoriasis*
Musculoskeletal and connective tissue disorders					Myalgia, systemic lupus erythematosus
Renal and urinary disorders			urolithiasis		
Reproductive system and breast disorders					sexual dysfunction, Peyronie's disease*, decreased libido
General disorders and administration site conditions					asthenia/ fatigue*

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*Additional adverse reactions have been seen with ophthalmic Timolol or Dorzolamide alone and may potentially occur with COSOPT
** Additional adverse reactions have been seen with ophthalmic beta-blockers and may potentially occur with COSOPT

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions.

OVERDOSE

No data are available in humans in regard to overdose by accidental or deliberate ingestion of COSOPT or COSOPT.

Symptoms
There have been reports of inadvertent overdoses with timolol maleate ophthalmic solution resulting in systemic effects similar to those seen with systemic beta-adrenergic blocking agents such as dizziness, headache, shortness of breath, bradycardia, bronchospasm, and cardiac arrest. The most common signs and symptoms to be expected with overdoses of dorzolamide are electrolyte imbalance, development of an acidotic state, and possibly central nervous system effects.

Only limited information is available with regard to human overdose by accidental or deliberate ingestion of dorzolamide hydrochloride. With oral ingestion, somnolence has been reported. With topical application the following have been reported: nausea, dizziness, headache, fatigue, abnormal dreams, and dysphagia.

Treatment
Treatment should be symptomatic and supportive. Serum electrolyte levels (particularly potassium) and blood pH levels should be monitored. Studies have shown that timolol does not dialyze readily.

PHARMACOLOGICAL PROPERTIES

A. PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Antiglaucoma preparations and miotics, Beta blocking agents, Timolol, combinations, ATC code: S01ED51

Mechanism of action

COSOPT is comprised of two components: dorzolamide hydrochloride and timolol maleate. Each of these two components decreases elevated intraocular pressure by reducing aqueous humor secretion, but does so by a different mechanism of action.

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Dorzolamide hydrochloride is a potent inhibitor of human carbonic anhydrase II. Inhibition of carbonic anhydrase in the ciliary processes of the eye decreases aqueous humor secretion, presumably by slowing the formation of bicarbonate ions with subsequent reduction in sodium and fluid transport. Timolol maleate is a nonselective beta-adrenergic receptor blocking agent. The precise mechanism of action of timolol maleate in lowering intraocular pressure is not clearly established at this time, although a fluorescein study and tonography studies indicate that the predominant action may be related to reduced aqueous formation. However, in some studies a slight increase in outflow facility was also observed. The combined effect of these two agents results in additional intraocular pressure reduction (IOP) compared to either component administered alone.

Following topical administration, COSOPT reduces elevated intraocular pressure, whether or not associated with glaucoma. Elevated intraocular pressure is a major risk factor in the pathogenesis of optic nerve damage and glaucomatous visual field loss. This medicinal product reduces intraocular pressure without the common side effects of miotics such as night blindness, accommodative spasm and pupillary constriction.

Pharmacodynamic effects

Clinical Effects
Clinical studies of up to 15 months duration were conducted to compare the IOP-lowering effect of COSOPT b.i.d. (dosed morning and bedtime) to individually- and concomitantly-administered 0.5% timolol and 2.0% dorzolamide in patients with glaucoma or ocular hypertension for whom concomitant therapy was considered appropriate in the trials. This included both untreated patients and patients inadequately controlled with timolol monotherapy. The majority of patients were treated with topical beta- blocker monotherapy prior to study enrollment. In an analysis of the combined studies, the IOP-lowering effect of COSOPT b.i.d. was greater than that of monotherapy with either 2% dorzolamide t.i.d. or 0.5% timolol b.i.d. The IOP-lowering effect of COSOPT b.i.d. was equivalent to that of concomitant therapy with dorzolamide b.i.d. and timolol b.i.d. The IOP-lowering effect of COSOPT b.i.d. was demonstrated when measured at various time points throughout the day and this effect was maintained during long-term administration.

In an active-treatment-controlled, parallel, double-masked study in 261 patients with elevated intraocular pressure ≥22 mmHg in one or both eyes, COSOPT had an IOP-lowering effect equivalent to that of COSOPT (preservative formulation). The safety profile of COSOPT was similar to COSOPT (preservative formulation).

B. PHARMACOKINETIC PROPERTIES

Dorzolamide Hydrochloride

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Unlike oral carbonic anhydrase inhibitors, topical administration of dorzolamide hydrochloride allows for the active substance to exert its effects directly in the eye at substantially lower doses and therefore with less systemic exposure. In clinical trials, this resulted in a reduction in IOP without the acid-base disturbances or alterations in electrolytes characteristic of oral carbonic anhydrase inhibitors.

When topically applied, dorzolamide reaches the systemic circulation. To assess the potential for systemic carbonic anhydrase inhibition following topical administration, active substance and metabolite concentrations in red blood cells (RBCs) and plasma and carbonic anhydrase inhibition in RBCs were measured. Dorzolamide accumulates in RBCs during chronic dosing as a result of selective binding to CA-II while extremely low concentrations of free active substance in plasma are maintained. The parent active substance forms a single N-desethyl metabolite that inhibits CA-II less potently than the parent active substance but also inhibits a less active isoenzyme (CA-I). The metabolite also accumulates in RBCs where it binds primarily to CA-I. Dorzolamide binds moderately to plasma proteins (approximately 33%). Dorzolamide is primarily excreted unchanged in the urine; the metabolite is also excreted in urine. After dosing ends, dorzolamide washes out of RBCs nonlinearly, resulting in a rapid decline of active substance concentration initially, followed by a slower elimination phase with a half-life of about four months.

When dorzolamide was given orally to simulate the maximum systemic exposure after long term topical ocular administration, steady state was reached within 13 weeks. At steady state, there was virtually no free active substance or metabolite in plasma; CA inhibition in RBCs was less than that anticipated to be necessary for a pharmacological effect on renal function or respiration. Similar pharmacokinetic results were observed after chronic, topical administration of dorzolamide hydrochloride. However, some elderly patients with renal impairment (estimated CrCl 30-60 ml/min) had higher metabolite concentrations in RBCs, but no meaningful differences in carbonic anhydrase inhibition and no clinically significant systemic side effects were directly attributable to this finding.

Timolol Maleate

In a study of plasma active substance concentration in six subjects, the systemic exposure to timolol was determined following twice daily topical administration of timolol maleate ophthalmic solution 0.5%. The mean peak plasma concentration following morning dosing was 0.46 ng/ml and following afternoon dosing was 0.35 ng/ml.

C. PRECLINICAL SAFETY DATA

The ocular and systemic safety profile of the individual components is well established.

Dorzolamide
In rabbits given maternotoxic doses of dorzolamide associated with metabolic acidosis, malformations of the vertebral bodies were observed.

Timolol
Animal studies have not shown teratogenic effect.

Furthermore, no adverse ocular effects were seen in animals treated topically with dorzolamide hydrochloride and timolol maleate ophthalmic solution or with concomitantly- administered dorzolamide hydrochloride and timolol maleate. *In vitro* and *in vivo* studies with each of the components did not reveal a mutagenic potential. Therefore, no significant risk for human safety is expected with therapeutic doses of COSOPT.

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SHELF LIFE

2 years

COSOPT should be used no longer than 15 days after first opening the sachet. Discard any unused single dose containers after that time.

Discard the opened single dose container immediately after first use.

STORAGE

Do not store above 30°C.
Store in the original package in order to protect from light.

PACKAGING

COSOPT is available in 0.2 ml low density polyethylene single dose containers in an aluminum sachet containing 15 single -dose containers.

Pack sizes:

30 x 0.2 ml (2 sachets with 15 single dose containers)
60 x 0.2 ml (4 sachets with 15 single dose containers)

Not all pack sizes may be marketed.

Reg. No.

HARUS DENGAN RESEP DOKTER

SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING

No special requirements.

Instructions for use

1. Open the foil sachet which contains 15 individual single dose containers. There are three strips of 5 single dose containers each in the sachet. Write the date of first opening on the sachet.

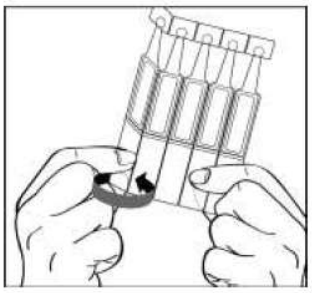
2. First wash your hands then break off one single dose container from the strip and twist open the

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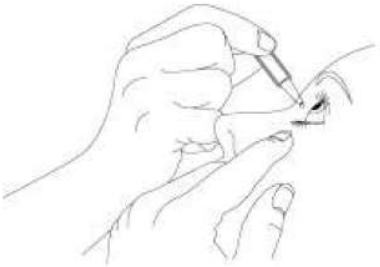
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top.





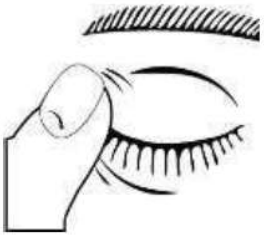
3. Tilt your head back and pull your lower eyelid down slightly to form a pocket between your eyelid and eye as shown. **Do not allow any part of the container to touch your eye or any area around your eye.**



If you are not sure how to administer your medicine, ask your doctor, pharmacist or nurse.

4. Put one drop in the affected eye(s) as directed by your doctor. Do not blink while applying the drop to your eye.
Each single dose container contains enough solution for both eyes.

5. When using nasolacrimal occlusion or closing the eyelids for 2 minutes, the systemic absorption is reduced. This may result in a decrease in systemic side effects and an increase in local activity.



6. After putting the drop into the eye, throw away the used single dose container even if there is solution remaining to avoid contamination of the preservative free solution.

7. Store the remaining containers in the foil sachet; the remaining containers must be used within 15 days after opening of the sachet. If there are any containers left 15 days after opening the

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sachet they should be safely thrown away and a fresh sachet opened. It is important to continue to use the eye drops as prescribed by your doctor.

Manufactured by:
Catalent Pharma Solutions
2210 Lake Shore Drive Woodstock,
IL 60098, USA

Licensed and Released by:
Santen Oy
Niittyhaankatu 20,
33720 Tampere, Finland

Imported and Marketed by:
meiji
PT. MEIJI INDONESIAN PHARMACEUTICAL INDUSTRIES
Bangil-Pasuruan, Jawa Timur-Indonesia

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Informasi Produk untuk Pasien

COSOPT®
Dorzolamide HCl / Timolol Maleate
Ophthalmic Solution

HARUS DENGAN RESEP DOKTER

Apa yang terdapat dalam leaflet ini

1. Apa COSOPT dan apa kegunaannya
2. Apa yang anda perlu ketahui sebelum menggunakan COSOPT
3. Bagaimana cara penggunaan COSOPT
4. Efek samping yang mungkin terjadi
5. Bagaimana cara penyimpanannya
6. Isi dari kemasan dan informasi lainnya.

1. Apa COSOPT dan Apa kegunaannya

COSOPT mengandung 2 zat aktif: dorzolamide dan timolol

- Dorzolamide masuk ke dalam golongan obat yang dinamakan "carbonic anhydrase inhibitors"
- Timolol masuk kedalam golongan obat "beta bloker".

Obat ini menurunkan tekanan pada mata dengan menggunakan cara yang berbeda.

COSOPT di resepkan untuk menurunkan tekanan pada mata pada pengobatan ocular hypertension atau glaucoma ketika penggunaan monoterapi beta blocker topical tidak adekuat.

2. Apa yang anda harus ketahui jika menggunakan COSOPT

Jangan menggunakan COSOPT

- Jika anda alergi terhadap dorzolamide hydrochloride, timolol maleate atau komposisi dari obat ini (lihat list section 6).
- Jika anda memiliki masalah pernapasan pada saat ini atau masa lampau, seperti asma, atau bronchitis obstruktif parah (penyakit paru parah yang dapat menyebabkan nafas berbunyi, kesulitan dalam bernafas dan/atau batuk dalam jangka lama).
- Jika anda memiliki detak jantung yang lemah, gagal jantung atau gangguan ritme jantung (detak jantung yang tidak beraturan).
- Jika anda memiliki masalah pada ginjal atau penyakit ginjal yang parah, atau pernah menderita batu ginjal.
- Jika anda memiliki keasaman darah yang berlebih yang disebabkan karena meningkatnya kloride di dalam darah (hiperkloremia asidosis)

Jika anda tidak yakin ketika menggunakan obat ini, hubungi dokter atau apoteker.

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Peringatan dan Pencegahan
Komunikasikan pada dokter anda sebelum menggunakan COSOPT

Beritahu dokter anda mengenai beberapa masalah medis atau masalah mata anda saat ini atau pernah terjadi pada masa lalu, seperti:

- Penyakit jantung koroner (gejala dapat termasuk nyeri dada atau sesak, sulit bernafas, atau tersedak), gagal jantung, tekanan darah rendah.
- Gangguan denyut jantung seperti detak jantung lambat.
- Gangguan pernafasan, asama atau penyakit obstructive paru kronis.
- Penyakit peredaran darah yang buruk (seperti penyakit Raynaud atau gejala Raynaud)
- Diabetes, timolol mungkin menutupi tanda dan gejala dari penurunan gula rendah.
- Peningkatan aktifitas dari kelenjar tiroid oleh timolol mungkin menutupi tanda dan gejala.

Beritau dokter anda sebelum dilakukan operasi bahwa anda menggunakan COSOPT karena, timolol mungkin dapat merubah efek dari beberapa obat yang digunakan selama proses anastesi.

Beritau dokter anda mengenai reaksi alergi atau anafilaksis

Beritau dokter anda jika anda memiliki kelemahan otot atau telah di diagnosa memiliki miastenia gravis

Jika anda menderita iritasi mata atau problem baru pada mata seperti kemerahan pada mata atau bengkak pada kelopak mata, segera hubungi dokter

Jika anda mengira bahwa COSOPT ini yang menyebabkan reaksi alergi atau hipersensitifitas (sebagai contoh, ruam kulit, reaksi kuit parah, atau kemerahan dan gatal pada mata), hentikan penggunaan obat dan hubungi dokter segera

Beritau dokter anda jika menderita infeksi mata, luka pada mata, operasi mata, atau terjadi reaksi termasuk gejala baru atau gejala yang memburuk

JIka COSOPT diteteskan ke mata ini dapat berefek pada seluruh tubuh

COSOPT belum pernah diteliti pada pasien yang menggunakan lensa kontak
Jika anda menggunakan lensa kontak, anda sebaiknya mengkonsultasikan terlebih dahulu dengan dokter sebelum menggunakan obat ini

Penggunaan pada Anak
Pengalaman terbatas dengan penggunaan COSOPT pada bayi dan anak.

Penggunaan pada Lansia
Penelitian dengan COSOPT, efek dari COSOPT mirip pada lansia dan pasien muda.

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Penggunaan pada pasien dengan Kerusakan Hati

Beritau dokter anda mengenai gangguan hati yang terjadi saat ini atau pernah diderita di masa lalu

Obat lain dan COSOPT

COSOPT dapat mempengaruhi atau dipengaruhi oleh obat lain yang di gunakan, termasuk tetes mata lain yang digunakan untuk glaucoma. Beritau dokter anda jika anda sedang menggunakan atau berniat untuk menggunakan obat dengan tujuan menurunkan tekanan darah, obat jantung atau obat diabetes

Beritau dokter anda atau apoteker jika anda menggunakan, sedang menggunakan atau mungkin menggunakan obat lain. Ini penting khususnnya jika anda;

- Minum obat untuk menurunkan kadar gula darah atau untuk mengobati penyakit jantung (seperti calcium channel bloker, beta bloker atau digoxin).
- Minum obat untuk mengobati gangguan atau detak jantung yang tidak beraturan seperti calcium channel blockers, beta-blockers atau digoxin.
- Menggunakan tetes mata lainnya yang mengandung beta bloker.
- Minum carbonic anhydrase inhibitor lainnya seperti asetazolamide.
- Minum monoamine oxidase inhibitors (MAOIs)
- Minum obat parasimpatomimetic yang mungkin pernah diresepkan untuk membantu anda buang air kecil. Parasympathomimetics juga tipe obat tertentu yang terkadang digunakan untuk membantu mengembalikan pergerakan normal pada perut bagian bawah.
- Minum narkotik seperi morfin digunakan untuk mengobati nyeri sedang atau berat.
- Minum obat untuk mengobati diabetes.
- Minum antidepresan dikenal sebagai fluoxetine dan paroxetine.
- Minum obat sulfa
- Minum quinidine (digunakan untuk mengobati kondisi Antung dan beberapa tipe malaria)

Kehamilan dan menyusui

Tanya dokter atau apoteker untuk saran sebelum menggunakan obat

Penggunaan pada Kehamilan

Jangan gunakan COSOPT jika anda sedang hamil kecuali jika penting menurut pertimbangan dokter

Penggunaan pada menyusui

Jangan menggunakan COSOPT jika anda dalam masa menyusui

Timolol mungkin dapat masuk kedalam ASI

Tanya pada dokter anda sebelum menggunakan obat ini dalam masa menyusui

Berkendara dan menggunakan mesin

Tidak ada studi yang dilaporkan terhadap efek pada kemampuan berkendara atau mengoperasikan mesin

Ada efek samping yang berkaitan dengan COSOPT, seperti penglihatan buram, mungkin dapat mempengaruhi kemampuan berkendara dan/atau mengoperasikan mesin

Jangan mengendarai atau mengoperasikan mesin sampai anda merasa lebih baik atau penglihatan sudah jelas

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3. Bagaimana Cara penggunaan COSOPT.

Gunakan selalu obat ini sesuai dengan anjuran dokter
Tanyakan pada dokter anda atau apoteker jika anda tidak yakin
Dosis yang sesuai dan jangka pengobatan akan di tentukan oleh dokter anda

Dosis yang di rekomendasikan adalah satu tetes pada mata yang sakit pada pagi dan sore hari

JIka anda menggunakan COSOPT dengan tetes mata lain, tetesan obat lain sebaiknya minimal di beri jarak 10 menit.

Jangan merubah dosis obat tanpa mengkonsultasikan dengan dokter

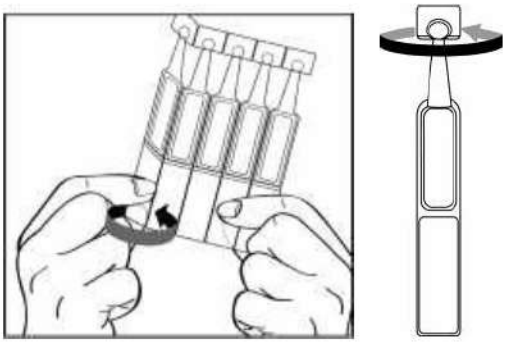
Jika anda kesulitan untuk meneteskan pada mata anda, cari bantuan dari anggota keluarga atau asisten

Tidak diperbolehkan kemasan dosis tunggal menyentuh mata atau area sekitar mata. Ini dapat menyebabkan cedera pada mata anda. Itu juga mungkin dapat mengkontaminasi bakter yang dapat menyebabkan infeksi mata yang akan menyebabkan bahaya pada mata, sampai kehilangan penglihatan. Untuk menghindari kontaminasi yang mungkin terjadi dari kemasan dosis tunggal, cuci tangan dengan sabun sebelum menggunakan obat ini dan lindungi ujung kemasan dosis tunggal terhadap kontak dari berbagai permukaan.

Instruksi penggunaan

Larutan dari setiap individu yang menggunakan COSOPT harus segera digunakan setelah kemasan di buka digunakan pada mata yang sakit. Dikarenakan sterilitas tidak dapat di jaga setelah kemasan dosis tunggal dibuka, kemasan baru harus dibuka sebelum digunakan dan harus segera dibuang setelah di pergunakan.

1. Buka kantong yang terdiri dari 15 kemasan dosis tunggal. Ada 3 strip yang berisi 5 kemasan dosis tunggal di dalam kantong. Tulis tanggal pertama kali membuaka kemasan.
2. Pertama cuci tangan anda kemudian lepaskan 1 kemasan dosis tunggal dari strip dan putarkan untuk membuka bagian atas kemasan dosis tunggal itu seperti terlihat di bawah ini.

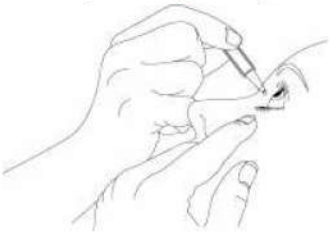


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3. Miringkan kepala anda kebelakang dan tarik bagian bawah kelopak mata anda sampai terbentuk kantung antara kelopak mata dengan mata, seperti terlihat pada gambar dibawah ini. **Jangan sampai bagian dari kemasan menyentuh mata anda atau area mata anda.**



Jika anda tidak yakin bagaimana menggunakan obat ini, tanya pada dokter atau apoteker atau perawat.

4. Teteskan 1 tetes pada mata yang sakit seperti yang dianjurkan dokter. Jangan berkedip ketika mengaplikasikan tetesan pada mata anda.
   Tiap kemasan dosis tunggal mengandung cukup cairan untuk kedua mata.
5. Setelah menggunakan COSOPT, tekan dengan jari pada pojok mata anda, sampping hidung, atau tutup mata anda selama 2 menit. Hal ini membantu agar obat tidak masuk dalam tubuh.
6. Setelah meneteskan ke mata, buang kemasan dosis tunggal yang tidak terpakai walaupun masih ada cairan tersisa untuk menghindari kontaminasai karena larutan ini tidak mengandung pengawet.
7. Simpan kemasan yang tersisa di dalam kantong; kemasan yang tersisa harus digunakan dalam waktu 15 hari setelah di buka dari kantong. Jika ada kemasan yang lebih dari 15 hari setelah kantong dibuka sebaiknya dibuang agar aman dan buka kantong baru. Penting untuk melanjutkan obat tetes mata ini seperti anjuran dokter.

Jika anda memakai COSOPT lebih dari yang disarankan

Jika anda menggunkaan COSOPT terlalu banyak pada mata nada atau menelan isi dari kemasan, efeknya antara lain, anda mungkin akan merasa kepala ringan, sulit bernafas, atau merasa detak jantung anda menjadi lambat. Hubungi dokter secepatnya.

Jika anda lupa menggunakan COSOPT

Penting untuk menggunakan COSOPT sesuai dengan anjuran dokter.

Jika anda terlewat, maka gunakan secepatnya. Jika anda ingat saat mendekati jadwal penggunaan dosis selanjutnya, maka lewatkan dosis yang terlupa dan kembali lagi ada penggunaan regular sesuai jadwal.

Jangan menggunakan dosis ganda untuk mengganti dosis yang terlewat.

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Jika anda menghentikan penggunaan COSOPT
Jika anda ingin menghentikan penggunaan obat ini, bicarakan dengan dokter anda terlebih dahulu.

Jika anda mempunyai pertanyaan lebih lanjut tentang penggunaan obat ini, tanyakan pada dokter atau apoteker.

4. Efek samping yang mungkin terjadi.
Seperti kebanyakan obat, obat ini dapat menyebabkan efek samping, walaupun tidak semua orang mengalaminya.

Anda dapat melanjutkan pemakaian obat, asalkan tidak ada efek yang serius. Jika anda ragu, bicarakan pada dokter atau apoteker. Jangan menghentikan COSOPT tanpa berbicara pada dokter.

Reaksi alergi umum termasuk bentol dapa terjadi pada area wajah dan anggota tubuh, dan dapat merusak jalannya udara yang dapat menyebabkan kesulitan dari menelan atau bernafas, gatal – gatal atau ruam gatal, secara lokal atau ruam seluruhnya, gatal, jarang terjadi reaksi alergi yang mengancam jiwa.

Berikut reaksi efek samping yng telah dilaporkan terkait COSOPT atau satu dari komponen obat lain selama uji klinik atau selama paska permasaran:

<u>Sangat Umum (kemungkinan terjadi lebih dari 1 dari 10 pengguna):</u>
Panas dan pedih pada mata, kelainan pengecapan rasa

<u>Umum (kemungkinan terjadi lebih dari 1 sampai 10 dari 100 pengguna):</u>
Kemerahan di dalam dan sekitar mata, mata berair atau gatal pada mata, erosi kornea (kerusakan pada lapisan depan dari bola mata), penglihatan kabur, sinusitis(perasaan tegang atau seperti penuh pada hidung).

<u>Tidak Umum (kemungkinan terjadi lebih dari 1 sampai 10 dari 1000 pengguna):</u>
Batu kemih.

<u>Jarang (kemungkinan terjadi lebih dari 1 sampai 10 dari 10.000 pengguna):</u>
Reaksi alergi seperti kemerahan, urtikaria, gatal, dan pada kasus yang jarang terjadi kemungkinan pembengkakan bibir, mata, mulut, bunyi mengi, dan reaksi alergi kulilt yang parah (Steven Johnsons syndrome, nekrolisis epidermis toksik), dermatitis kontak, sesak napas, gagal napas, rhinitis, penyempitan saluran pernapasan.

Seperti obat lain yang di aplikasikan pada mata, timolol diserap kedalam darah. Ini mungkin di sebabkan efeksamping yang mirip yang terlihat dengan penggunaan betabloker. Kejadian dari efek samping setelah penggunaan obat mata secara topical lebih rendah dari obat adalah, contoh, melalui mulut atau injeksi.

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Daftar efek samping tambahan termasuk reaksi yang terlihat antara golongan beta bloker ketika di gunakan untuk mengobati mata.

Tidak diketahui (kemungkinan terjadi tidak dapat diperkirakan dari data yang tersedia)
Glukosa darah rendah, gagal jantung, tipe dari kerusakan ritme jantung, insomnia, mimpi buruk, hilang ingatan, depresi, pusing, kesemutan atau mati rasa pada tangan atau kaki, sakit kepala, pingsan, peningkatan pada tanda dan gejala dari myasthenia gravis (gangguan otot), pembengkakan dan/ atau iritasi pada atau sekitar mata, perasaan ada sesuatu pada mata, sakit mata, pengerasan kulit kelopak mata, penurunan sensitifitas kornea (tidak sadar jika kemasukan benda asing pada mata atau tidak merasa sakit), mata kering, gangguan penglihatan termasuk perubahan refraksi (pada beberapa kasus disebabkan karena penarikan terapi miopi), kelopak mata terkulai (membuat mata terjaga setengah tertutup), visual ganda, pembengkakan pada kornea, (dengan gejala gangguan penglihatan), tekanan pada mata rendah, pelepasan lapisan pada bagian bawah retina yang terdapat pembuluh darah, diikuti dari operasi penyaringan dimana dapat menyebabkan gangguan visual, penglihatan memendek sementara dan dapat disembuhkan dengan memberhentikan terapi, inflamasi pada iris, suara dengung pada telinga, serangan jantung, gagal jantung kongestif (sakit jantung dengan sesak napas dan pembengkakan kaki karena penumpukan cairan), detak jantung melambat, nyeri dada, palpitasi (detak jantung lebih cepat/ tidak beraturan), udem (penumpukan cairan), perubahan ritme atau kecepatan detak jantung, tekanan darah rendah, dan/ atau sakit pada kaki ketika berjalan (klaudikasi), fenomena Raynaud, pembengkakan atau mendingin pada bagian tangan, dan kaki dan mengurangi sirkulasi pada tangan dan kaki, pendarahan pada hidung, kesusahan bernafas (dyspnea), batuk, mual, iritasi tenggorokan, mulut kering, diare, gangguan pencernaan, nyeri abdomen, muntah, rambut rontok, ruam kulit dengan muncul warna putih keperakan, nyeri otot yang tidak disebabkan oleh olahraga. Sistemik Lupus erithematosus (penyakit autoimun dimana dapat menyebabkan pembengkakan organ internal), disfungsi seks, penyakit Peyronic (menyebabkan penis melengkung), penurunan nafsu seksual, kelemahan dan kelelahan.

5. Bagaimana Cara Penyimpanan COSOPT

Simpan obat ini jauh dari pandangan dan jangkauan anak-anak

Jangan gunakan kemasan COSOPT yang telah terbuka setelah masa kadaluarsa yang tercantum dalam 6 digit berikut EX (atau EXP) pada kemasan aluminium foil. Digit pertama menunjukkan bulan; empat digit terakhir menunjukkan tahun. Masa kadaluarsa mengacu pada hari terakhir dari bulan tersebut.

Jangan simpan pada suhu diatas 30°C.
Simpan pada kemasan aluminium foil agar terhindar dari cahaya.
Anda dapat gunakan COSOPT dalam jangka 15 hari setelah kantong pertama kali buka. Buang kemasan tunggal yang tidak terpakai setelah dibuka.
Buang kemasan dosis tunggal yang telah terbuka disertai cairan yang tersisa sesaat setelah penggunaan pertama.

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Jangan membuang obat melalui pembuangan air atau pembuangan sampah rumah tangga. Tanya pada apoteker bagaimana cara membuang obat yang telah lama tidak terpakai. Dengan cara ini kan membantu melindungi lingkungan.

6. Isi dari kemasan dan informasi lainnya.

Apa isi COSOPT:

- Zat aktif terdiri dari dorzolamide dan timolol

Tiap ml mengandung 20 mg dorzolamide (22.26 sebagai dorzolamide hydrochloride) dan 5 mg timolol (6.83 sebagai timolol maleate)

- Komposisi lain yaitu hydroxyethyl cellulose, mannitol, sodium citrate, sodium hydroxide, dan water for injection

Seperti apa COSOPT dan isi dari kemasannya.

COSOPT berupa bening, tidak berwarna sampai mendekati tidak berwarna larutan sedikit kental. Tiap kantung aluminium mengandung berat jenis rendah dari 15 polyethylene dalam kemasan tunggal yang mengandung 0,2 ml larutan.

Besar kemasan:

30 x 0.2 ml (2 sachet dengan 15 kemasan dosis tunggal)
60 x 0.2 ml (4 sachet dengan 15 kemasan dosis tunggal)

Reg. No :

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