Merck Announces FDA Approval of COSOPT® PF (dorzolamide hydrochloride-timolol maleate ophthalmic solution) 2%/0.5%

Dear Customer:

I am very excited to inform you that on February 1, 2012, the US Food and Drug Administration (FDA) approved COSOPT PF, Merck’s new, preservative-free formulation of branded COSOPT® (dorzolamide hydrochloride-timolol maleate ophthalmic solution). COSOPT PF is a carbonic anhydrase inhibitor with a beta-adrenergic receptor blocking agent indicated for the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension who are insufficiently responsive to beta-blockers (failed to achieve target IOP determined after multiple measurements over time). The IOP-lowering of COSOPT twice daily was slightly less than that seen with the concomitant administration of 0.5% timolol twice daily and 2.0% dorzolamide 3 times daily.

COSOPT PF, the first preservative-free, fixed-dose combination therapy for lowering IOP, has been proven to provide the same powerful efficacy as original COSOPT. In an active-treatment controlled, parallel, double-masked study in 261 patients with elevated IOP ≥22 mmHg in 1 or both eyes, COSOPT PF had an IOP-lowering effect equivalent to that of COSOPT. The IOP-lowering effect of COSOPT twice daily was greater (1–3 mmHg) than that of monotherapy with either 2.0% dorzolamide 3 times daily or 0.5% timolol twice daily. The IOP-lowering effect of COSOPT twice daily was approximately 1 mmHg less than that of concomitant therapy with 2.0% dorzolamide 3 times daily and 0.5% timolol twice daily.

COSOPT PF is approved only as a branded product from Merck. There are no generic versions of COSOPT PF available.

COSOPT PF is contraindicated in patients with bronchial asthma, a history of bronchial asthma, severe chronic obstructive pulmonary disease, sinus bradycardia, second- or third-degree atrioventricular block, overt cardiac failure, cardiogenic shock, or hypersensitivity to any component of this product.

COSOPT PF is an important addition to Merck’s ophthalmics portfolio and underscores our commitment to provide additional treatment options for patients with open-angle glaucoma and/or ocular hypertension.

Merck expects to make COSOPT PF available in mid 2012. Merck is committed to delivering COSOPT PF as soon as feasible.
Additional Select Important Safety Information

COSOPT® PF (dorzolamide hydrochloride-timolol maleate ophthalmic solution)
2%/0.5% contains timolol maleate, a beta-adrenergic blocking agent; and although
administered topically, it is absorbed systemically. Therefore, the same types of adverse
reactions that are attributable to systemic administration of beta-adrenergic blocking
agents may occur with topical administration of COSOPT PF. For example, severe
respiratory reactions, including death due to bronchospasm in patients with asthma, and
rarely death in association with cardiac failure, have been reported following systemic or
ophthalmic administration of timolol maleate.

Sympathetic stimulation may be essential for support of the circulation in individuals
with diminished myocardial contractility, and its inhibition by beta-adrenergic receptor
blockade may precipitate more severe failure. In patients without a history of cardiac
failure continued depression of the myocardium with beta-blocking agents over a period
of time can, in some cases, lead to cardiac failure. At the first sign or symptom of
cardiac failure, COSOPT PF should be discontinued.

COSOPT PF contains dorzolamide, a sulfonamide; and although administered topically,
it is absorbed systemically. Therefore, the same types of adverse reactions that are
attributable to sulfonamides may occur with topical administration of COSOPT PF.
Fatalities have occurred, although rarely, due to severe reactions to sulfonamides,
including Stevens-Johnson syndrome, toxic epidermal necrolysis, fulminant hepatic
necrosis, agranulocytosis, aplastic anemia, and other blood dyscrasias.

Patients with chronic obstructive pulmonary disease (eg, chronic bronchitis,
emphysema) of mild or moderate severity, bronchospastic disease, or a history of
bronchospastic disease (other than bronchial asthma or a history of bronchial asthma,
in which COSOPT PF is contraindicated) should, in general, not receive beta-blocking
agents, including COSOPT PF.

While taking beta-blockers, patients may be more reactive to allergens. Such patients
may be unresponsive to the usual doses of epinephrine used to treat anaphylactic
reactions.

Beta-adrenergic blockade has been reported to potentiate muscle weakness consistent
with certain myasthenic symptoms (eg, diplopia, ptosis, and generalized weakness).

Beta-adrenergic receptor blocking agents may mask the signs and symptoms of acute
hypoglycemia.

Beta-adrenergic blocking agents may also mask certain clinical signs (eg, tachycardia)
of hyperthyroidism. Patients suspected of developing thyrotoxicosis should be managed
carefully to avoid abrupt withdrawal of beta-adrenergic blocking agents that might
precipitate a thyroid storm.
Additional Select Important Safety Information (continued)
Dorzolamide has not been studied in patients with severe renal impairment (CrCl <30 mL/min). Because dorzolamide and its metabolite are excreted predominantly by the kidney, COSOPT® PF (dorzolamide hydrochloride-timolol maleate ophthalmic solution) 2%/0.5% is not recommended in such patients. Dorzolamide has not been studied in patients with hepatic impairment and should therefore be used with caution in such patients.

Some patients receiving beta-adrenergic receptor blocking agents have experienced protracted severe hypotension during anesthesia. Difficulty in restarting and maintaining the heartbeat has also been reported. For these reasons, in patients undergoing elective surgery, some authorities recommend gradual withdrawal of beta-adrenergic receptor blocking agents.

There is an increased potential for developing corneal edema in patients with low endothelial cell counts. Caution should be used when prescribing COSOPT PF to this group of patients.

In clinical trials evaluating COSOPT and COSOPT PF, the most frequently reported adverse reactions occurring in up to 30% of patients were taste perversion (bitter, sour, or unusual taste) or ocular burning and/or stinging. The following adverse reactions were reported in 5% to 15% of patients: conjunctival hyperemia, blurred vision, superficial punctate keratitis, or eye itching.

Due to the potential for an additive effect on the known systemic effects of carbonic anhydrase inhibition, the concomitant administration of COSOPT PF and oral carbonic anhydrase inhibitors is not recommended. The concomitant use of 2 topical beta-adrenergic blocking agents is not recommended, and patients receiving a beta-adrenergic blocking agent orally and COSOPT PF should be observed for potential additive effects of beta-blockade, both systemic and on IOP.

The potential for acid-base and electrolyte disturbances should be considered in patients receiving COSOPT PF. Caution should be used with coadministration of calcium antagonists because of possible atrioventricular conduction disturbances, left ventricular failure, and hypotension, and should be avoided in patients with impaired cardiac function. Close observation is recommended with coadministration of catecholamine-depleting drugs because of possible additive effects and the production of hypotension and/or marked bradycardia. The concomitant use of beta-adrenergic blocking agents with digitalis and calcium antagonists may have additive effects in prolonging atrioventricular conduction time. Potentiated systemic beta-blockade has been reported during combined treatment with CYP2D6 inhibitors and timolol.

There are no adequate and well-controlled studies in pregnant women. COSOPT PF should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
Additional Select Important Safety Information (continued)
It is not known whether dorzolamide is excreted in human milk. Timolol maleate has been detected in human milk following oral and ophthalmic drug administration. Because of the potential for serious adverse reactions from COSOPT® PF (dorzolamide hydrochloride-timolol maleate ophthalmic solution) 2%/0.5% in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Dosage and Administration
The dose is 1 drop of COSOPT PF in the affected eye(s) 2 times daily. If more than 1 topical ophthalmic drug is being used, the drugs should be administered at least 5 minutes apart. The solution from 1 individual unit is to be used immediately after opening for administration to 1 or both eyes. Since sterility cannot be maintained after the individual unit is opened, the remaining contents should be discarded immediately after administration.

Before prescribing COSOPT PF, please read the accompanying Prescribing Information. For additional copies of the Prescribing Information, please call 800-672-6372 or contact your Merck representative.

In summary, the FDA approved COSOPT PF on February 1, 2012. COSOPT PF will be available for use in mid 2012. We will keep you updated on the availability of the product.

Sincerely,

Michael A. Stanton
US Region Marketing Leader – Ophthalmics

Enclosure: Prescribing Information for COSOPT PF