Wyeth

March 10, 2005

Dear Health Care Professional:

Wyeth Pharmaceuticals is announcing that **Trecator®-SC (ethionamide tablets, USP) Sugar-Coated Tablets** have been reformulated from sugar-coated tablets to film-coated tablets.

The new name of the product is **Trecator® (ethionamide tablets, USP) Tablets**. The immediate bottle label has been revised. Copies of both Trecator and Trecator-SC labels are enclosed.

The new formulation was designed for improved stability. However, because the new film-coated tablet is more rapidly absorbed, resulting in higher peak concentrations (C_{max}) of ethionamide, it may potentially lead to patient intolerance when introduced at the same initial dose as the old sugar-coated tablet. As shown in the table below, in a study of 40 healthy adult volunteers, although the mean ethionamide area-under-the-curve (AUC) for the film-coated tablet was not significantly different from that of the sugar-coated tablet, the mean C_{max} for the film-coated tablet was significantly higher (approximately 46%) than that of the sugar-coated tablet. The median time to reach C_{max} (T_{max}) was also significantly shorter for the film-coated tablet as compared to that of the sugar-coated tablet. Therefore, patients should be monitored and have their dosages re-titrated (see Dosing discussion below) when switching from the sugar-coated tablet to the film-coated tablet.

Mean (SD) Pharmacokinetic Parameters for Ethionamide Following Single-Dose Administration of 250-mg Trecator Film-Coated and Sugar-Coated Tablets to Healthy Adult Volunteers[1,2]

	C_{max} (μg/mL)	T_{max} (hrs)	AUC (μg•hr/mL)
Film-Coated Tablet	2.16 (0.61)	1.02 (0.55)	7.67 (1.69)
Sugar-Coated Tablet	1.48 (0.64)	1.49 (0.87)	6.59 (1.76)

Trecator is primarily indicated in combination with other anti-tuberculous drugs for the treatment of active tuberculosis in patients with *M. tuberculosis* that is resistant to isoniazid or rifampin or when there is intolerance on the part of the patient to other drugs.

The usual adult dose is 15 to 20 mg/kg/day administered once daily or, if the patient exhibits poor gastrointestinal tolerance, in divided doses, with a maximum daily dose of 1 g. Therapy should be initiated at a dose of 250 mg daily, with gradual titration to optimal doses as tolerated by the patient. A regimen of 250 mg daily for 1 or 2 days followed by 250 mg twice daily for 1 or 2 days with a subsequent increase to 1 g in 3 or 4 divided doses has been reported with the sugar-coated formulation.[3,4] This regimen has not been studied with the film-coated formulation.

The use of Trecator alone in the treatment of tuberculosis results in rapid development of resistance. Ethionamide is contraindicated in patients with severe hepatic impairment and in patients who are hypersensitive to the drug. The most common side effects of ethionamide are gastrointestinal disturbances, including nausea, vomiting, diarrhea, abdominal pain, excessive salivation, metallic taste, stomatitis, anorexia, and weight loss. Adverse gastrointestinal effects appear to be dose related, with approximately 50% of patients unable to tolerate 1 g as a single dose. Gastrointestinal effects may be minimized by decreasing dosage, by changing the time of drug administration, or by the concurrent administration of an antiemetic agent.

Other adverse events include the following:

Nervous System: Psychotic disturbances (including mental depression), drowsiness, dizziness, restlessness, headache, and postural hypotension have been reported with ethionamide. Peripheral neuritis, optic neuritis, diplopia, blurred vision, and a pellagra-like syndrome also have been reported rarely. Concurrent administration of pyridoxine has been recommended to prevent or relieve neurotoxic effects.

Hepatic: Transient increases in serum bilirubin, SGOT, SGPT; hepatitis (with or without jaundice).

Other: Hypersensitivity reactions (including rash), photosensitivity, thrombocytopenia, and purpura have been reported rarely. Hypoglycemia, gynecomastia, impotence, and acne also have occurred. The management of patients with diabetes mellitus may become more difficult.

Before prescribing Trecator, please see the enclosed prescribing information. If you have any questions, please call 1-800-934-5556 for Product Information.

Sincerely,

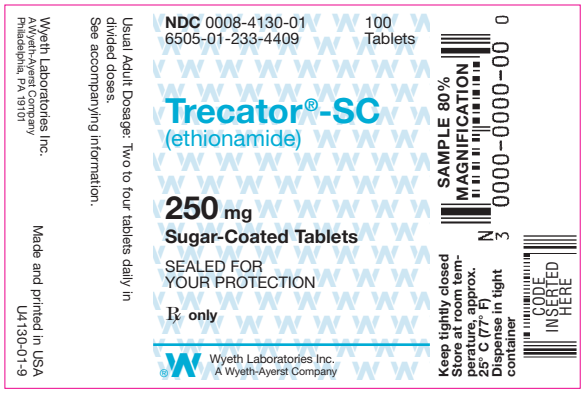
Hal R. Tucker, DO

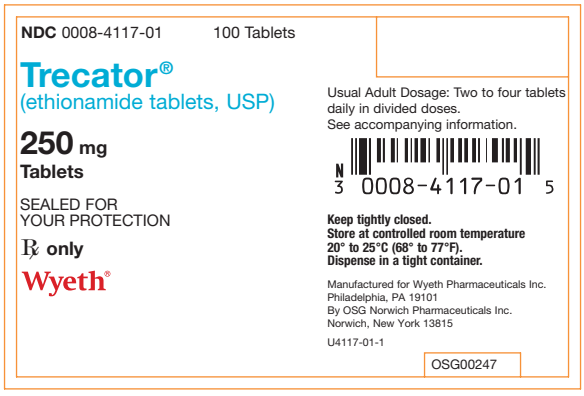
Hal R. Tucker, D.O.
Associate Director, Infectious Disease

Enclosures: Trecator® (ethionamide tablets, USP) Tablets Prescribing Information
Trecator and Trecator-SC Bottle Labels

References

1. Trecator® (ethionamide tablets, USP) Tablets Prescribing Information. Wyeth Pharmaceuticals Inc., Philadelphia, Pa.
2. Data on file, Wyeth Pharmaceuticals Inc.
3. Peloquin CA. Pharmacology of the antimycobacterial drugs. *Med Clin North Am.* 1993;77:1230-1262.
4. American Thoracic Society. *Am J Respir Crit Care Med.* 1997;156:S1-S25.


Wyeth Laboratories Inc.
A Wyeth-Ayerst Company
Philadelphia, PA 19101
Made and printed in USA
U4130-01-9
Usual Adult Dosage: Two to four tablets daily in divided doses.
See accompanying information.
NDC 0008-4130-01
6505-01-233-4409
100 Tablets
Trecator®-SC
(ethionamide)
250 mg
Sugar-Coated Tablets
SEALED FOR YOUR PROTECTION
℞ only
Wyeth Laboratories Inc.
A Wyeth-Ayerst Company
SAMPLE 80% MAGNIFICATION
N 3 0000-0000-00 0
Keep tightly closed
Store at room temperature, approx. 25° C (77° F)
Dispense in tight container
CODE INSERTED HERE


NDC 0008-4117-01
100 Tablets
Trecator®
(ethionamide tablets, USP)
250 mg
Tablets
SEALED FOR YOUR PROTECTION
℞ only
Wyeth®
Usual Adult Dosage: Two to four tablets daily in divided doses.
See accompanying information.
N 3 0008-4117-01 5
Keep tightly closed.
Store at controlled room temperature 20° to 25°C (68° to 77°F).
Dispense in a tight container.
Manufactured for Wyeth Pharmaceuticals Inc.
Philadelphia, PA 19101
By OSG Norwich Pharmaceuticals Inc.
Norwich, New York 13815
U4117-01-1
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