PROPYLTHIOURACIL (PTU)-INDUCED LIVER FAILURE

This New Drug FAX Sheet issue provides updated information from the FDA regarding liver failure associated with propylthiouracil. The verbatim communication from the FDA is provided below. If you need further information, please contact the Samford University Drug Information Service at (205) 726-2659.

FDA is notifying healthcare professionals of the risk of serious liver injury, including liver failure and death, with the use of propylthiouracil (PTU) in adult and pediatric patients. Reports to FDA’s Adverse Event Reporting System (AERS) suggest there is an increased risk of hepatotoxicity with PTU when compared to methimazole (MMI). Although both PTU and MMI are indicated for the treatment of hyperthyroidism due to Graves’ disease, healthcare professionals should carefully consider which drug to initiate in a patient recently diagnosed with Graves’ disease. Physicians should closely monitor patients on PTU therapy for symptoms and signs of liver injury, especially during the first six months after initiation of therapy. PTU and MMI were approved in 1947 and 1950, respectively.

FDA has identified 32 AERS cases (22 adult and 10 pediatric) of serious liver injury associated with PTU use. Of the adult cases, 12 deaths and 5 liver transplants occurred. Among the pediatric patients, 1 case resulted in death and 6 in liver transplants. In contrast, for MMI 5 AERS cases of serious liver injury were identified. All five cases were in adult patients and 3 resulted in death.

In general, PTU is considered second-line drug therapy except in patients who are allergic to or intolerant of methimazole. Rare cases of embryopathy, including aplasia cutis, have been reported with use of MMI during pregnancy, while no such cases have been reported with PTU use. Thus, PTU may be more appropriate for patients with Graves’ disease who are in their first trimester of pregnancy.

On April 18, 2009, FDA held a public workshop with the American Thyroid Association (ATA) to discuss PTU-related hepatotoxicity. FDA is continuing to monitor these serious reported adverse events and working to make changes to the PTU prescribing information, particularly for use in pediatric patients. Also, the ATA plans to update its treatment guidelines for Graves’ disease in the upcoming months.

Recommendations and Information for Healthcare Professionals:
- Reserve PTU use for patients who are in their first trimester of pregnancy, or who are allergic to or intolerant of methimazole.
- Closely monitor patients on PTU therapy for signs and symptoms of liver injury, especially during the first six months after initiation of therapy.
- If liver injury is suspected, promptly discontinue PTU therapy and evaluate the patient for evidence of liver injury and provide supportive care.
- PTU should not be used in pediatric patients unless the patient is allergic to or intolerant of MMI, and there are no other treatment options available.
- Rare cases of embryopathy, including aplasia cutis, have been reported with use of MMI during pregnancy. No such cases have been reported with PTU use during pregnancy. Therefore, PTU may be more appropriate for patients with Graves’ disease who are in their first trimester of pregnancy.
- Counsel patients to promptly advise you if they note any of the following signs or symptoms: fatigue, weakness, vague abdominal pain, loss of appetite, itching, easy bruising or yellowing of the eyes or skin.

Adverse reactions or quality problems experienced with the use of this Product may be reported to the FDA’s MedWatch Adverse Event Reporting program either online, by regular mail or by fax, using the contact information at the bottom of this sheet.

References

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