Prime Drug Alert

PRIME Therapeutics

DRUG THERAPY CHALLENGES AND SOLUTIONS TO ADDRESS THEM

MARCH 24, 2005

Avonex and hepatic injury

Changes in Avonex's label:

As of March 2005, changes to the warnings section of the label of Avonex (interferon beta-1a), an injectable drug indicated for use in patients with multiple sclerosis, have been made:

Severe hepatic injury, including cases of hepatic failure, has been reported rarely in patients taking AVONEX®. Asymptomatic elevation of hepatic transaminases has also been reported, and in some patients has recurred upon rechallenge with AVONEX®. In some cases, these events have occurred in the presence of other drugs that have been associated with hepatic injury. The potential risk of AVONEX® used in combination with known hepatotoxic drugs or other products (e.g. alcohol) should be considered prior to AVONEX® administration, or when adding new agents to the regimen of patients already on AVONEX®. Patients should be monitored for signs of hepatic injury.

Laboratory monitoring recommendations with Avonex:

In addition to those laboratory tests normally required for monitoring patients with multiple sclerosis, complete blood and differential white blood cell counts, platelet counts, and blood chemistries, including liver function tests, are recommended during AVONEX® therapy. During the placebo-controlled studies in multiple sclerosis, these tests were performed at least every 6 months.

Comparison to Rebif:

The warnings section for Rebif, which is also interferon beta-1a and indicated for use in multiple sclerosis, has similar language concerning liver injury:

Severe liver injury, including some cases of hepatic failure requiring liver transplantation, has been reported rarely in patients taking Rebif®. Symptoms of liver dysfunction began from one to six months following the initiation of Rebif®. If jaundice or other symptoms of liver dysfunction appear, treatment with Rebif® should be discontinued immediately due to the potential for rapid progression to liver failure. Asymptomatic elevation of hepatic transaminases (particularly SGPT) is common with interferon therapy. Rebif® should be initiated with caution in patients with active liver disease, alcohol abuse, increased serum SGPT (> 2.5 times ULN), or a history of significant liver disease. Also, the potential risk of Rebif® used in combination with known hepatotoxic products should be considered prior to Rebif® administration, or when adding new agents to the regimen of patients already on Rebif®. Reduction of Rebif® dose should be considered if SGPT rises above 5 times the upper limit of normal. The dose may be gradually re-escalated when enzyme levels have normalized.

Laboratory monitoring recommendations with Rebif:

In addition to those laboratory tests normally required for monitoring patients with multiple sclerosis, blood cell counts and liver function tests are recommended at regular intervals (1, 3, and 6 months) following introduction of Rebif® therapy and then periodically thereafter in the absence of clinical symptoms.

References:

- FDA MedWatch Alert, Avonex (interferon beta-1a): http://www.fda.gov/medwatch/SAFETY/2005/safety05.htm#Avonex
- Dear Healthcare Professional letter: http://www.fda.gov/medwatch/SAFETY/2005/avonex_DHCP.pdf
- Revised label: http://www.fda.gov/medwatch/SAFETY/2005/Avonex_PI.pdf
- Rebif prescribing information: http://www.rebif.com/assets/pdfs/Rebif_PI.pdf