Asthma drug zafirlukast (Accolate): serious hepatic events

Reason for posting: Zafirlukast is an oral leukotriene receptor antagonist used in the treatment of chronic asthma. Since the drug was first marketed in 1996, more than 100 cases of significant liver dysfunction have been reported worldwide, including 14 of liver failure.¹ In some cases, no symptoms or signs of liver dysfunction were reported before the severe hepatic injury occurred. Ten cases, none fatal, have been reported in Canada. The growing number of hepatic adverse events recently prompted the drug's manufacturer, AstraZeneca, to warn health care professionals about this rare but potentially serious adverse event.

The drug: Zafirlukast selectively competes for the leukotriene D₄ and E₄ receptors, both of which are implicated in the pathophysiology of asthma. The drug does not relieve acute bronchospasm, but instead it is used for

the prophylaxis and chronic treatment of asthma in patients older than 12 years.² Several drugs have been recognized to interact with zafirlukast, including warfarin, erythromycin, ASA, theophylline and terfenadine. According to the product monograph, other adverse effects associated with the drug include hypereosinophilia, hematologic abnormalities (e.g., bruising, bleeding and agranulocytosis), edema, arthralgias and myalgias.

What to do: Zafirlukast should not be prescribed to patients with hepatic dysfunction. Patients receiving the drug should be warned of these rare but potentially serious hepatic adverse effects and urged to immediately report any symptoms of concern, including pain in the right upper quadrant, nausea, vomiting, anorexia, fatigue, lethargy, flu-like symptoms, pruritus or jaundice. Serum transaminase levels should be monitored periodically

and the drug stopped if hepatotoxic effects develop. In most cases, mild hepatic dysfunction seems to reverse after discontinuation of the drug, but in some cases the condition progresses to fulminant hepatitis or hepatic failure despite early detection of a problem and discontinuation of the medication. It is unclear whether this adverse effect is shared with other members of the leukotriene receptor inhibitor class, including montelukast.

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References

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