IRISH MEDICINES BOARD

Notice Information: Human Medicines - 3rd Party Publications 31 July 2006

Part 1. Product Information

a)	Title:	Co-Amoxiclav and Hepatobiliary Reactions
b)	Product Name/Type:	Co-Amoxiclav and Hepatobiliary Reactions MIMS Advisory
c)	Reference:	MIMS Publication July 2006
d)	Prescription Required:	No

Part 2. Problem/Issue

a)	Problem/Issue:	Co-amoxiclav (amoxicillin / clavulanic acid) is a broad spectrum antibiotic approved in Ireland for the short term treatment of bacterial infections caused by gram-negative or gram-positive amoxicillin resistant beta-lactamase producing bacteria. If there is good reason to assume that a certain infection is due to the above-mentioned micro organisms then treatment with co-amoxiclav may be considered. However, in other situations, amoxicillin alone should be considered. Further to an earlier review of hepatobiliary effects associated with use of co-amoxiclav, the IMB has continued to monitor the safety profile of products containing this active substance. A review of all adverse reactions reported in association with coamoxiclav indicates that just under a third of adverse reaction reports notified to the Irish Medicines Board with co-amoxiclav involve hepatobiliary type reactions. In addition to those reactions reported directly to the IMB, reports of hepatobiliary reactions with co-amoxiclav have also appeared in the scientific literature over that time. The potential for hepatobiliary adverse reactions with co-amoxiclav is well documented, with moderate and asymptomatic rises in liver enzymes reported occasionally and hepatitis and cholestatic jaundice reported rarely. It is important to note that these types of reactions have been reported more commonly with co-amoxiclav than with amoxicillin alone or with other penicillins. Although hepatic reactions are usually reversible, they may be severe and, very rarely, deaths have been reported. Signs and symptoms usually occur during or shortly after treatment but in some cases may not occur until several weeks after treatment has ended. Of note, hepatic reactions have been reported more frequently in males and elderly patients, particularly those over 60 years and have also been associated with prolonged use. The IMB would therefore like to take this opportunity to remind healthcare professionals of the following recommendations in relation to products containing co-amoxiclav: • Co-amoxiclav is contra-indicated in patients who have suffered previous co-amoxiclav associated jaundice/hepatic dysfunction. • Co-amoxiclav should be given with caution to patients with known hepatic impairment, as there are insufficient data on which to base a dosage recommendation for such patients. • Hepatic function should be monitored at regular intervals in patients treated with co-amoxiclav who have known hepatic dysfunction and in patients with signs or symptoms of hepatic impairment; a change of therapy should be considered in case of deterioration of liver function parameters during treatment. • It is recommended that the duration of treatment should be appropriate to the indication and should not exceed 14 days without review. Finally healthcare professionals are reminded that any suspected adverse reactions should be reported to the IMB in the usual way. A downloadable version of the ADR report form is available from the IMB' s website (www.imb.ie). Downloaded forms may be completed and sent by freepost to the IMB. Envelopes should be marked “Freepost”, Pharmacovigilance Unit, Irish Medicines Board, The Earlsfort Centre, Earlsfort Terrace, Dublin 2. Alternatively, completed forms may be submitted by fax (01- 6762517). Post-paid report cards are also availab

available from the Pharmacovigilance Unit at the IMB (01- 6764971)

Part 3. Keywords

a) Keywords: Co-Amoxiclav Hepatobiliary Reactions