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Dear Healthcare Professionals,

Adverse Drug Reaction Report of Suspected Colchicine Toxicity Associated with Drug Interaction between Colchicine and Clarithromycin

Your attention is drawn to a local case report received by the Department of Health (DH) concerning suspected colchicine toxicity associated with drug interaction between colchicine and clarithromycin

The case involved a 77 year-old woman with a history of hypertension, diabetes, gout and renal impairment. She was prescribed with colchicine for acute gouty attack, together with triple therapy (pantoprazole, clarithromycin and amoxicillin) for helicobacter associated active chronic gastritis. Five days later, the patient was admitted to hospital and subsequently found to have pancytopenia, which was compatible with the presentation of colchicine toxicity. She was later admitted to intensive care unit and her conditions gradually improved upon supportive treatment.

Colchicine has been used for the relief of acute gout and prophylaxis of acute attacks. The most frequent adverse effects of colchicine included diarrhea, nausea, vomiting and abdominal pain. Colchicine has a narrow therapeutic index and is extremely toxic in overdose. Early features of toxicity include nausea, vomiting, abdominal pain, and diarrhea. Features occurring after 1 to 7 days include confusion, decreased cardiac output, cardiac arrhythmias, renal and hepatic impairment, respiratory distress, hyperpyrexia, and bone marrow depression. These can progress in severe cases to multiple organ damage with bone marrow aplasia, convulsions, coma, rhabdomyolysis, and disseminated intravascular coagulation.

Colchicine is a substrate for P-glycoprotein and the cytochrome P450 isoenzyme CYP3A4. Inhibitors of these such as clarithromycin may increase colchicine blood concentrations and the potential for toxicity. Life-threatening or fatal colchicine toxicity has been reported with use of colchicine and clarithromycin, erythromycin, ciclosporin or calcium channel antagonists such as verapamil and diltiazem.

Healthcare professionals are advised that:

P-glycoprotein (P-gp) or strong CYP3A4 inhibitors not be used in patients with renal or hepatic impairment who are currently taking colchicine; and

a dose reduction or interruption of colchicine treatment be considered in patients with normal renal and hepatic function if treatment with a P-gp or a strong CYP3A4 inhibitor is required.

In Hong Kong, there are 12 registered pharmaceutical products containing colchicine. So far, DH has just received the above adverse drug reaction case on colchicine. Healthcare professionals are reminded to pay attention on drug-drug interaction, and balance the risk of possible adverse effects against the benefit of treatment.

Please report any adverse events caused by drugs to the Pharmacovigilance Unit of the DH (tel. no.: 2319 2920, fax: 2319 6319 or email: adr@dh.gov.hk). For details, please refer to the website at Drug Office under "ADR Reporting": http://www.drugoffice.gov.hk/adr.html. You may wish to visit the Drug Office's website for subscription and browsing of "Drug News" which is a monthly digest of drug safety news and information issued by Drug Office.

Yours faithfully,

(Christine CHEUNG)
for Assistant Director (Drug)