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19 December 2018

(來函請敍明此檔案號碼)
(IN REPLY PLEASE QUOTE THIS FILE REF.)

Dear Healthcare Professionals,

Direct-acting antivirals for chronic hepatitis C: risk of hypoglycaemia in patients with diabetes

Your attention is drawn to the United Kingdom Medicines and Healthcare products Regulatory Agency's (MHRA) announcement that studies show some patients with diabetes initiating direct-acting antiviral therapy for hepatitis C have experienced hypoglycaemia. The studies indicate that achieving sustained virological response (SVR) is associated with improvements in glycaemic control, compared to patients who relapse or are non-responders. Many studies recorded these changes in glycaemic control in the first 3 months of treatment. Some studies reported the need to adjust patient's diabetic medication following changes in glucose metabolism, with up to 30% of patients requiring adjustments to their treatment.

An European Union (EU) review confirmed the risk of hypoglycaemia in patients with diabetes who had been initiated on direct-acting antivirals for chronic hepatitis C. Information on the risk is being added to the Summary of Product Characteristics and Patient Information Leaflet for these medicines.

Patients with diabetes should be closely monitored for changes in glucose levels, particularly in the first 3 months of treatment, and adjustments to their diabetic medication or doses made where necessary.

In the United Kingdom, direct-acting antivirals for chronic hepatitis C infection include: daclatasvir (Daklinza▼); sofosbuvir/velpatasvir (Epclusa▼); ledipasvir/sofosbuvir (Harvoni▼); sofosbuvir (Sovaldi▼); sofosbuvir/velpatasvir/voxilaprevir (Vosevi▼); dasabuvir (Exviera▼); ombitasvir/paritaprevir/ritonavir (Viekirax ▼); glecaprevir/pibrentasvir (Maviret ▼); and elbasvir/grazoprevir (Zepatier▼).

Healthcare professionals are advised:

- rapid reduction in hepatitis C viral load during direct-acting antiviral therapy for hepatitis C may lead to improvements in glucose metabolism in patients with diabetes, potentially resulting in symptomatic hypoglycaemia if diabetic treatment is continued at the same dose.
- be vigilant for changes in glucose tolerance and advise patients of the risk of hypoglycaemia during direct-acting antiviral therapy, particularly within the first 3 months when the viral load is being reduced, and modify diabetic medication or doses when necessary.
- physicians who initiate direct-acting antiviral therapy in patients with diabetes should inform the healthcare professional in charge of the diabetic care of the patient.

- report any suspected adverse drug reactions associated with direct-acting antiviral therapies.

Please refer to the following website in MHRA for details:
https://www.gov.uk/drug-safety-update/direct-acting-antivirals-for-chronic-hepatitis-c-risk-of-hypoglycaemia-in-patients-with-diabetes

In Hong Kong, there are eight registered pharmaceutical products which are direct-acting antivirals, namely: Sovaldi Tablets 400mg containing sofosbuvir (HK-63501), Harvoni Tablets containing the combination of sofosbuvir and ledipasvir (HK-63886), Epclusa Tablets 400mg/100mg containing the combination of sofosbuvir and velpatasvir (HK-65046), and Vosevi Tablets containing the combination of sofosbuvir, velpatasvir and voxilaprevir (HK-65775), which are registered by Gilead Sciences Hong Kong Limited; Viekira Pak Tablets containing the combination of ombitasvir, paritaprevir, ritonavir and dasabuvir (HK-63695), and Maviret Tablets containing the combination of glecaprevir and pibrentasvir (HK- 65653) which are registered by Abbvie Limited; Daklinza Tablets 60mg containing daclatasvir (HK-64505) which is registered by Bristol-Myers Squibb Pharma (HK) Ltd; and Zepatier Tablets containing the combination of grazoprevir and elbasvir (HK-65571) which is registered by Merck Sharp & Dohme (Asia) Ltd. All are prescription-only medicines.

So far, the Department of Health (DH) has received 46 cases of adverse drug reaction related to above mentioned registered direct-acting antivirals, including 3 cases related to sofosbuvir, 5 cases related to sofosbuvir and ledipasvir combination products, 34 cases related to ombitasvir, paritaprevir, ritonavir and dasabuvir combination products, 1 case related to daclatasvir, and 3 cases related to glecaprevir and pibrentasvir combination products; but none of these cases was related to hypoglycaemia. In view of the above MHRA's announcement, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board. Healthcare professionals are advised to 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,

(Daniel CHEUNG)
for Assistant Director (Drug)