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Pharmacovigilance Risk Assessment Committee (PRAC)

New product information wording – Extracts from PRAC recommendations on signals

Adopted at the 30 August-2 September 2016 PRAC

The product information wording in this document is extracted from the document entitled 'PRAC recommendations on signals' which contains the whole text of the PRAC recommendations for product information update, as well as some general guidance on the handling of signals. It can be found ***here*** (in English only).

New text to be added to the product information is underlined. Current text to be deleted is ~~struck through~~.

1. Agomelatine – Urinary retention (EPITT no 18637)

Summary of product characteristics

4.8. Undesirable effects

Renal and urinary disorders

Frequency "rare": Urinary retention

Package leaflet

4 - Possible side effects

Frequency "rare": Inability to completely empty the bladder

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2. Boceprevir ; daclatasvir; dasabuvir; elbasvir, grazoprevir; ledipasvir, sofosbuvir; ombitasvir, paritaprevir, ritonavir; simeprevir; sofosbuvir; sofosbuvir, velpatasvir – Drug interaction between direct-acting antivirals (DAAV) and vitamin K antagonists leading to a reduced international normalised ratio (INR) (EPITT no 18654)

Summary of product characteristics

4.5. Interaction with other medicinal products and other forms of interaction

Patients treated with vitamin K antagonists:

As liver function may change during treatment with {product name}, a close monitoring of International Normalised Ratio (INR) values is recommended.

Moreover, the tables with information on interactions should be modified according to the following instructions:

For Olysio, Viekirax and Exviera (products for which pharmacokinetic studies with warfarin have been performed)

Warfarin and other vitamin K antagonists	Interaction	Recommendation/clinical comments
	Results of interaction studies with warfarin should be included here as applicable	While no change in the pharmacokinetics of warfarin is expected, close monitoring of INR is recommended with all vitamin K antagonists. This is due to liver function changes during treatment with {product name}.

For Victrelis, Sovaldi, Harvoni, Daklinza, Zepatier and Epclusa (products for which pharmacokinetic studies with warfarin have not been performed)

Vitamin K antagonists	Interaction	Recommendation/ clinical comments
	Interaction not studied	Close monitoring of INR is recommended with all vitamin K antagonists. This is due to liver function changes during treatment with {product name}.

Package leaflet

2 - What you need to know before you <take> <use> {product name}

Other medicines and {product name}

<Tell your <doctor> <or> <pharmacist> if you are <taking> <using>, have recently <taken> <used> or might <take> <use> any other medicines.>

Warfarin and other similar medicines called vitamin K antagonists used to thin the blood. Your doctor may need to increase the frequency of your blood tests to check how well your blood can clot.

Note: it is acknowledged that the package leaflet for some products may need to be slightly modified in order to incorporate the above message.

3. Cobicistat containing products: cobicistat; cobicistat, atazanavir sulfate; cobicistat, darunavir; cobicistat, elvitegravir, emtricitabine, tenofovir alafenamide; cobicistat, elvitegravir, emtricitabine, tenofovir disoproxil fumarate – Drug interaction with corticosteroids leading to adrenal suppression (EPITT no 18647)

Summary of product characteristics of cobicistat containing products

N.B: For Evotaz, Section 4.4 warning should be maintained.

4.5. Interaction with other medicinal products and other forms of interaction

Corticosteroids primarily metabolised by CYP3A (including betamethasone, budesonide, fluticasone, mometasone, prednisone, triamcinolone).	Interaction not studied with any of the components of <product name>. Plasma concentrations of these medicinal products may be increased when co–administered with <product name>, resulting in reduced serum cortisol concentrations.	Concomitant use of <product name> and corticosteroids that are metabolised by CYP3A (e.g. fluticasone propionate or other inhaled or nasal corticosteroids) may increase the risk of development of systemic corticosteroid effects, including Cushing's syndrome and adrenal suppression Co-administration with CYP3A-metabolised corticosteroids is not recommended unless the potential benefit to the patient outweighs the risk, in which case patients should be monitored for systemic corticosteroid effects. Alternative corticosteroids which are less dependent on CYP3A metabolism e.g.

		beclomethasone for intranasal or inhalational use should be considered, particularly for long term use.

Package leaflet of cobicistat containing products

2 - What you need to know before you take {product name}

It is important to tell your doctor if you are taking:

Corticosteroids including betamethasone, budesonide, fluticasone, mometasone, prednisone, triamcinolone. These medicines are used to treat allergies, asthma, inflammatory bowel diseases, inflammatory conditions of the eyes, joints and muscles and other inflammatory conditions. If alternatives cannot be used, its use should only take place after medical evaluation and under close monitoring by your doctor for corticosteroid side effects.

Summary of product characteristics of corticosteroids (excluding topical formulations)

4.4. Special warnings and precautions for use *or* 4.5. Interaction with other medicinal products and other forms of interaction, *as appropriate*

Co-treatment with CYP3A inhibitors, including cobicistat-containing products, is expected to increase the risk of systemic side-effects. Cases of Cushing's syndrome and adrenal suppression have been reported. The combination should be avoided unless the benefit outweighs the increased risk of systemic corticosteroid side-effects, in which case patients should be monitored for systemic corticosteroid effects.

4. Iomeprol – Haemolysis (EPITT no 18625)

Summary of product characteristics

4.8. Undesirable effects

Blood and lymphatic system disorders (frequency not known):

Haemolytic anaemia

Package leaflet

4 - Possible side effects

Frequency not known

Haemolytic anaemia (abnormal breakdown of red blood cells, which may cause fatigue, rapid heart rate and shortness of breath)