10 November 2016
EMA/PRAC/700135/2016
Pharmacovigilance Risk Assessment Committee (PRAC)

New product information wording – Extracts from PRAC recommendations on signals

Adopted at the 24-27 October 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. 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)

1. Cobicistat containing products

No changes have been made to the product information wording for cobicistat containing products as compared to the PRAC recommendation published on the 26th September 2016. The wording for these products remains as per the below.

Summary of product characteristics (SmPC) 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,	Interaction not studied with any of the components of <product name>.	Concomitant use of <product name> and corticosteroids that are metabolised by CYP3A (e.g.

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budesonide, fluticasone, mometasone, prednisone, triamcinolone).	Plasma concentrations of these medicinal products may be increased when co–administered with <product name>, resulting in reduced serum cortisol concentrations.	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 (PL) 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.

2. Beclomethasone containing products (excluding cutaneous formulations)

SmPC of beclomethasone containing products (excluding cutaneous formulations)

Section 4.4 or 4.5, as applicable:

Beclomethasone is less dependent on CYP3A metabolism than some other corticosteroids, and in general interactions are unlikely; however the possibility of systemic effects with concomitant use of strong CYP3A inhibitors (e.g. ritonavir, cobicistat) cannot be excluded, and therefore caution and appropriate monitoring is advised with the use of such agents.

PL of beclomethasone containing products (excluding cutaneous formulations)

- Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

- Some medicines may increase the effects of [product name] and your doctor may wish to monitor you carefully if you are taking these medicines (including some medicines for HIV: ritonavir, cobicistat).

3. All corticosteroids other than beclomethasone (excluding cutaneous formulations)

SmPC of all corticosteroids other than beclomethasone (excluding cutaneous formulations) - Double strikethrough represents deletion as compared to the PRAC recommendation published on the 26th September 2016.

Section 4.4 or 4.5, as applicable:

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 side-effects. ~~Alternative corticosteroids which are less dependent on CYP3A metabolism eg: beclomethasone for intranasal or inhalational use should be considered, particularly for long term use~~.

PL of all corticosteroids other than beclomethasone (excluding cutaneous formulations)

- Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.
- Some medicines may increase the effects of [product name] and your doctor may wish to monitor you carefully if you are taking these medicines (including some medicines for HIV: ritonavir, cobicistat).

2. Flucloxacillin – Acute generalized exanthematous pustulosis (AGEP)(EPITT no 18773)

Summary of product characteristics

4.4. Special warnings and precautions for use

The occurrence at the treatment initiation of a feverish generalised erythema associated with pustula may be a symptom of acute generalised exanthematous pustulosis (AGEP) (see section 4.8). In case of AGEP diagnosis, flucloxacillin should be discontinued and any subsequent administration of flucloxacillin contra-indicated.

4.8. Undesirable effects

Skin and subcutaneous tissue disorders

Frequency not known: AGEP - acute generalized exanthematous pustulosis (see section 4.4)

Package leaflet

4 - Possible side effects

Other side effects (frequency not known)

Serious skin reactions

A red, scaly rash with bumps under the skin and blisters (exanthematous pustulosis).

Contact a doctor immediately if you get any of these symptoms.

3. Olanzapine – Restless legs syndrome (EPITT no 18659)

Summary of product characteristics

4.8. Undesirable effects (Table)

Nervous system disorders

Restless legs syndrome (frequency uncommon (≥ 1/1,000 to < 1/100))

Package leaflet

4 - Possible side effects

[...]

Uncommon side effects (may affect up to 1 in 100 people) include hypersensitivity (e.g. swelling in the mouth and throat, itching, rash); diabetes or the worsening of diabetes, occasionally associated with ketoacidosis (ketones in the blood and urine) or coma; seizures, usually associated with a history of seizures (epilepsy); muscle stiffness or spasms (including eye movements); restless legs syndrome; problems with speech; slow heart rate; sensitivity to sunlight; bleeding from nose; abdominal distension; memory loss or forgetfulness; urinary incontinence; lack of ability to urinate; hair loss; absence or decrease in menstrual periods; and changes in breasts in males and females such as an abnormal production of breast milk or abnormal growth.