



30 September 2019¹
EMA/PRAC/474668/2019
Pharmacovigilance Risk Assessment Committee (PRAC)

New product information wording – Extracts from PRAC recommendations on signals

Adopted at the 2-5 September 2019 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. Ibrutinib – Ischaemic stroke (EPITT no 19369)

Summary of product characteristics

4.4. Special warnings and precautions for use

Cerebrovascular accidents

Cases of cerebrovascular accident, transient ischaemic attack and ischaemic stroke including fatalities have been reported with the use of ibrutinib, with and without concomitant atrial fibrillation and/or hypertension. Latency from the initiation of treatment with ibrutinib to the onset of ischemic central nervous vascular conditions was in the most cases after several months (more than 1 month in 78% and more than 6 months in 44% of cases) emphasizing the need for regular monitoring of patients (please see section 4.4 Cardiac arrhythmia and Hypertension and section 4.8).

4.8. Undesirable effects

Tabulated list of adverse reactions

Nervous system disorders

¹ Intended publication date. The actual publication date can be checked on the webpage dedicated to [PRAC recommendations on safety signals](#).



Uncommon: cerebrovascular accident, transient ischaemic attack, ischaemic stroke

Package leaflet

2. What you need to know before you take IMBRUVICA

Warnings and precautions

Tell your doctor immediately if you notice or someone notices in you: sudden numbness or weakness in the limbs (especially on one side of the body), sudden confusion, trouble speaking or understanding speech, sight loss, difficulty walking, loss of balance or lack of coordination, sudden severe headache with no known cause. These may be signs and symptoms of stroke.

4. Possible side effects

Tell a doctor straight away if you notice any of the following side effects:

Uncommon (may affect up to 1 in 100 people):

temporary episode of neurologic dysfunction caused by loss of blood flow, stroke.

2. Ibuprofen – Acute generalised exanthematous pustulosis (AGEP) (EPITT no 19409)

Summary of product characteristics

1. For ibuprofen monotherapy or ibuprofen in combinations excluding combinations with pseudoephedrine

4.4. Special warnings and precautions for use

Severe skin reactions

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis have been reported rarely in association with the use of NSAIDs (see section 4.8). Patients appear to be at highest risk of these reactions early in the course of therapy, the onset of the reaction occurring in the majority of cases within the first month of treatment. Acute generalised exanthematous pustulosis (AGEP) has been reported in relation to ibuprofen-containing products. Ibuprofen should be discontinued, at the first appearance of signs and symptoms of severe skin reactions, such as skin rash, mucosal lesions, or any other sign of hypersensitivity.

4.8. Undesirable effects

Skin and subcutaneous tissue disorders

Not known: Acute generalised exanthematous pustulosis (AGEP)

2. For ibuprofen and pseudoephedrine combinations

4.4. Special warnings and precautions for use

Severe skin reactions

Severe skin reactions such as acute generalised exanthematous pustulosis (AGEP) may occur with ibuprofen and pseudoephedrine-containing products. [...]

4.8. Undesirable effects¹

Skin and subcutaneous tissue disorders

Not known: Acute generalised exanthematous pustulosis (AGEP)

Package leaflet²

2. What you need to know before you use <product name>

Warnings and precautions - Take special care with <product name>

Skin reactions²

Serious skin reactions have been reported in association with <product name> treatment. You should stop taking <product name> and seek medical attention immediately, if you develop any skin rash, lesions of the mucous membranes, blisters or other signs of allergy since this can be the first signs of a very serious skin reaction. See section 4.

4. Possible side effects

Frequency "Not known"

A red, scaly widespread rash with bumps under the skin and blisters mainly localized on the skin folds, trunk, and upper extremities accompanied by fever at the initiation of treatment (acute generalised exanthematous pustulosis). Stop using <product name> if you develop these symptoms and seek medical attention immediately. See also section 2.

Footnotes:

1 Only if the already existing AGEP ADR in section 4.8 is listed specifically for pseudoephedrine.

2 The following text should replace any current information regarding serious skin reactions in section Warnings and precautions.

3. Sodium-glucose co-transporter 2 (SGLT2) inhibitors² – New information on the known association between SGLT2 inhibitors and diabetic ketoacidosis in surgical patients (EPITT no 19355)

Summary of product characteristics

4.4. Special warnings and precautions for use

Diabetic ketoacidosis

[...]

² Canagliflozin; canagliflozin, metformin; dapagliflozin; dapagliflozin, metformin; empagliflozin; empagliflozin, metformin; empagliflozin, linagliptin; ertugliflozin, metformin; ertugliflozin, sitagliptin; saxagliptin, dapagliflozin

Treatment should be interrupted in patients who are hospitalised for major surgical procedures or acute serious medical illnesses. Monitoring of ketones is recommended in these patients. Measurement of blood ketone levels is preferred to urine. ~~In both cases, t~~Treatment with <product name> may be restarted ~~once~~ when the ketone values are normal and the patient's condition has stabilised.

4. Teriflunomide – Psoriasis (EPITT no 19366)

Summary of product characteristics

4.4. Special warnings and precautions for use

Skin reactions

[...]

New onset of psoriasis (including pustular psoriasis) and worsening of pre-existing psoriasis have been reported during the use of teriflunomide. Treatment withdrawal and initiation of an accelerated elimination procedure may be considered taking into account patient's disease and medical history.

4.8. Undesirable effects

Tabulated list of adverse reactions

Skin and subcutaneous tissue disorders

Frequency not known: Psoriasis (including pustular psoriasis)^b

b: see section 4.4

Package leaflet

4. Possible side effects

Not known (frequency cannot be estimated from the available data)

[...]

- Psoriasis