28 September 2020[1]
EMA/PRAC/458930/2020
Pharmacovigilance Risk Assessment Committee (PRAC)

New product information wording – Extracts from PRAC recommendations on signals

Adopted at the 31 August–3 September 2020 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. Abiraterone – Anaphylactic reaction (EPITT no 19535)

Summary of product characteristics

4.8. Undesirable effects

Immune system disorders

Frequency 'not known': anaphylactic reactions

Package leaflet

4. Possible side effects

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

Heart attack, changes in ECG - electrocardiogram (QT prolongation), and serious allergic reactions with difficulty swallowing or breathing, swollen face, lips, tongue or throat, or an itchy rash.

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

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

2. Fluoroquinolones for systemic and inhalation formulations[2] – Heart valve regurgitation, cervical artery dissection, and aortic aneurysm and dissection (EPITT no 19522)

New text in **bold underlined**

Summary of product characteristics

4.4. Special warnings and precautions for use

Aortic aneurysm and dissection**, and heart valve regurgitation/incompetence**

Epidemiologic studies report an increased risk of aortic aneurysm and dissection**, particularly in elderly patients, and of aortic and mitral valve regurgitation** after intake of fluoroquinolones ~~particularly in the older population~~. **Cases of aortic aneurysm and dissection, sometimes complicated by rupture (including fatal ones), and of regurgitation/incompetence of any of the heart valves have been reported in patients receiving fluoroquinolones (see section 4.8).**

Therefore, fluoroquinolones should only be used after a careful benefit-risk assessment and after consideration of other therapeutic options in patients with positive family history of aneurysm disease **or congenital heart valve disease**, or in patients diagnosed with pre-existing aortic aneurysm and/or dissection **or heart valve disease**, or in presence of other risk factors or conditions predisposing

- for **both** aortic aneurysm and dissection **and heart valve regurgitation/incompetence** (e.g. **connective tissue disorders such as** Marfan syndrome **or** ~~vascular~~ Ehlers-Danlos syndrome, **Turner syndrome**, ~~Takayasu arteritis, giant cell arteritis~~, Behçet´s disease, hypertension, **rheumatoid arthritis** ~~known atherosclerosis~~) **or additionally**
- **for aortic aneurysm and dissection (e.g. vascular disorders such as Takayasu arteritis or giant cell arteritis, or known atherosclerosis, or Sjögren's syndrome) or additionally**
- **for heart valve regurgitation/incompetence (e.g. infective endocarditis).**

The risk of aortic aneurysm and dissection, and their rupture may also be increased in patients treated concurrently with systemic corticosteroids.

In case of sudden abdominal, chest or back pain, patients should be advised to immediately consult a physician in an emergency department.

Patients should be advised to seek immediate medical attention in case of acute dyspnoea, new onset of heart palpitations, or development of oedema of the abdomen or lower extremities.

4.8. Undesirable effects

Cardiac disorders******

Vascular disorders******

** **Cases of aortic aneurysm and dissection, sometimes complicated by rupture (including fatal ones), and of regurgitation/incompetence of any of the heart valves have been**

[2] Ciprofloxacin; delafloxacin; levofloxacin; lomefloxacin; moxifloxacin; norfloxacin; ofloxacin; pefloxacin; prulifloxacin; rufloxacin

reported in patients receiving fluoroquinolones (see section 4.4).

Package leaflet

2. What you need to know before you take [product name]

Warning and precautions

Talk to your doctor before taking [product name]:

[…]

- if you have been diagnosed with leaking heart valves (heart valve regurgitation).

- if you have a family history of aortic aneurysm or aortic dissection or **congenital heart valve disease, or** other risk factors or predisposing conditions (e.g. connective tissue disorders such as Marfan syndrome~~,~~ or ~~vascular~~ Ehlers-Danlos syndrome, **Turner syndrome, Sjögren's syndrome [an inflammatory autoimmune disease],** or vascular disorders such as Takayasu arteritis, giant cell arteritis, Behçet´s disease, high blood pressure, or known atherosclerosis**, rheumatoid arthritis [a disease of the joints] or endocarditis [an infection of the heart]**).

[…]

While taking [product name]:

[…]

- If you feel sudden, severe pain in your abdomen, chest or back**, which can be symptoms of aortic aneurysm and dissection**, go immediately to an emergency room. **Your risk may be increased if you are being treated with systemic corticosteroids.**

- If you start experiencing a rapid onset of shortness of breath, especially when you lie down flat in your bed, or you notice swelling of your ankles, feet or abdomen, or a new onset of heart palpitations (sensation of rapid or irregular heartbeat), you should inform a doctor immediately.

4. Possible side effects

[…]

Cases of an enlargement and weakening of the aortic wall or a tear in the aortic wall (aneurysms and dissections), which may rupture and may be fatal, and of leaking heart valves have been reported in patients receiving fluoroquinolones. See also section 2.

3. Interferon alfa-2a; peginterferon alfa-2a – Neuromyelitis optica spectrum disorder (EPITT no 19532)

Summary of product characteristics

4.8. Undesirable effects

Eye disorders

Frequency "not known": Optic neuritis

4. Pomalidomide – Progressive multifocal leukoencephalopathy (PML) (EPITT no 19546)

Summary of product characteristics

4.4. Special warnings and precautions for use

Progressive multifocal leukoencephalopathy (PML)

Cases of progressive multifocal leukoencephalopathy, including fatal cases, have been reported with pomalidomide. PML was reported several months to several years after starting the treatment with pomalidomide. Cases have generally been reported in patients taking concomitant dexamethasone or prior treatment with other immunosuppressive chemotherapy. Physicians should monitor patients at regular intervals and should consider PML in the differential diagnosis in patients with new or worsening neurological symptoms, cognitive or behavioural signs or symptoms. Patients should also be advised to inform their partner or caregivers about their treatment, since they may notice symptoms that the patient is not aware of.

The evaluation for PML should be based on neurological examination, magnetic resonance imaging of the brain, and cerebrospinal fluid analysis for JC virus (JCV) DNA by polymerase chain reaction (PCR) or a brain biopsy with testing for JCV. A negative JCV PCR does not exclude PML. Additional follow-up and evaluation may be warranted if no alternative diagnosis can be established.

If PML is suspected, further dosing must be suspended until PML has been excluded. If PML is confirmed, pomalidomide must be permanently discontinued.

Package leaflet

2. What you need to know before you take Imnovid

[…]

Warnings and precautions

At any time during or after your treatment, tell your doctor or nurse immediately if you experience: blurred, loss of or double vision, difficulty speaking, weakness in an arm or a leg, a change in the way you walk or problems with your balance, persistent numbness, decreased sensation or loss of sensation, memory loss or confusion. These may all be symptoms of a serious and potentially fatal brain condition known as progressive multifocal leukoencephalopathy (PML). If you had these symptoms prior to treatment with Imnovid, tell your doctor about any change in these symptoms.