



26 May 2016
EMA/PRAC/313237/2016
Pharmacovigilance Risk Assessment Committee (PRAC)

New product information wording – Extracts from PRAC recommendations on signals

Adopted at the 10-13 May 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. Natalizumab – Necrotising retinitis (EPI TT no 18605)

Summary of Product Characteristics

Section 4.4 - Special warnings and precautions for use

Infections including other opportunistic infections

[...] If herpes encephalitis or meningitis occurs, TYSABRI should be discontinued and appropriate treatment for herpes encephalitis or meningitis should be administered.

Acute retinal necrosis (ARN) is a rare fulminant viral infection of the retina caused by the family of herpes viruses (e.g. varicella zoster). ARN has been observed in patients being administered TYSABRI and can be potentially blinding. Patients presenting with eye symptoms such as decreased visual acuity, redness and painful eye should be referred for retinal screening for ARN. Following clinical diagnosis of ARN, discontinuation of TYSABRI should be considered in these patients.

Section 4.8 - Undesirable effects

Infections, including PML and opportunistic infections

[...] The duration of treatment with TYSABRI prior to onset ranged from a few months to several years (see section 4.4).



In post-marketing experience, rare cases of acute retinal necrosis (ARN) have been observed in patients receiving TYSABRI. Some cases have occurred in patients with central nervous system (CNS) herpes infections (e.g. herpes meningitis and encephalitis). Serious cases of ARN, either affecting one or both eyes, led to blindness in some patients. The treatment reported in these cases included anti-viral therapy and in some cases, surgery (see section 4.4).

Package Leaflet

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Speak to your doctor or nurse immediately if you notice any of the following

Symptoms of serious infections including:

- An unexplained fever
- Severe diarrhoea

[...]

- Impaired vision
- Pain or redness of the eye(s)

2. Warfarin – Calciphylaxis (EPITT no 18545)

Summary of Product Characteristics

Section 4.4 - Special warnings and precautions for use

Calciphylaxis is a rare syndrome of vascular calcification with cutaneous necrosis, associated with high mortality. The condition is mainly observed in patients with end-stage renal disease on dialysis or in patients with known risk factors such as protein C or S deficiency, hyperphosphataemia, hypercalcaemia or hypoalbuminaemia. Rare cases of calciphylaxis have been reported in patients taking warfarin, also in the absence of renal disease. In case calciphylaxis is diagnosed, appropriate treatment should be started and consideration should be given to stopping treatment with warfarin.

Section 4.8 - Undesirable effects

Skin and subcutaneous tissue disorders

Frequency 'not known': Calciphylaxis

Package Leaflet:

4. Possible side effects

Tell your doctor straight away if you have any of the following side effects...:

[...]

A painful skin rash. On rare occasions warfarin can cause serious skin conditions, including one called calciphylaxis that can start with a painful skin rash but can lead to other serious complications. This adverse reaction occurs more frequently in patients with chronic kidney disease.