



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Pharmacovigilance Risk Assessment Committee (PRAC)

New product information wording – Extracts from PRAC recommendations on signals – Part 2

Adopted at the 27-30 September 2021 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. COVID-19 mRNA² vaccine (nucleoside-modified) – Comirnaty – Erythema multiforme (EPITT no 19721)

Summary of product characteristics

4.8. Undesirable effects

Skin and subcutaneous tissue disorders

"Erythema multiforme" with frequency "Not Known"

Package leaflet

4. Possible side effects

Frequency "Not known": a skin reaction that causes red spots or patches on the skin, that may look like a target or "bulls-eye" with a dark red centre surrounded by paler red rings (erythema multiforme).

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

² Messenger ribonucleic acid



2. COVID-19 mRNA³ vaccine (nucleoside-modified) – Spikevax – Erythema multiforme (EPITT no 19720)

Summary of product characteristics

4.8. Undesirable effects

Skin and subcutaneous tissue disorders

“Erythema multiforme” with frequency “Not Known”

Package leaflet

4. Possible side effects

Frequency “Not known”: a skin reaction that causes red spots or patches on the skin, that may look like a target or "bulls-eye" with a dark red centre surrounded by paler red rings (erythema multiforme).

3. Piperacillin; piperacillin, tazobactam – Haemophagocytic lymphohistiocytosis (EPITT no 19676)

Summary of product characteristics

4.4. Special warnings and precautions for use

Haemophagocytic lymphohistiocytosis (HLH)

Cases of HLH have been reported in patients treated with <piperacillin/tazobactam><piperacillin>, often following treatment longer than 10 days. HLH is a life-threatening syndrome of pathologic immune activation characterised by clinical signs and symptoms of an excessive systemic inflammation (e.g. fever, hepatosplenomegaly, hypertriglyceridaemia, hypofibrinogenaemia, high serum ferritin, cytopenias and haemophagocytosis). Patients who develop early manifestations of pathologic immune activation should be evaluated immediately. If diagnosis of HLH is established, <piperacillin/tazobactam><piperacillin> treatment should be discontinued.

Package leaflet

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

Warnings and precautions

Haemophagocytic lymphohistiocytosis

There have been reports about a disease in which the immune system makes too many of otherwise normal white blood cells called histiocytes and lymphocytes, resulting in inflammation (haemophagocytic lymphohistiocytosis). This condition may be life-threatening if not diagnosed and treated early. If you experience multiple symptoms such as fever, swollen glands, feeling weak, feeling lightheaded, shortness of breath, bruising, or skin rash, contact your doctor immediately.

³ Messenger ribonucleic acid

4. Warfarin – Anticoagulant-related nephropathy (EPITT no 19652)

Summary of product characteristics

4.4. Special warnings and precautions for use

~~Use in patients with altered glomerular function~~ Anticoagulant-related nephropathy

In patients with altered glomerular integrity or with a history of kidney disease, acute kidney injury may occur, possibly in relation to episodes of excessive anticoagulation and hematuria. A few cases have been reported in patients with no pre-existing kidney disease. Close monitoring including renal function evaluation is advised in patients with a supratherapeutic INR and hematuria (including microscopic).

4.8. Undesirable effects

Renal and urinary disorders

Frequency 'not known': Anticoagulant-related nephropathy (see section 4.4)

Package leaflet

4. Possible side effects

Adverse effects with no known frequency: Impairment of renal function occurring with excessive anticoagulation and presence of blood in urine (anticoagulant-related nephropathy).