25 January 2018
EMA/PRAC/8436/2018
Pharmacovigilance Risk Assessment Committee (PRAC)

New product information wording – Extracts from PRAC recommendations on signals

Adopted at the 8-11 January 2018 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. Dulaglutide – Gastrointestinal stenosis and obstruction (EPITT no 18931)

Summary of product characteristics

4.8. Undesirable effects

Gastrointestinal disorders

Frequency 'not known': Non-mechanical intestinal obstruction

Package leaflet

4. Possible side effects

Frequency 'not known'

Bowel obstruction - a severe form of constipation with additional symptoms such as stomach ache, bloating or vomiting

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5525
Send a question via our website www.ema.europa.eu/contact

2. Methotrexate – Pulmonary alveolar haemorrhage (EPITT no 18850)

2.1. For methotrexate-containing medicinal products with non-oncologic indications

Summary of product characteristics

4.4. Special warnings and precautions for use

Assessment of respiratory system
Questioning the patient with regard to possible pulmonary dysfunctions, if necessary lung function test. Acute or chronic interstitial pneumonitis, often associated with blood eosinophilia, may occur and deaths have been reported. Symptoms typically include dyspnoea, cough (especially a dry non-productive cough), thoracic pain and fever for which patients should be monitored at each follow-up visit. Patients should be informed of the risk of pneumonitis and advised to contact their doctor immediately should they develop persistent cough or dyspnoea.

In addition, pulmonary alveolar haemorrhage has been reported with methotrexate used in rheumatologic and related indications. This event may also be associated with vasculitis and other comorbidities. Prompt investigations should be considered when pulmonary alveolar haemorrhage is suspected to confirm the diagnosis.

4.8. Undesirable effects

Respiratory, thoracic and mediastinal disorders

Not known: Epistaxis, Pulmonary alveolar haemorrhage

Package leaflet

2. What you need to know before you take [MTX]

Warnings and precautions

Acute bleeding from the lungs in patients with underlying rheumatologic disease has been reported with methotrexate. If you experience symptoms of spitting or coughing up blood you should contact your doctor immediately.

4. Possible side effects

Serious side effects

If you develop any of the following side effects, contact your doctor immediately:

- inflammation of the lungs (symptoms may be general illness, dry, irritating cough, shortness of breath, breathlessness at rest, chest pain, or fever)

- spitting or coughing blood

The following side effects have also been reported:

Frequency not known (cannot be estimated from the available data): bleeding from the lungs

2.2. For methotrexate-containing medicinal products with oncologic indications

Summary of product characteristics

4.4. Special warnings and precautions for use

Respiratory system
Acute or chronic interstitial pneumonitis, often associated with blood eosinophilia, may occur and deaths have been reported. Symptoms typically include dyspnoea, cough (especially a dry non-productive cough), thoracic pain and fever for which patients should be monitored at each follow-up visit. Patients should be informed of the risk of pneumonitis and advised to contact their doctor immediately should they develop persistent cough or dyspnoea.

In addition, pulmonary alveolar haemorrhage has been reported with methotrexate used in rheumatologic and related indications. This event may also be associated with vasculitis and other comorbidities. Prompt investigations should be considered when pulmonary alveolar haemorrhage is suspected to confirm the diagnosis.

Package leaflet

2. What you need to know before you take [MTX]

Warnings and precautions

Acute bleeding from the lungs in patients with underlying rheumatologic disease has been reported with methotrexate.

2.3. For methotrexate-containing medicinal products with both non-oncologic and oncologic indications

Summary of product characteristics

4.4. Special warnings and precautions for use

Respiratory system
Acute or chronic interstitial pneumonitis, often associated with blood eosinophilia, may occur and deaths have been reported. Symptoms typically include dyspnoea, cough (especially a dry non-productive cough), thoracic pain and fever for which patients should be monitored at each follow-up visit. Patients should be informed of the risk of pneumonitis and advised to contact their doctor immediately should they develop persistent cough or dyspnoea.

In addition, pulmonary alveolar haemorrhage has been reported with methotrexate used in rheumatologic and related indications. This event may also be associated with vasculitis and other comorbidities. Prompt investigations should be considered when pulmonary alveolar haemorrhage is suspected to confirm the diagnosis.

4.8. Undesirable effects

Respiratory, thoracic and mediastinal disorders

Not known: Epistaxis, Pulmonary alveolar haemorrhage*

*(has been reported for methotrexate used in rheumatologic and related indications)

Package leaflet

2. What you need to know before you take [MTX]

Warnings and precautions

Acute bleeding from the lungs in patients with underlying rheumatologic disease has been reported with methotrexate. If you experience symptoms of spitting or coughing up blood you should contact your doctor immediately.

4. Possible side effects

Serious side effects

If you develop any of the following side effects, contact your doctor immediately:

- inflammation of the lungs (symptoms may be general illness, dry, irritating cough, shortness of breath, breathlessness at rest, chest pain, or fever)

- spitting or coughing blood*

*(has been reported for methotrexate used in patients with underlying rheumatologic disease)

The following side effects have also been reported:

Frequency not known (cannot be estimated from the available data): bleeding from the lungs*

*(has been reported for methotrexate used in patients with underlying rheumatologic disease).

3. Pemetrexed – Nephrogenic diabetes insipidus (EPITT no 18930)

Summary of product characteristics

4.4. Special warnings and precautions for use

Serious renal events, including acute renal failure, have been reported with pemetrexed alone or in association with other chemotherapeutic agents. Many of the patients in whom these occurred had underlying risk factors for the development of renal events including dehydration or pre-existing hypertension or diabetes. Nephrogenic diabetes insipidus and renal tubular necrosis were also reported in post marketing setting with pemetrexed alone or with other chemotherapeutic agents. Most of these events resolved after pemetrexed withdrawal. Patients should be regularly monitored for acute tubular necrosis, decreased renal function and signs and symptoms of nephrogenic diabetes insipidus (e.g. hypernatraemia).

4.8. Undesirable effects

Uncommon cases of acute renal failure have been reported with pemetrexed alone or in association with other chemotherapeutic agents (see section 4.4). Nephrogenic diabetes insipidus and renal tubular necrosis have been reported in post marketing setting with an unknown frequency.

Package leaflet

4. Possible side effects

Not known: frequency cannot be estimated from the available data

Increased urine output

Thirst and increased water consumption

Hypernatraemia – increased sodium in blood