6 July 2026[1]
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Pharmacovigilance Risk Assessment Committee (PRAC)

New product information wording – Extracts from PRAC recommendations on signals

Adopted at the 8-11 June 2026 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 on the webpage for PRAC recommendations on safety signals (in English only).

New text to be added to the product information is underlined. Current text to be deleted is ~~struck through~~.

1. Darolutamide – Angioedema (EPITT no 20237)

Summary of product characteristics

4.8 Undesirable effects

Table 1

Skin and subcutaneous tissue disorders

Frequency "Not known": Angioedema [g, h]

[g] Includes laryngeal oedema, lip swelling, swelling face, and swollen tongue

[h] Spontaneous reports from post-marketing experience

Package leaflet

4 Possible side effects

Other side effects that have been reported with frequency not known (cannot be estimated from the available data):

- swelling under the skin in areas such as the face, lips, tongue and throat

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

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2. Gemcitabine – Drug reaction with eosinophilia and systemic symptoms (DRESS) (EPITT no 20256)

Taking into account the already existing wording in some nationally authorised products, the text may need to be adapted by marketing authorisation holders to individual products.

Summary of product characteristics

4.4 Warning and precautions for use

Severe cutaneous adverse reactions (SCARs)

~~Severe cutaneous adverse reactions (SCARs) including~~ Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), and acute generalized exanthematous pustulosis (AGEP), which can be life-threatening or fatal, have been reported in association with gemcitabine treatment (see section 4.8). Patients should be advised of the signs and symptoms of the severe cutaneous adverse reactions and should seek medical advice from their physician immediately when observing any indicative signs or symptoms. ~~and monitored closely for skin reactions.~~ If signs and symptoms suggestive of these reactions appear, gemcitabine should be withdrawn immediately and an alternative treatment considered (as appropriate).

If the patient has developed a severe cutaneous adverse reaction with the use of gemcitabine, treatment with gemcitabine must not be restarted at any time.

4.8 Undesirable effects

Tabulated list of adverse reactions

Skin and subcutaneous tissue disorders

Frequency: Not known

Drug reaction with eosinophilia and systemic symptoms (DRESS)

Package leaflet

2. What you need to know before you take Gemcitabine

Warnings and precautions

Talk to your doctor before using gemcitabine if:

- you have ever developed a severe skin rash or skin peeling, blistering and/or mouth sores after using gemcitabine.

~~Serious skin reactions including Stevens-Johnson syndrome, toxic epidermal necrolysis, and acute generalized exanthematous pustulosis (AGEP) have been reported in association with gemcitabine treatment. Seek medical attention immediately if you notice any of the symptoms related to these serious skin reactions described in section 4.~~

This medicine can cause serious skin reactions. Seek medical attention immediately if you notice any of the symptoms related to these serious skin reactions described in section 4.

4. Possible side effects

You should contact your doctor immediately if you develop any of the following symptoms:

(*Note: Add the following heading if the existing one differs and does not adequately reflect the urgency of the required action, ensuring it applies to all listed severe cutaneous adverse reactions:* "Seek medical attention immediately if you notice any of the following symptoms of serious skin reactions:")

- Widespread rash, high body temperature and enlarged lymph nodes (DRESS syndrome or drug hypersensitivity syndrome) (frequency: not known).

3. Valproate and related substances[2] – Neurodevelopmental disorders with paternal exposure (EPITT no 20191)

Taking into account the already existing wording in some nationally authorised products, the text may need to be adapted by marketing authorisation holders to individual products.

Summary of product characteristics

4.4 Special warnings and precautions for use

Use in male patients

A retrospective observational study suggests an increased risk of neuro-developmental disorders (NDDs) in children born to men treated with valproate in the 3 months prior to conception compared to those born to men treated with lamotrigine or levetiracetam. However, other studies do not suggest an increased risk of NDDs after paternal valproate exposure. Thus, available evidence is inconsistent and the causal role of valproate is uncertain (see section 4.6).

[…]

4.6 Fertility, pregnancy and lactation

Males and potential risk of neuro-developmental disorders in children of fathers treated with valproate in the 3 months prior to conception

[…] ~~The study was not large enough to investigate associations with specific NDD subtypes and study limitations included potential confounding by indication and differences in follow-up time between exposure groups. The mean follow-up time of children in the valproate group ranged between 5.0 and 9.2 years compared to 4.8 and 6.6 years for children in the lamotrigine/levetiracetam group. Overall an increased risk of NDDs in children of fathers treated with valproate in the 3 months prior to conception is possible however the causal role of valproate is not confirmed. In addition, the study did not evaluate the risk of NDDs to children born to men stopping valproate for more than 3 months prior to conception (i.e., allowing a new spermatogenesis without valproate exposure).~~

Other observational population-based studies did not show an increased risk of NDDs in children born to men treated with valproate as monotherapy in the 3–4 months prior to conception compared with men treated with lamotrigine or levetiracetam as monotherapy.

Differences in study design, including control for confounding and population selection, may contribute to differences in study findings. In addition, available data suggest that factors other than valproate exposure, including underlying paternal disease, may contribute to the observed association. Overall, the evidence regarding an increased risk of NDDs in children of fathers treated with valproate in the 3 months prior to conception is inconsistent, and the causal role of valproate is uncertain.

[…]

[2] Valproic acid, sodium valproate, valproate semisodium, valpromide

Package leaflet

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

Important advice for male patients

Potential risks related to taking valproate in the 3 months before conception of a child

[…] ~~The risk for children born to fathers who stopped valproate treatment 3 months (the time needed to form new sperm) or longer before conception is not known.~~ ~~The study has limitations and therefore it is not clear if~~ ~~the increased risk for movement and mental developmental disorders suggested by this study is caused by valproate. The study has limitations and was not large enough to show which particular specific type of movement and mental developmental disorder children may be at risk of developing.~~

Other studies did not suggest an increased risk of mental developmental disorders (problems with early childhood development) in children born to fathers treated with valproate in the 3-4 months before conception. In these studies the risk was similar compared to children of fathers treated with lamotrigine or levetiracetam before conception.

Differences in how these studies were designed may explain the different results. Overall, it is not known whether any possible risk of childhood developmental disorders is caused by valproate itself or by other factors, such as the father's underlying medical condition.

[…]

4. X-ray contrast agents: iobitridol; iodixanol; iohexol; iomeprol; iopamidol; iopromide; ioversol; ioxitalamic acid – Fixed drug eruption (EPITT no 20229)

Taking into account the already existing wording in some nationally authorised products, the text may need to be adapted by marketing authorisation holders to individual products.

Summary of product characteristics

4.8 Undesirable effects

Skin and subcutaneous tissue disorders

Frequency 'Not known': Fixed drug eruption

Package leaflet

4 Possible side effects

Side effects reported/described with frequency 'Not known' (frequency cannot be estimated from the available data)

An allergic skin reaction that may include round or oval patches of redness and swelling of the skin, blistering, and itching (fixed drug eruption). Darkening of the skin in affected areas, which might persist after healing, may also occur.

Fixed drug eruption usually reoccurs at the same site(s) if the medication is <taken> <used> again.

5. Zolbetuximab – Protein-losing gastroenteropathy (EPITT no 20236)

Summary of product characteristics

4.8 Undesirable effects

Gastrointestinal disorders

Gastritis (frequency: uncommon)

Protein-losing gastroenteropathy (frequency: not known)

Package leaflet

4. Possible side effects

Other possible side effects:

Uncommon (may affect up to 1 in 100 people)

Inflammation of the stomach lining (gastritis)

Other side effects that have been reported with frequency not known (cannot be estimated from the available data)

Loss of protein from the digestive tract (protein-losing gastroenteropathy)