3 August 2026[1]
EMA/PRAC/155652/2026
Pharmacovigilance Risk Assessment Committee (PRAC)

PRAC recommendations on signals

Adopted at the 6-9 July 2026 PRAC meeting

This document provides an overview of the recommendations adopted by the Pharmacovigilance Risk Assessment Committee (PRAC) on the signals discussed during the meeting of 6-9 July 2026 (including the signal European Pharmacovigilance Issues Tracking Tool [EPITT][2] reference numbers).

PRAC recommendations to provide supplementary information are directly actionable by the concerned marketing authorisation holders (MAHs). PRAC recommendations for regulatory action (e.g. amendment of the product information) are submitted to the Committee for Medicinal Products for Human Use (CHMP) for endorsement when the signal concerns Centrally Authorised Products (CAPs), and to the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) for information in the case of Nationally Authorised Products (NAPs). Thereafter, MAHs are expected to take action according to the PRAC recommendations.

When appropriate, the PRAC may also recommend the conduct of additional analyses by the Agency or Member States.

MAHs are reminded that in line with Article 16(3) of Regulation No (EU) 726/2004 and Article 23(3) of Directive 2001/83/EC, they shall ensure that their product information is kept up to date with the current scientific knowledge including the conclusions of the assessment and recommendations published on the European Medicines Agency (EMA) website (currently acting as the EU medicines webportal).

For CAPs, at the time of publication, PRAC recommendations for update of product information have been agreed by the CHMP at their plenary meeting (20-23 July 2026) and corresponding variations will be assessed by the CHMP.

For nationally authorised medicinal products, it is the responsibility of the National Competent Authorities (NCAs) of the Member States to oversee that PRAC recommendations on signals are adhered to.

Variations for CAPs are handled according to established EMA procedures. MAHs are referred to the available guidance. Variations for NAPs (including via mutual recognition and decentralised procedures) are handled at national level in accordance with the provisions of the Member States.

[1] Expected publication date. The actual publication date can be checked on the webpage dedicated to PRAC recommendations on safety signals.
[2] The relevant EPITT reference number should be used in any communication related to a signal.

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

The timeline recommended by PRAC for submission of variations following signal assessment is applicable to both innovator and generic medicinal products, unless otherwise specified.

For procedural aspects related to the handling of PRAC recommendations on signals (e.g. submission requirements, contact points, etc.) please refer to the Questions and Answers on signal management.

1. Recommendations for update of the product information[3]

1.1. Desogestrel; etonogestrel – Meningioma

Authorisation procedure	Non-centrally authorised
EPITT No	20167
PRAC Rapporteur	Karin Bolin (SE)
Date of adoption	9 July 2026

Recommendation *[see also section 3]*

Having considered the available evidence in EudraVigilance and literature, including the data submitted by the Marketing Authorisation Holder (MAH), the PRAC has agreed that the MAHs of all desogestrel and etonogestrel containing products should submit a variation within 2 months from the publication of the PRAC recommendation, to amend the product information as described below taking into account the already existing wording in some nationally authorised products the text needs to be adapted by MAHs to individual products (new text underlined):

Summary of product characteristics

4.3 Contraindications

Meningioma or history of meningioma (see section 4.4)

4.4 Special warnings and precautions for use

Meningioma

Current, prolonged use (≥1 year) of desogestrel has been associated with a small increased risk of meningioma (see sections 4.3 and 4.8). [For etonogestrel-containing products: Desogestrel is metabolised to etonogestrel.] The risk increased with longer duration of treatment. The risk may be higher in women with previous exposure to progestogens associated with an increased risk of meningioma, which should be considered before initiating treatment. Patients treated with <substance> should be monitored for signs and symptoms of meningioma. If a patient is diagnosed with meningioma, treatment with <substance> must be discontinued. Available data suggest that the risk of meningioma may decrease after treatment discontinuation.

4.8 Undesirable effects

The following adverse reaction should be added under the SOC Neoplasms benign, malignant and unspecified, with a frequency 'not known':

Meningioma

Under Description of selected adverse reactions:

Meningioma

A case-control study found that current, prolonged use (≥1 year) of desogestrel 75 µg was associated with a small increased risk of intracranial meningioma requiring surgery (odds ratio, 1.3 [95%

[3] Translations in all official EU languages of the new product information adopted by PRAC are also available to MAHs on the EMA website.

confidence interval (CI), 1.1 to 1.5]). The estimated number needed to harm was overall 67 300 women for one intracranial meningioma. The risk increased with longer duration (≥7 years) of treatment (odds ratio, 2.1 [95% CI, 1.5 to 2.9]). Excess risk was greater in women who had previously used a progestogen with a known association to meningioma (odds ratio 3.3 [95% CI 2.6 to 4.1]). The increased risk was no longer observed one year after discontinuation of desogestrel. [For etonogestrel-containing products: Since desogestrel is metabolised to etonogestrel, the results of this study are also of clinical relevance for <product name>.]

Package leaflet

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

Do not take [product name]

- […]
- If you have meningioma or have ever been diagnosed with a meningioma (a tumour of the tissue layer surrounding the brain and spinal cord that is usually benign). See section Warnings and precautions.
- […]

Warnings and precautions

[…]

Meningiomas

Use of [active substance] has been linked to a small increased risk for tumours of the tissue surrounding the brain and spinal cord that are usually benign (meningiomas). The risk appears to increase with longer use and in women who have previously used progestogens associated with meningioma. Overall, about one additional case of meningioma is estimated to occur for every 67,300 women treated with [active substance]. If you are diagnosed with meningioma, your doctor will stop treatment with [Product name] (see section 'Do not use [Product name]'). If you notice any symptoms such as changes in vision (e.g. double vision or blurred vision), hearing loss or ringing in the ears, loss of smell, headaches that get worse over time, memory loss, seizures, or weakness in your arms or legs you must tell your doctor straight away.

[…]

4. Possible side effects

Not known (cannot be estimated from the available data)

- Tumour of the tissue surrounding the brain and spinal cord that is usually benign (meningioma).

1.2. Levonorgestrel intrauterine device 13.5 mg – Increased risk of ectopic pregnancy

Authorisation procedure	Non-centralised
EPITT No	20251
PRAC Rapporteur	Dennis Lex (DE)
Date of adoption	9 July 2026

Recommendation

Having considered the responses to the LoQ on the study by Roland et al. submitted by the Marketing Authorisation Holder (MAH), the PRAC has agreed that the MAH of Jaydess (Bayer) should submit a variation within 2 months from the publication of the PRAC recommendation, to amend the product information as described below (new text underlined, text to be deleted ~~strikethrough~~):

Summary of product characteristics

4.4 Special warnings and precautions for use

Ectopic pregnancy

In clinical trials, the overall incidence of ectopic pregnancy with Jaydess was approximately 0.11 per 100 woman-years. Approximately half of the pregnancies that occur during Jaydess use are likely to be ectopic. Data from post-authorisation observational studies report higher incidence rates of ectopic pregnancy with Jaydess (13.5 mg), compared to other IUSs and copper IUDs (see section 4.8, description of selected adverse reactions).

Women considering Jaydess should be counselled on the signs, symptoms and risks of ectopic pregnancy. For women who become pregnant while using Jaydess, the possibility of an ectopic pregnancy must be considered and evaluated.

Women with a previous history of ectopic pregnancy, tubal surgery or pelvic infection carry an increased risk of ectopic pregnancy. The possibility of ectopic pregnancy should be considered in the case of lower abdominal pain, especially in connection with missed periods or if an amenorrheic woman starts bleeding.

Because an ectopic pregnancy may ~~impact~~ compromise future fertility, the benefits and risks of using Jaydess should be carefully evaluated~~, in particular for nulliparous women~~ on an individual basis. This includes consideration of other IUSs/IUDs, particularly in women who may wish to become pregnant in the future.

~~*Use in nulliparous women:* Jaydess is not first choice for contraception in nulliparous women as clinical experience is limited.~~

4.8 Undesirable effects

c. Description of selected adverse reactions

[…]

If a woman becomes pregnant while using Jaydess, the relative likelihood of this pregnancy being ectopic is increased (see section 4.4 under Ectopic Pregnancy).

In a nationwide cohort study using data from the French National Healthcare Data System, hormonal IUSs and copper IUDs were compared. At 1-year, ectopic pregnancy incidence rates were 0.18 (95%

CI 0.14–0.23), 0.10 (95% CI 0.08–0.11), 0.04 (95% CI 0.03–0.05), and 0.07 (95% CI 0.07–0.08) per 100 person-years, for the levonorgestrel 13.5 mg, 19.5 mg, 52 mg IUSs and copper IUDs, respectively. Compared with copper IUDs, hazard ratios for ectopic pregnancy were 2.57 (95% CI 1.92–3.43), 1.37 (95% CI 1.15–1.62), and 0.62 (95% CI 0.49–0.80) for the levonorgestrel 13.5 mg, 19.5 mg, and 52 mg IUSs, respectively.

Package leaflet

2. What you need to know before you use Jaydess

[…]

Extrauterine pregnancy (pregnancy outside the womb)

It is uncommon to become pregnant while using Jaydess. However, if you become pregnant while using Jaydess, the risk that the pregnancy could develop outside the womb (have an extrauterine or ectopic pregnancy) is increased. Women who have already had an extrauterine pregnancy, surgery of the fallopian tubes or a pelvic infection carry a higher risk for this type of pregnancy. Real-world studies report higher risk of ectopic pregnancy with Jaydess compared with other IUSs (levonorgestrel 19.5 and 52 mg) and copper intrauterine devices (IUDs). An extrauterine pregnancy is a serious condition, which calls for *immediate* medical attention (see section 2, "Warnings and precautions" for signs and symptoms) and may ~~impact~~ compromise future fertility.

2. Recommendations for submission of supplementary information

INN	Signal (EPITT No)	PRAC Rapporteur	Action for MAH	MAH
Atogepant	Insomnia (20291)	Rugile Pilviniene (LT)	Assess in the ongoing PSUR (submission by 30 September 2026 with the MAH comments to the PSUR preliminary assessment report)	AbbVie Deutschland GmbH & Co. KG
Atogepant; eptinezumab; erenumab; fremanezumab; galcanezumab; rimegepant	Raynaud's phenomenon (20292)	Terhi Lehtinen (FI)	Supplementary information requested (submission by 14 October 2026)	AbbVie Deutschland GmbH & Co. KG, Eli Lilly Nederland B.V., H. Lundbeck A/S, Novartis Europharm Limited, Pfizer Europe MA EEIG, Teva GmbH

INN	Signal (EPITT No)	PRAC Rapporteur	Action for MAH	MAH
Oseltamivir; intravenous zanamivir	New information on safety in patients critically ill with influenza (20299)	Terhi Lehtinen (FI)	Supplementary information requested (submission by 26 August 2026)	Roche Registration GmbH, GlaxoSmithKline Trading Services Limited
Sacituzumab govitecan	Interstitial lung disease (20290)	Bianca Mulder (NL)	Supplementary information requested (submission by 23 September 2026)	Gilead Sciences Ireland UC
Selpercatinib	Lymphangiectasia intestinal (20289)	Bianca Mulder (NL)	Assess in the next PSUR (submission by 17 January 2027)	Eli Lilly Nederland B.V.
Sevoflurane	Acute encephalopathy in patients carrying the mitochondrial DNA variant m.11232T>C (20285)	Eamon O Murchu (IE)	Supplementary information requested (submission by 23 September 2026)	AbbVie SA, Baxter SA, Piramal Critical Care B.V.

3. Other recommendations

INN	Signal (EPITT No)	PRAC Rapporteur	Action for MAH	MAH
Desogestrel; etonogestrel	Meningioma (20167)	Karin Bolin (SE)	· See section 1.1	· All MAHs of desogestrel containing medicinal products and etonogestrel-containing medicinal products
			· Distribute a Direct Healthcare Professional Communication (DHPC) by 6 August 2026	· Organon
Venlafaxine	Cardiotoxicity (20230)	Karin Bolin (SE)	Monitor in PSUR	Viatris Limited (innovator MAH of venlafaxine)