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Media and Public Relations

News announcement

Meeting highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 1 – 4 September 2025

PRAC starts safety review of levamisole, a medicine used to treat parasitic worm infections

Review will assess risk of leukoencephalopathy, a condition affecting the brain

EMA's safety committee (PRAC) has started a review of medicines containing levamisole, authorised in four countries of the European Union (EU) to treat infections caused by parasitic worms in adults and children.

The review follows concerns about a risk of leukoencephalopathy, a potentially serious condition that damages the white matter of the brain. White matter is made of nerve fibres covered by a protective layer called myelin, which allows efficient communication between different parts of the brain. Leukoencephalopathy can be life-threatening and debilitating, especially when left undiagnosed or untreated. It may lead to a range of neurological symptoms, including but not limited to confusion, weakness or impaired muscle function, difficulties with movement coordination, and impaired or lost speech or vision.

Leukoencephalopathy has already been identified as a potential risk with levamisole, and the product information of levamisole medicines include the general term encephalopathy (a group of brain dysfunction conditions).

The review follows new data gathered as part of the continuous safety monitoring of medicines authorised in the EU. These include reported serious cases of leukoencephalopathy following levamisole use, one of which resulted in death, as well as additional data published in the medical literature. PRAC will review all available evidence regarding the risk of leukoencephalopathy with medicines containing levamisole, including any risk minimisation measures already in place.

Because some of the reported cases describe demyelination in the central nervous system (loss of myelin in the brain and spinal cord) which is a form of leukoencephalopathy, the review will also address this safety concern.

The committee will also assess the impact of the risk of leukoencephalopathy and demyelination on the benefit-risk balance of these medicines and issue a recommendation on whether their marketing authorisations should be maintained, varied, suspended or withdrawn across the EU.

More information is available in EMA's public health communication (link)

New safety information for healthcare professionals

Caspofungin: new warning against use of polyacrylonitrile-based membranes during continuous renal replacement therapy

PRAC has endorsed a direct healthcare professional communication (DHPC) warning about the use of polyacrylonitrile (PAN)-based membranes during continuous renal replacement therapy (CRRT) in critically ill patients receiving caspofungin. CRRT involves non-stop dialysis in patients with acute kidney injury and fluid overload.

Caspofungin is an antifungal medicine, given by intravenous infusion for the treatment of fungal infections in adults and children.

Laboratory data suggest that the PAN-based membranes used to filter the blood in CRRT can bind caspofungin and decrease its effectiveness. In addition, lack of caspofungin effectiveness has been reported in patients undergoing CRRT with these membranes.

Antifungal treatment failure may lead to worsening of the systemic fungal infection, which may be fatal in these critically ill patients.

Healthcare professionals should verify the type of haemofiltration membrane used before initiating and during treatment with caspofungin. If PAN-derived membranes are being used, healthcare professionals should either switch to an alternative membrane or consider an alternative antifungal medicine.

Crysvita (burosumab): new recommendations for monitoring due to risk of severe hypercalcaemia

PRAC discussed a DHPC to inform healthcare professionals about the risk of severe hypercalcaemia (high blood levels of calcium) in people treated with burosumab. Increases in serum calcium, including severe hypercalcaemia, and/or parathyroid hormone (a substance made by the parathyroid gland that helps the body store and use calcium) have been reported in patients treated with burosumab. In particular, severe hypercalcaemia has been reported in

patients with tertiary hyperparathyroidism (overproduction of parathyroid hormone that leads to hypercalcaemia).

Patients with moderate to severe hypercalcaemia (> 3.0 mmol/L) should not be given burosumab until hypercalcaemia is adequately treated and resolved.

In patients treated with burosumab, blood calcium levels should be measured before treatment initiation, one to two weeks after initiation or dose adjustment, and every six months during the treatment (or every three months in one to two-year-old children). Parathyroid hormones should also be measured every six months (or every three months in one to two-year-olds).

Healthcare professionals should also be aware that factors such as hyperparathyroidism, prolonged lack of movement, dehydration, hypervitaminosis D (vitamin D toxicity) or renal impairment may increase the risk of hypercalcaemia.

The product information for Crysvita will be updated to include these monitoring recommendations and to add the following possible side effects: hyperparathyroidism, hypercalcaemia, hypercalciuria (increased levels of calcium in the urine) and increased blood parathyroid hormone levels.

Crysvita is used to treat X-linked hypophosphataemia, a hereditary disorder characterised by low levels of phosphate in the blood. It is also used to treat osteomalacia (softening and weakening of the bones) caused by phosphaturic mesenchymal tumours. This type of tumour produces hormones, particularly a substance called fibroblast growth factor 23 (FGF23), which cause the body to lose phosphate.

Remsima (infliximab): new intravenous formulation contraindicated in patients with hereditary fructose intolerance

Remsima is a biosimilar medicine containing infliximab and is used to treat rheumatoid arthritis, Crohn’s disease, ulcerative colitis, ankylosing spondylitis, psoriatic arthritis and psoriasis.

The PRAC discussed a direct healthcare professional communication (DHPC) about a new intravenous formulation of Remsima that must not be given to people with hereditary fructose intolerance (HFI) as it contains sorbitol. In people with HFI, even small amounts of sorbitol given intravenously can result in severe and potentially life-threatening adverse reactions, including hypoglycaemia (low blood glucose levels), acute liver failure, haemorrhagic syndrome (excessive bleeding), kidney failure and death.

The new formulation is a concentrate for solution for infusion under evaluation by EMA’s human medicines committee (CHMP). Once approved, it will replace the existing formulation of a powder to be made up into a solution for infusion which does not contain sorbitol. Remsima is also available as a subcutaneous solution for injection in a prefilled syringe or pen. Although this subcutaneous formulation also contains sorbitol, it is considered safe for people with HFI.

Before starting treatment with the new Remsima concentrate for solution for infusion, healthcare professionals must confirm that the patient does not have hereditary fructose intolerance. The product information and patient reminder card for Remsima will be updated to reflect this new information.

Tegretol (carbamazepine): use restricted in neonates as concentration of one excipient, propylene glycol, exceeds recommended threshold

PRAC discussed a DHPC to inform healthcare professionals that the use of Tegretol 100 mg/5 mL oral suspension is restricted in neonates.

Tegretol 100 mg/5 mL oral suspension should not be used in neonates below 4 weeks of age for term babies, or 44 weeks post-menstrual age for pre-term babies, unless there is no other treatment option available and the expected benefit outweighs the risks. This is because this formulation of Tegretol contains 25 mg of the excipient (ingredient) propylene glycol per 1 mL, which exceeds the recommended threshold for neonates of 1 mg/kg/day[1]. At doses of 1 mg/kg/day or higher, propylene glycol accumulates in neonates as their liver and kidneys are not mature enough to fully process and remove it from the body. This increases the risk of serious adverse reactions such as metabolic acidosis (a condition in which the blood is too acidic), renal (kidney) dysfunction including acute tubular necrosis (damage to the structures in the kidneys that filter blood), acute renal failure and liver dysfunction.

Neonates treated with Tegretol 100 mg/5 mL should be monitored by healthcare professionals, including measurements of osmolarity and/or anion gap (tests to assess the body's fluid balance and detect abnormal levels of acids in the blood). Healthcare professionals should also be aware that if Tegretol 100 mg/5 mL is given with other medicines containing propylene glycol or with any substance that is broken down by the enzyme alcohol dehydrogenase, such as ethanol, the risk of propylene glycol accumulation and toxicity is increased.

The product information of Tegretol 100 mg/5 mL is being updated to reflect its restricted use in neonates and to inform about the risk of serious adverse reactions in these patients due to the concentration of this excipient. This restriction does not apply to other liquid formulations of carbamazepine that do not contain propylene glycol.

Tegretol 100 mg/5 mL oral suspension is a nationally authorised medicine that is used to treat various conditions including some forms of epilepsy.

The DHPCs for Caspofungin, Crysvita, Remsima and Tegretol will be disseminated to healthcare professionals by the marketing authorisation holders, according to an agreed communication plan, and published on the direct healthcare professional communications page and/or in national registers in EU Member States.

[1] Questions and answers on propylene glycol used as an excipient in medicinal products for human use (EMA/CHMP/704195/2013)

PRAC statistics: September 2025

[infographic]

Glossary:

Safety signal assessments. A safety signal is information which suggests a new potentially causal association, or a new aspect of a known association between a medicine and an adverse event that warrants further investigation. Safety signals are generated from several sources such as spontaneous reports, clinical studies and the scientific literature. More information can be found under 'Signal management'.

Periodic safety update reports, abbreviated as PSURs, are reports prepared by the marketing authorisation holder to describe the worldwide safety experience with a medicine in a defined period after its authorisation. PSURs for medicinal products that contain the same active substance or the same combination of active substances but have different marketing authorisations and are authorised in different EU Member States, are jointly assessed in a single assessment procedure. More information can be found under 'Periodic safety update reports: questions and answers'.

Risk management plans, abbreviated as RMPs, are detailed descriptions of the activities and interventions designed to identify, characterise, prevent or minimise risks relating to medicines. Companies are required to submit an RMP to EMA when applying for a marketing authorisation. RMPs are continually updated throughout the lifetime of the medicine as new information becomes available. More information is available under 'Risk-management plans'.

Post-authorisation safety studies, abbreviated as PASSs, are studies carried out after a medicine has been authorised to obtain further information on its safety, or to measure the effectiveness of risk-management measures. The PRAC assesses the protocols (aspects related to the organisation of a study) and the results of PASSs. More information can be found under 'Post-authorisation safety studies'.

Referrals are procedures used to resolve issues such as concerns over the safety or benefit-risk balance of a medicine or a class of medicines. In a referral related to safety of medicines, the PRAC is requested by a Member State or the European Commission to conduct a scientific assessment of a particular medicine or class of medicines on behalf of the EU. More information can be found under referral procedures.

Notes

1. This press release, together with all related documents, is available on the Agency's website.
2. More information on the work of the European Medicines Agency can be found on its website: www.ema.europa.eu

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