boletim de FARMACOVIGILÂNCIA

VOLUME 25
NUMBER 3
MARCH 2021

March highlights from the Pharmacovigilance Risk Assessment Committee (PRAC)

AstraZeneca Vaccine for COVID-19 (Vaxzevria®): benefits still outweigh potential risks

The PRAC's review of all cases of thromboembolic events and other coagulation related conditions reported following administration of Vaxzevria® is ongoing. The AstraZeneca vaccine can continue to be given since its benefit-risk ratio is still favourable. More on this assessment **here**.

NB: The PRAC concluded the assessment of this safety signal on 20 April 2021: unusual blood clotting combined with thrombocytopenia is now listed in the Summary of the Product's Characteristics (SmPC) and in the Patient Information Leaflet (PL) as a very rare adverse effect.

Meanwhile, following an assessment of cases of serious allergic reactions (**anaphylaxis**), the PRAC has recommended that the Summary of the Product's Characteristics (SmPC) and the Patient Information Leaflet (PL) be updated to include anaphylaxis and hypersensitivity as listed (very rare) adverse reactions. Anyone developing an anaphylactic reaction after receiving the first dose of the vaccine should not be given a second dose. This is a recommendation that is common to all COVID-19 vaccines approved in the EU.

COVID-19 Vaccines and low platelets: start of safety signal assessment

The PRAC has started an assessment of reported cases of immune thrombocytopenia in persons who have received any of the following three vaccines: Comirnaty®, COVID-19 Vaccine AstraZeneca / Vaxzevria®, and COVID-19 Vaccine Moderna®. A causal nexus cannot be ascertained at this time. The PRAC is analyzing all available data.

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Design and production: Letras & Sinais, Comunicação e Imagem, Lda.
ISSN: 0873-7118

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March highlights from the Pharmacovigilance Risk Assessment Committee (PRAC)

Xeljanz® (tofacitinib): increased risk of major adverse cardiovascular events and malignant neoplasms compared to TNF-alpha inhibitor therapy

Based on the initial results of a recent clinical trial (A3921133), it has been agreed that a Dear Healthcare Professional Communication (DHPC) should be sent out to raise awareness of this risk. EMA, with the Marketing Authorization Holder's cooperation, is assessing the data from the above trial in full and will report on this matter as soon as a conclusion is reached.

Tofacitinib is a Janus kinase (JAK) inhibitor that is indicated in:
- moderate to severe active rheumatoid arthritis or active psoriatic arthritis, in adult patients who have responded inadequately to, or who are intolerant to one or more disease-modifying antirheumatic drugs (DMARDs).
- moderately to severely active ulcerative colitis in adult patients who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a biologic agent.

Eylea® (aflibercept): correct handling of pre-filled syringes

A higher than expected number of reports have been received of cases of raised intraocular pressure with administration of Eylea® in pre-filled syringes. The PRAC has concluded that this may be caused by incorrect handling of the syringe.

Aflibercept, intravitreal injection, is indicated in neovascular (wet) age-related macular degeneration and in loss of vision due to macular oedema secondary to retinal vein occlusion, diabetic macular oedema or pathologic myopia associated choroidal neovascularization.

Márcia Silva

Thrombotic Microangiopathy

Thrombotic microangiopathy (TMA) covers a diverse range of conditions including haemolytic uraemic syndrome (HUS) and thrombotic thrombocytopenic purpura (TTP). It is characterized by endothelial capillary injury and microvascular thrombosis. Clinically it is diagnosed based on the findings of thrombocytopenia, haemolytic anaemia and acute renal injury. It supervenes due to deregulation and/or excessive activation of the alternative complement pathway. It is an exceedingly rare acute condition and is life threatening for both adults and children.
The aetiology of TMA can be **genetic or acquired** (either iatrogenic or from exposure to toxins or infection). Drugs reportedly associated with TMA include **immunosuppressants, vaccines and antimicrobials**. Treatment includes removal of the causal agent (when possible) and support therapy. There is also a good response to plasmapheresis, systemic corticosteroids and transfusion.
Cases of TMA have been reported in patients with **spinal muscular atrophy (SMA)** treated with onasemongene abeparvovec (Zolgensma®). There are currently about 800 patients undergoing treatment with this medicine and TMA has been confirmed in five cases only, which is a very low incidence. TMA in these cases presented within **6 to 11 days after** infusion. Symptoms included vomiting, hypertension, oliguria/anuria and/or oedema; lab results showed thrombocytopenia, haemolytic anaemia, raised serum creatinine, proteinuria and/or haematuria.
These cases of ATM with onasemongene abeparvovec have triggered a communication to healthcare professionals (on 18-03-2021) to advise on monitoring for an early diagnosis. Likewise, the product's SmPC will be updated to reflect this risk.

Gonçalo Almeida

Communications to Healthcare Professionals published in the Infomed product information webpage

Click on the links.

INN Medicinal product	Target	Communication? Online publication date
Atezolizumab *Tecentriq*	**Physicians:** pneumology, urology, oncology, radio-oncology, gynaecology, gastroenterology, internal medicine **Nurses:** day care hospitals **Pharmacists:** hospital	Risk of serious adverse skin reactions 25-03-2021
Onasemnogene abeparvovec *Zolgensma*	**Physicians:** neuropaediatricians running a structured spinal muscular atrophy clinic as part of a neuromuscular disease treatment unit	Risk of thrombotic microangiopathy 19-03-2021
Tofacitinib *Xeljanz*	**Physicians:** rheumatologists, internists and dermatologists consulting on rheumatoid and psoriatic arthritis; gastroenterologists (indication: ulcerative colitis)	Increased risk of major adverse cardiovascular events and malignant neoplasms 24-03-2021
Tramadol + Paracetamol *Tramadol + Paracetamol Krka comprimidos de libertação prolongada, Zilpen LP*	**Physicians:** general medicine, surgery, intensive medicine, pain, oncology, rheumatology, orthopaedic surgery	Risk of overdosing and of serious liver injury following overdosing 03-03-2021
Anti-COVID-19 non-replicating viral vector (chimpanzee adenovirus) vaccine *Vaxzevria (formerly COVID-19 Vaccine AstraZeneca)*	**Healthcare professionals:** at vaccination centres, general/family medicine, emergency services, and Portuguese National Health Service 24-hr Helpline	Risk of thrombocytopenia and coagulation disorders 24-03-2021

Compiled by Patrícia Catalão

Educational Materials published in the Infomed product information webpage

Click on the links

INN Medicinal product	Target	Materials? Online publication date
Axicabtagene ciloleucel *Yescarta*	**Healthcare professionals:** multidisciplinary teams at centres in charge of managing patients undergoing therapy with Yescarta and Tecartus	Guide on management of serious neurological adverse reactions and cytokine release syndrome
Autologous anti-CD19-transduced CD3+ cells *Tecartus*		Guide on handling and administration, and recommendations regarding collection of samples from secondary malignant neoplasms
	Patients	Alert card 16-03-2021
Sebelipase alfa *Kanuma*	**Physicians:** paediatrics, gastroenterology, internal medicine, endocrinology	Guide for healthcare professionals
	Nurses	04-03-2021
Talimogene laherparepvec *Imlygic*	**Physicians:** oncology and dermatology	Information: risks of herpetic transmission and complications, and safe use and handling
	Nurses: oncology and dermatology departments	
	Pharmacists: hospital	Guide
	Patients, caregivers and close contacts	Alert card 03-03-2021
Tocilizumab *Roactemra*	**Physicians:** internal medicine, rheumatology, paediatrics, haematology and oncology, and corresponding heads of department	Brochure
	Nurses	Administration guide
	Patients	Brochure Alert card 05-03-2021

Compiled by Patrícia Catalão

Portal **RAM**

Notificação de Reações Adversas a Medicamentos

Report an adverse drug reaction here.
Find answers to your questions about the ADR Portal here.