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# October highlights from the Pharmacovigilance Risk Assessment Committee (PRAC)

## Ongoing assessments and conclusions regarding COVID-19 vaccines

### Assessment of additional data on the risk of myocarditis and pericarditis with mRNA vaccines

The PRAC is continuing a risk assessment concerning myocarditis and pericarditis following immunization with Comirnaty® and Spikevax®. This risk had initially been assessed based on spontaneous reports from the EU, and a recommendation was previously made for myocarditis and pericarditis to be listed as undesirable effects of the above vaccines. The Committee has now asked the MA holders to further review this issue in depth by including all published data, as well as all data from clinical trials, the literature and any source in the public domain.

### COVID-19 vaccines in general and multisystem inflammatory syndrome

*Multisystem inflammatory syndrome (MIS) is an inflammatory condition that affects several body systems and organs. Manifestations can range from fatigue, high, persistent fever, diarrhoea, vomiting and abdominal pain, to headache, chest pain and difficulty breathing.* ***MIS has previously been reported in association with COVID-19 infection itself.***

*MIS is very rare; based on data from five European studies, its pre-pandemic incidence was estimated to be at around 2 to 6 cases per 100,000 per year in children and adolescents younger than 20 years, to fewer than two cases per 100,000 per year in adults older than 20.*

The PRAC has concluded that there currently is insufficient evidence to support a causal nexus between COVID-19 vaccines and the very rare reported cases of multisystem inflammatory syndrome (MIS). Any new reports of MIS will be closely monitored.

**INDEX CARD**

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## Safety signal concerning capillary leak syndrome and Spikevax®:

*Capillary leak syndrome is very rare and potentially serious. It is characterized by leakage of fluids from the blood vessels resulting in tissue oedema and a drop in blood pressure.*

The PRAC has started an assessment of six reports of capillary leak syndrome in persons vaccinated with Spikevax®. For the time being and awaiting conclusion of this assessment, a causal nexus cannot be established. See also here.

# Other safety issues

## Imbruvica®: risk of cardiac death / sudden death not associated with concomitant administration of angiotensin converting enzyme (ACE) inhibitors

*Imbruvica® is indicated for the treatment of mantle cell lymphoma, chronic lymphocytic leukaemia (CLL) and Waldenström's macroglobulinaemia (lymphoplasmacytic lymphoma). Its active ingredient is ibrutinib, a potent Bruton tyrosine kinase (BTK) inhibitor, with a limiting effect on the malignant proliferation of B cells.*

The clinical trials conducted by the MA holder of Imbruvica® have found no statistically significant differences in cardiac death / sudden death events between patients receiving ibrutinib and an ACE inhibitor versus patients receiving an ACE inhibitor and a comparator. See also here.

*Márcia Silva*

## What do they mean?

| | |
|---|---|
| **ADR** | Adverse Drug Reaction |
| **EMA** | European Medicines Agency |
| **MA** | Marketing Authorization |
| **PL** | Patient Information Leaflet |
| **PRAC** | Pharmacovigilance Risk Assessment Committee (EMA) |
| **SmPC** | Summary of Product Characteristics |

# Excipients: safety information in patient leaflets – part 1

This is the first of a series of instalments on the Annex of the European Commission guideline on excipients in packages and patient information leaflets (SANTE-2017-11668). Authorized excipients are presented in alphabetical order (in Portuguese) with their route(s) of administration and information that should be included in the leaflets addressing patients. Additional comments are extracted from the guideline or from other literature sources.

| Excipient | Route(s) of administration | Information in PL | Comments |
|---|---|---|---|
| **Benzoic acid (E210) and benzoates** | Various | *This medicine contains x mg <benzoic acid/benzoate salt> in each <dosage unit><unit volume> <which is equivalent to x mg/<weight><volume>>.*<br>*<Benzoic acid/Benzoate salt> may increase jaundice (yellowing of the skin and eyes) in newborn babies (up to 4 weeks old).*<br>*<Benzoic acid/Benzoate salt> may cause local irritation.* | • Occurring naturally in several plants.<br>• Absorption through immature newborn skin is significant. Increased serum billirubin following its displacement from albumin can increase neonatal jaundice and develop into kernicterus (deposits of non-conjugated billirubin in brain tissue).<br>• It can cause non-immunologic immediate contact reactions through a possible cholinergic mechanism. |
| **Boric acid and borates** | Various | From 1 mg boron/day:<br>*Do not give to a child less than 2 years old as this medicine contains boron and may impair fertility in the future.*<br>From 3 mg boron/day:<br>*. . . a child less than 12 years old . . .*<br>From 7 mg boron/day:<br>*. . . a child less than 18 years old . . .* | • 1 mg boron = 5.7 mg boric acid<br>• Used as an antimicrobial preservative in eye drops, in creams and ointments, as well as in food products. |
| **Sorbic acid** | Topical | *May cause local skin reactions, (e.g. contact dermatitis).* | • A preservative with antibacterial and antifungal properties. It is used in medicines, foods, enteral and cosmetic products, as well as with proteins, enzymes, gelatins and vegetable gums. |
| **Invert sugar** | Oral, including oral liquids, lozenges and chewable tablets | *If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.*<br>*May be harmful to the teeth (nformation to be included only when the medicinal product may be intended for chronic use, e.g. for two weeks or more).*<br>From 5 g:<br>*Contains x g of a mixture of fructose and glucose per dose. This should be taken into account in patients with diabetes mellitus.* | • Caution in patients with rare hereditary conditions such as fructose intolerance or glucose-galactose malabsorption. |

## Communications to Healthcare Professionals published on the Infomed product information webpage

**Click on the links.**

| INN<br>Medicinal product | Target | Communication?<br>Online publication date |
|---|---|---|
| **COVID-19 non-replicating viral vector vaccine (type 26 human adenovirus)**<br>*COVID-19 Vaccine Janssen* | **Healthcare professionals:** vaccination centres, internal medicine, general/family medicine, clinical haematology, immuno-haemotherapy, intensive care units, hospital emergency services, and Portuguese NHS 24-hr helpline | Risk of immune thrombocytopenia and of venous thromboembolism<br>13-10-2021 |
| **COVID-19 non-replicating viral vector vaccine (chimpanzee adenovirus)**<br>*Vaxzevria previously COVID-19 Vaccine AstraZeneca* | **Healthcare professionals:** vaccination centres, internal medicine, general/family medicine, haematology, emergency services, and Portuguese NHS 24-hr helpline | Risk of thrombocytopenia (including immune thrombocytopenia) with or without associated haemorrhage<br>13-10-2021 |

*Compiled by Patrícia Catalão*

## Educational Materials publishedon the Infomed product information webpage

**Click on the links**

| INN<br>Medicinal product | Target | Materials?<br>Online publication date |
|---|---|---|
| **Blinatumomab**<br>*Blincyto* | **Physicians:** haematology and paediatrics, at units treating ALL patients<br>**Nurses:** hospital haematology services treating ALL patients, including paediatric hospitals<br>**Pharmacists:** hospitals treating ALL patients, including paediatric hospitals<br>**Patients** | Guide<br>Guide<br>Guide<br>Guide for patients and caregivers<br>Alert card<br>25-10-2021 |
| **Glasdegib**<br>*Daurismo* | **Male patients** | Alert card<br>21-10-2021 |

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