

2018: key messages

LIVER TOXICITY

- **GADOLINIUM (CONTRAST AGENTS)** Due to risk of accumulation in tissues, namely in the brain, marketing authorization for various contrast agents containing gadolinium has been suspended. The contrast agents that can still be used are under **specific restrictions** – see [BoIFVG 2–2018](#)
- **ESMYA® (ULIPRISTAL)** Possible serious adverse liver reactions have led to the definition of a set of risk minimization measures which should be taken into account whenever considering starting treatment or during treatment. Look up the safety measures here: [BoIFVG 1–2018](#) and [9–2018](#)
- **METANOR® (FLUPIRTINE)** This analgesic has been withdrawn from the market on account of an unfavourable benefit-risk balance to do with serious hepatotoxicity. [BoIFVG 3–2018](#)

- **TRAMAL® (Tramadol)** In order to minimize the risk of accidental overdose it is essential to bear in mind the following equivalence when using the dosing pump: **1 full activation of pump = 5 drops = 12.5 mg = 0.125 ml.** [BoIFVG 4–2018](#)

- **VARENICLINE** Patients on varenicline (Champix®) should not drive, operate complex machinery or undertake potentially hazardous activities before it has been confirmed that the medicine does not affect their ability to do so. Special attention should be given to the possible occurrence of **dizziness**, **sleepiness** and even episodes of **loss of consciousness**. [BoIFVG 8–2018](#)

PREGNANCY

- **VALPROATE** Given the **risks associated with fetal exposure** to medicines containing valproate, namely congenital malformations, developmental problems with learning difficulties, autism-spectrum disorders, and manifestations of attention deficit hyperactivity disorder, a set of **educational materials** for healthcare professionals and patients has been put together with an aim to minimize the above risks. You can download those materials at [BoIFVG 11–12–2018](#)
- **LEVETIRACETAM** Although levetiracetam does not seem to be associated with teratogenicity or neurodevelopmental disorders in children who have been exposed in utero, those risks cannot be excluded. The following is therefore recommended: use the **lowest effective dose**, in **monotherapy** and under **appropriate clinical monitoring**, especially during the third trimester when the physiological changes associated with pregnancy can lead to a decrease in the dose/plasma concentration ratios. [BoIFVG 7–2018](#)

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INDEX CARD

Director: Fátima Canedo

Editor: Rui Pombal

Contributors: Ana Severiano, Ana Sofia Martins, Cristina Mousinho, Elsa de Fátima Costa, Fátima Bragança, Fátima Hergy, Fernanda Marques, Magda Pedro, Márcia Silva, Miguel Antunes, Sílvia Duarte

Publishing Assistant: Inocência Pinto

Advisory Board: Conselho Diretivo do INFARMED, I.P.
INFARMED – Autoridade Nacional do Medicamento e Produtos de Saúde, I.P.
Parque de Saúde de Lisboa, Av. do Brasil, N.º 53, 1749-004 Lisboa

Phone: +351 217 987 100

E-mail: farmacovigilancia@infarmed.pt

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- **METHOTREXATE** Clinical awareness is recommended for the possibility of occurrence of pulmonary alveolar haemorrhage with methotrexate in rheumatological and other related indications. [BoIFVG 7-2018](#)

INTERACTIONS

- **DIRECT ANTICOAGULANTS AND SSRIs/SNRIs** Similarly to antiplatelet agents and NSAIDs, there is an increased risk of haemorrhage when direct anticoagulants (**apixaban, edoxaban**) are administered concomitantly with selective serotonin reuptake inhibitors or with serotonin-norepinephrine reuptake inhibitors. [BoIFVG 8-2018](#)
- **RITONAVIR AND LEVOTHYROXINE** Ritonavir can interact with **levothyroxine** thereby **reducing the efficacy** of the latter. In patients on levothyroxine, thyroid function should be assessed at the initial stages of treatment with ritonavir, as well as when ritonavir is discontinued. [BoIFVG 4-2018](#)

VIRUSES AND ADRs

- **DASATINIB** The chemotherapy agent Sprycel® is associated with an increased risk of complications due to **reactivation of herpesvirus latent infection**, namely cytomegalovirus (CMV). [BoIFVG 5-2018](#)
- **LENALIDOMIDE** Cases of **progressive multifocal leucoencephalopathy** (PML) have been reported several months to several years after starting treatment in patients concomitantly on dexamethasone or who had previously been treated with other **immunosuppressive chemotherapeutic** agents. [BoIFVG 9-2018](#)

Educational Materials published in the [Infomed](#) product information webpage

Click on the links.



INN Medicinal product	Target	Materials? Online publication date
Aflibercept Eylea	Physicians: ophthalmologists who prescribe and administer Eylea.	Safety information Intravitreal injection procedure: Pictogram Video
	Patients	Guides for patients with: Neovascular (wet) age-related macular degeneration Or with loss of vision due to: Diabetic macular oedema Macular oedema secondary to branch or central retinal vein occlusion Choroidal neovascularization associated with pathological myopia 08-01-2019
Dienogest + Ethinylestradiol Amelye	Physicians: gynaecologists, general/family physicians conducting family planning, and dermatologists.	Checklist
	Patients	Information card 22-01-2019

Educational Materials published in the **Infomed** product information webpage

Click on the links.



INN Medicinal product	Target	Materials? Online publication date
Efavirenz + Emtricitabine + Tenofovir disoproxil Efavirenz + Emtricitabina + Tenofovir disoproxil Zentiva	Physicians: infectious diseases and internal medicine.	Recommendations on renal impairment and dose adjustments in HIV1 infected ADULT patients treated with tenofovir disoproxil Creatinine clearance calculation ruler 09-01-2019
Emtricitabine + Tenofovir disoproxil Emtricitabina + Tenofovir disoproxil Zentiva	Physicians: infectious diseases and internal medicine.	Recommendations on renal impairment and dose adjustments in HIV1 infected ADULT patients treated with tenofovir disoproxil Creatinine clearance calculation ruler
	Physicians: infectious diseases, internal medicine and paediatrics. Pharmacists: directors of hospital paediatrics departments.	Recommendations on the use of tenofovir disoproxil in the treatment of HIV1 infected ADOLESCENTS
	Physicians: potential prescribers of PrEP (adults), namely infectious diseases and internal medicine specialists. Pharmacists: hospital pharmaceutical services.	Important safety information on PRE-EXPOSURE PROPHYLAXIS (PrEP) Checklist for the prescribing physician – PrEP
	High risk individuals	Important information on reducing the risk of acquiring HIV infection – PrEP PrEP – Reminder card 09-01-2019
Oral retinoids (acitretin and isotretinoin)	Physicians: general/family medicine, dermatology and gynaecology/obstetrics.	Physician guide
Isotretinoína Generis, Isotretinoína Mer, Isotretinoína Orotrex, Isotretinoína Aurovitas, Neotigason	Pharmacists: community pharmacies.	Pharmacist guide
	Patients	Patient guide 14/01/2019
Trastuzumab emtansine Kadcyla	Physicians: oncology, radiotherapy, general surgery, gynaecology, and internal medicine (senology and with experience in anti-HER2 therapy). Pharmacists: hospital. Nurses: hospital.	Safety information 28-01-2019

INN

Communication

Online publication date

Risk of Fournier gangrene (perineal necrotizing fasciitis)

Nurses: in Diabetes Clinics at primary care health centres and family health units.

24/01/2019

Results of an imposed post-approval study did not confirm clinical benefit of olaratumab for the approved indication

Nurses: day care hospital nursing directors.

28/01/2019

New recommendations on teratogenicity risks and psychiatric disorders

11/01/2019

Compiled by Fernanda Marques and Magda Pedro

SmPC Summary of Product Characteristics