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Call for expressions of interest from Independent Scientific Experts for the EMA Pharmacovigilance Risk Assessment Committee (PRAC)

The European Commission is launching a selection procedure to appoint independent scientific experts to the PRAC, one of the European Medicines Agency's committees. The activities undertaken by the PRAC encompass every aspect of risk management of human medicinal product use, including detection, assessment, minimization and communication concerning adverse drug reaction risks. Six experts will be appointed for a three-year mandate starting on 2 July 2018. Applications can be submitted until 30 September 2017. For further information on this procedure go to this **Calls for expression of interest** at the European Commission's website.

Public Hearing at PRAC

Following earlier approval of rules in 2015, the Pharmacovigilance Risk Assessment Committee (PRAC) at EMA is starting **public hearings** from September. This initiative aims to involve every EU citizen in the supervision of medicines by sharing their opinions and experiences on the therapeutic effects of medicines and available alternatives. The participants will also have an opportunity to express their views on proposed risk management and minimization measures, thus being able to influence PRAC's decisions.

The first public hearing will be looking for the opinion of patients, affected families and the European public at large on three specific questions to do with the use of valproate and related substances during pregnancy. Products containing valproate and valproic acid authorized in Portugal are indicated for the treatment of epilepsy and bipolar disorder and are: Ácido Valpróico Generis, Ácido Valpróico Ratiopharm, Ácido Valpróico Sandoz, Depakine, Depakine Chrono, Depakine Chronosphere, Diplexil, and Diplexil-R (also for migraine prophylaxis). The three questions are:

1. What is your view of the risks of taking valproate during pregnancy, including its potential effect on the child?

2. What are your views on the measures currently in place to reduce the risks of using valproate during pregnancy?

3. What other measures should be taken to reduce the risks of using valproate during pregnancy?

The hearing will take place at 1 pm on 26 September at EMA headquarters in London and will last for approximately one hour. EMA will cover the speakers' travel expenses. Those speakers who will not be able to travel may participate by teleconference. Applications need to be made no later than 25 August by sending in the enrolment form to publichearings@ema.europa.eu. Anyone can participate as an observer. The hearing can also be followed live by teleconference on the EMA website. No application is required to attend this video broadcast - a link will be made available on the site on the day.

On the EMA website you will find a **Guide for the Participants**, as well as a summary of **safety concerns** that prompted this hearing.

Rita Amado Dias

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Brentuximab vedotin
Citomegalovirus reactivation

Quick Read

The possibility of an association between the use of the monoclonal antibody brentuximab vedotin and potentially serious infections is well known. CMV reactivation has recently been added to the list.

Brentuximab vedotin is a monoclonal antibody directed to protein CD30 for the treatment of adult patients with recurrent or refractory CD30+ Hodgkin's lymphoma, following autologous stem-cell transplantation (ASCT) or following at least two previous therapeutic trials whenever ASCT or combined chemotherapy are not an option.

During its routine pharmacovigilance activities, the French medicines agency detected a safety signal (potential problem) to do with the use of brentuximab vedotin and citomegalovirus (CMV) reactivation. Taking into account the cases from the European database (EudraVigilance), clinical trials and the literature[1], as well as the known association between brentuximab vedotin and infections, the PRAC at EMA has concluded that the SmPC and PIL texts need to be changed to reflect that risk, i.e. the uncommon occurrence (in over 1 out of every one thousand exposed patients but in fewer than 1 out of 100) of CMV reactivation.

Summary of the Product's Characteristics

4.4. Special warnings and precautions for use

[…]

Serious infections such as pneumonia, staphylococcal bacteraemia, sepsis/septic shock (including fatal outcomes) and herpes zoster, Cytomegalovirus (CMV) (reactivation) and opportunistic infections such as Pneumocystis jiroveci pneumonia and oral candidiasis have been reported in patients treated with brentuximab vedotin. Patients should be carefully monitored during treatment for the emergence of possible serious and opportunistic infections.

4.8. Undesirable effects

[…] 'uncommon': Cytomegalovirus infection or reactivation

Márcia Silva

Reference

[1] Lebrun. J et al. Brentuximab and cytomegalovirus reactivation: about 3 cases. Fundamental & Clinical Pharmacology. 2016; 30, 38-38.

Temozolomide
Risk of Herpetic Meningoencephalitis

Quick Read

Although uncommon, serious and potentially fatal cases of herpetic meningoencephalitis can occur in patients on therapy with the alkylating agent temozolamide (TMZ).

Temozolomide is an alkylating antineoplastic agent indicated in the treatment of adult patients with recently diagnosed glioblastoma multiforme, together with radiotherapy and, subsequently, as monotherapy. It is also indicated for the treatment of children from three years of age, adolescents and adults with a malignant glioma (such as glioblastoma multiforme or anaplastic astrocytoma) that progresses or recurs after standard therapy.

Taking into account the cases of herpetic meningoencephalitis in patients on temozolamide recorded in the European ADR database (EudraVigilance), as well as the evidence from the literature[1-6], the PRAC at EMA has concluded for changes to sections 4.4 and 4.8 of the SmPC and section 4 of the PIL. In the Summary of the Product's Characteristics the following is to be included:

Summary of the Product's Characteristics

4.4 Special warnings and precautions for use Meningoencephalitis herpetic

In post marketing cases, meningoencephalitis herpetic (including fatal cases) has been observed in patients receiving TMZ in combination with radiotherapy, including cases of concomitant steroids administration.

4.8 [. . .]

Frequency 'uncommon'*: Meningoencephalitis herpetic (including cases with fatal outcome)

* In over 1 out of every one thousand exposed patients but in fewer than 1 out of 100.

Márcia Silva

References:

[1] Kocher M et al. Efficacy and toxicity of postoperative temozolomide radiochemotherapy in malignant glioma. Strahlenther Onkol. 2005 Mar;181(3):157-63.

[2] Christman MP et al. Recurrence of herpes simplex encephalitis associated with temozolomide chemoradiation for malignant glioma: a case report and review of the literature. Oxf Med Case Reports. 2014 Mar 12;2014(1):1-4.

[3] Toler J et al. Cognitive Dysfunction After Cranial Radiation for a Brain Tumor. J Pediatric Infect Dis Soc. 2016 Mar;5(1):96-9.

[4] Tsai JP et al. Concomitant viral and bacterial encephalitis after temozolomide for glioblastoma. Can J Neurol Sci. 2014 Jan;41(1):84-5.

[5] Berzero G et al. Herpes simplex encephalitis in glioma patients: a challenging diagnosis. J Neurol Neurosurg Psychiatry. 2015 Apr;86(4):374-7.

[6] Okada M et al. Relapse of herpes encephalitis induced by temozolomide-based chemoradiation in a patient with malignant glioma. J Neurosurg. 2013 Feb;118 (2):258-63.

What do they mean?

ADR	Adverse Drug Reaction
EMA	European Medicines Agency
MA	Marketing Authorisation
PIL	Patient Information Leaflet
PRAC	Pharmacovigilance Risk Assessment Committee
SmPC	Summary of Product Characteristics

Educational Materials published in the Infomed product information webpage

Medicinal product (DCI)	Click on the links (in Portuguese)
Angiox (bivalirudine)	**Educational materials for healthcare professionals** Instruções de posologia e administração para intervenção coronária percutânea (ICP) e ICP primária - 4ª versão Instruções de posologia e administração para intervenção coronária percutânea (ICP) urgente ou precoce - 4ª versão For healthcare professionals involved in prescribing, dispensing or administering the product. Published on 06-07-2017
Benepali (etarnecept)	**Educational materials for healthcare professionals** Breve formação sobre medidas adicionais de minimização do risco - 2ª versão Guia de consulta rápida para o médico prescritor sobre a caneta auto-injetora - 2ª versão Guia de consulta rápida para o médico prescritor sobre a seringa pré-cheia - 2ª versão For rheumatologists and dermatologists. Published on 21-07-2017
Diane 35 (ciproterone + ethinylestradiol)	**Educational materials for healthcare professionals** Lista de verificação para prescritores - 2ª versão For gynaecologists/obstetricians, dermatologists and family doctors. **Educational materials for healthcare patients** Cartão de informação da doente - 2ª versão To be handed out to patients by doctors. Published on 11-07-2017
MabThera (rituximab)	**Educational materials for healthcare professionals** Cartão comparativo dirigido ao profissional de saúde - 2ª versão Guia para a utilização segura e eficiente do medicamento dirigido ao profissional de saúde - 2ª versão For haematologists and oncologists, hospital pharmacists and hospital nurses. Informação Importante de Segurança de Mabthera em Indicações não-oncológicas - 3ª Versão For rheumatologists and internists. **Educational materials for healthcare patients** Folheto educacional para o doente - 3ª versão To be handed out to patients by doctors. Published on 21-07-2017

Educational Materials published in the Infomed product information webpage

Medicinal product (DCI)	Click on the links (in Portuguese)
Qutenza (capsaícina)	**Educational materials for healthcare professionals** Guia de Administração - 5ª Versão For prescribers and users. Published on 10-07-2017
Strensiq (asfotase alfa)	**Educational materials for healthcare patients** Guia de autoinjeção - 2ª versão To be handed out to patients by doctors or hospital pharmaceutical services. Guia de injeção para pais e acompanhantes de crianças - 2ª versão To be handed out to children's parents and caregivers by doctors or hospital pharmaceutical services. Published on 21-07-2017

Compiled by Magda Pedro

Communications to Healthcare Professionals published on the Infarmed website

Medicinal product (DCI)	Click on the links (in Portuguese)
Imbruvica (ibrutinib)	Risk of hepatitis B reactivation – viral assessment before starting therapy For specialist doctors in haematology and oncology, for pharmacies in hospitals with a haematology/oncology department, and for doctors in internal medicine departments in hospitals without a haematology or an oncology department and whose patients are potentially attended to in internal medicine. Published on 18-07-2017.

Compiled by Magda Pedro