7th August 2018

Daclizumab beta (Zinbryta®): Cases of immune-mediated encephalitis, including anti-NMDA receptor encephalitis, reported several months after discontinuation of treatment

Dear Healthcare Professional,

Biogen in agreement with the European Medicines Agency and the Healthcare Products Regulatory Authority (HPRA) would like to inform you of the following:

Summary

- **Cases of immune-mediated encephalitis, including anti- N-methyl-D- aspartate (NMDA) receptor encephalitis, have been reported in patients during treatment and also several months after discontinuation of Zinbryta.**
- **All patients who have discontinued Zinbryta and their carers should be reminded to contact the patient's physician immediately if any of the common prodromal symptoms or early common behavioural, neurological, cognitive or movement-related symptoms occur.**
- **In cases where encephalitis is suspected in patients who have discontinued treatment with Zinbryta, the NMDA receptor antibody test in cerebrospinal fluid (CSF) and serum should be considered as early as possible to assist diagnosis.**
- **Cases should be reviewed by a specialist with experience in diagnosis and management of autoimmune encephalitis.**
- **Monitoring for encephalitis should continue for up to 12 months following discontinuation of daclizumab.**

Background on the safety concern

The marketing authorisation of Zinbryta (daclizumab beta) was suspended and the medicine recalled from the European market in March 2018, following reports of serious and potentially fatal immune reactions affecting the brain (including encephalitis and meningoencephalitis), liver and other organs in patients treated with Zinbryta. Physicians were advised to monitor patients at least monthly following discontinuation of the product and more frequently as clinically indicated, for up to six months after the last dose.

As of 10 July 2018, 7 cases of encephalitis have been reported after discontinuation of Zinbryta, two of them are confirmed cases of anti-NMDA receptor encephalitis. The cases of anti-NMDA receptor encephalitis have occurred around 3 to 4 months after discontinuation of treatment with Zinbryta. The patients with anti-NMDA receptor encephalitis presented with headache, fever, vomiting, confusion, tremor, visual disturbances and seizures.

Biogen Idec (Ireland) Limited
Registered Office: United Drug House, Magna Business Park, Citywest Road, Dublin 24 | Ireland
Phone +353 1 463 7725 | Fax +353 1 481 1730
Company Registration No 421718

Anti-NMDA receptor encephalitis can be diagnosed with a specific antibody test in cerebrospinal fluid and serum in the appropriate clinical setting. If cases of encephalitis are suspected in patients who have discontinued Zinbryta, physicians are advised to consider performing NMDA receptor antibody tests in cerebrospinal fluid and serum. Testing of a broad panel of autoantibodies may be considered (e.g. antigens for neuronal cell surface and synaptic proteins).

Zinbryta is no longer authorised in the European Union (EU).

On 27 March 2018, the European Commission withdrew the marketing authorisation of the medicine at the request of the marketing authorisation holder Biogen Idec Ltd.

Call for reporting

Healthcare professionals should report any suspect adverse reactions associated with the use of Zinbryta in accordance with the national requirements via the national spontaneous reporting system, to:

HPRA Pharmacovigilance, Earlsfort Terrace, IRL – Dublin 2; Tel: +353 1 676 4971; Fax: +353 1 676 2517; Website: www.hpra.ie; e-mail: medsafety@hpra.ie.

ADRs can also be reported to the Marketing Authorisation Holder (MAH) by telephone (1800 812 719), fax [+44 (0) 1628 501 010] or email (MedInfoUKI@biogen.com).

Company contact point

Further information can be requested from Biogen by telephone (1800 812 719), fax [+44 (0) 1628 501 010] or email (MedInfoUKI@biogen.com).

Annexes

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

Yours faithfully

Dr Simon Beck
Medical Director, UK and Ireland