



## Direct Healthcare Professional Communication

7<sup>th</sup> 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 Medicines and Healthcare products Regulatory Agency (MHRA), 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 6 months after the last dose.

As of 10 July 2018, seven 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 3–4 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 Limited**

Registered Office: Innovation House, 70 Norden Road, Maidenhead, Berkshire SL6 4AY | United Kingdom

Phone +44 1628 501000 | Fax +44 1628 501010 | [www.biogen.uk.com](http://www.biogen.uk.com)

Registered in England and Wales No 01497267

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***

Please continue to report suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card Scheme. Please report:

- all suspected ADRs that are serious or result in harm. Serious reactions are those that are fatal, life-threatening, disabling or incapacitating, those that cause a congenital abnormality or result in hospitalisation, and those that are considered medically significant for any other reason
- all suspected ADRs associated with new drugs and vaccines identified by the black triangle▼

It is easiest and quickest to report ADRs online via the Yellow Cards website - <https://yellowcard.mhra.gov.uk/> or via the Yellow Card app available from the Apple App Store or Google Play Store. Alternatively, prepaid Yellow Cards for reporting are available:

- by writing to FREEPOST YELLOW CARD (no other address details necessary)
- by emailing [yellowcard@mhra.gov.uk](mailto:yellowcard@mhra.gov.uk)
- at the back of the British National Formulary (BNF)
- by telephoning the Commission on Human Medicines (CHM) free phone line: 0800-731-6789 or
- by downloading and printing a form from the Yellow Card website (see link above)

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset, treatment dates, and product brand name.

### ***Company contact point***

Further information can be requested from Biogen by telephone (0800 008 7401), fax [+44 (0) 1628 501 010] or email ([MedInfoUKI@biogen.com](mailto:MedInfoUKI@biogen.com)).

Yours faithfully



**Dr Simon Beck**  
**Medical Director, UK and Ireland**