Direct Healthcare Professional Communication

07 November 2016

Dear Healthcare professional

▼Otezla (apremilast): New important advice regarding suicidal ideation and behaviour

Celgene Europe Limited in agreement with the European Medicines Agency and the Medicines & Healthcare Products Regulatory Agency would like to inform you of the following:

Summary

- **Suicidal ideation and behaviour have been reported from clinical trials and post-marketing experience (with or without a history of depression) with a frequency of uncommon (≥1/1,000 to ≤1/100), while cases of completed suicide were reported postmarketing in patients taking apremilast**
- **Carefully assess the balance of benefits and risks of treatment with apremilast for patients with a history of psychiatric symptoms or patients taking medicines which are likely to cause psychiatric symptoms**
- **If patients suffer from new or worsening psychiatric symptoms, or if suicidal ideation or suicidal behavior is identified, it is recommended to discontinue treatment with apremilast**
- **Instruct patients and caregivers to notify the prescriber of any changes in behaviour or mood or of any signs of suicidal ideation**

Background on the safety concern

Otezla (apremilast) alone or in combination with disease modifying antirheumatic drugs (DMARDs) is indicated for the treatment of active psoriatic arthritis (PsA) in adult patients who have had an inadequate response or who have been intolerant to a prior DMARD therapy. It is also indicated for the treatment of moderate to severe chronic plaque psoriasis in adult patients who failed to respond to or who have a contraindication to, or are intolerant to other systemic therapy including cyclosporine, methotrexate or psoralen and ultraviolet-A light (PUVA).

Although suicidal behaviour-related events and depression are more common in patients with psoriasis and psoriatic arthritis than in the general population, evidence from clinical trials and post-marketing experience suggests a causal association between suicidal ideation and behaviour with the use of apremilast. This conclusion is based on a thorough regulatory review of this issue.

In relation to suicidal ideation and behaviour:

- Post-marketing data up to 20 March 2016 reported 65 cases distributed as follows: 5 completed suicides, 4 suicide attempts, 50 cases of suicidal ideation, 5 cases of depression suicidal and 1 case of suicidal behaviour. In 32 cases out of 65, for which information was available, the patients reported improvement after treatment discontinuation. (From launch to 20 March 2016, there were approximately 105,000 patients exposed to apremilast.)
- In controlled clinical trials, a slight imbalance of suicidal ideation and behaviour events were observed in patients treated with apremilast versus placebo.

In relation to depression, a number of cases of this adverse drug reaction, some of which were serious, have been reported in the postmarketing setting. In clinical trials, an imbalance of cases of depression in patients treated with apremilast was identified vs placebo.

Based on the above data, it is recommended that risks and benefits of starting or continuing treatment with apremilast should be carefully assessed in patients with previous or existing psychiatric symptoms or if concomitant treatment with other medicinal products likely to cause psychiatric events are in use or

intended. Additionally, it is recommended to discontinue treatment with apremilast in patients suffering from new or worsening psychiatric symptoms, or suicidal ideation or suicidal attempt is identified. The product information (SmPC and package leaflet) of Otezla is being updated to add a warning about depression and suicidal behavior and ideation.

Call for reporting

▼ This medicinal product is subject to additional monitoring. This is intended to facilitate early identification of new safety information.

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/

Alternatively, prepaid Yellow Cards for reporting are available:

- by writing to FREEPOST YELLOW CARD (no other address details necessary)
- by emailing yellowcard@mhra.gsi.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 section of the MHRA website.

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

Adverse reactions associated with the use of apremilast may also be reported to Celgene: Celgene Drug Safety, Celgene Ltd, 1 Longwalk Road, Stockley Park, Uxbridge, UB11 1DB Telephone: 0808 238 9908 Fax: 0844 801 0468
email: drugsafetyuk@celgene.com

Communication information

If you have any further questions or require further information, please contact your local Celgene representative at:
Celgene Medical Information, Celgene Ltd, 1 Longwalk Road, Stockley Park, Uxbridge, UB11 1DB
Telephone: 0844 801 0045
Fax: 0844 801 0046
email: medinfo.uk.ire@celgene.com

Yours faithfully

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