Pomalidomide (Imnovid ® ▼): New important advice to minimise the risk of serious hepatotoxicity, interstitial lung disease and cardiac failure

24 April 2015

Dear Healthcare Professional:

Celgene, in agreement with the European Medicines Agency (EMA) and the Health Products Regulatory Authority (HPRA), wishes to inform you about important new safety information regarding pomalidomide. This relates to the newly identified risks of serious hepatotoxicity, interstitial lung disease (ILD) and cardiac failure.

Summary

Hepatotoxicity

- ***Serious cases of acute hepatitis due to pomalidomide have occurred that led to hospitalisation and discontinuation of treatment.***

- ***Regular monitoring of liver function is recommended for the first 6 months of treatment with pomalidomide and thereafter as clinically indicated.***

Interstitial lung disease (ILD)

- ***ILD and related events have been observed with pomalidomide.***

- ***Patients with an acute onset or unexplained worsening of pulmonary symptoms should be carefully assessed to exclude ILD. Treatment with pomalidomide should be interrupted pending investigation of these symptoms.***

- ***If ILD is confirmed, appropriate treatment should be initiated. Pomalidomide should only be resumed after a thorough evaluation of the benefits and risks.***

Cardiac failure

- ***Cardiac failure has been reported, mainly in patients with pre-existing cardiac disease or risk factors***

- ***Pomalidomide should be used with caution in patients with cardiac disease or risk factors and if used, patients should be monitored for signs or symptoms of cardiac failure.***

Further background information to this safety update

Pomalidomide in combination with dexamethasone is indicated in the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least two prior treatment regimens, including both lenalidomide and bortezomib, and have demonstrated disease progression on the last therapy.

A European review as part of regular safety monitoring concluded that pomalidomide can cause serious hepatotoxicity (acute hepatitis), ILD and cardiac failure. The safety review of pomalidomide was based on data from clinical trials, reports from clinical practice as well as published case reports.

The summary of product characteristics will be updated to include these newly identified risks.

Hepatotoxicity

Pomalidomide is known to cause markedly elevated levels of alanine aminotransferase and bilirubin. The safety review identified evidence that pomalidomide can also cause serious hepatotoxicity, mainly in the form of acute hepatitis, which has resulted in hospitalisation and discontinuation of treatment with pomalidomide. There have also been cases of acute hepatic failure (including fatal cases) although a causal relationship with pomalidomide has not been established. Given that pomalidomide can cause serious hepatotoxicity, monitoring of liver function is recommended. The available data do not provide sufficient evidence to support specific guidance on the frequency of liver function monitoring. Nevertheless, the period during which the risk of serious hepatic events is highest appears to be in the first 6 months of treatment and therefore regular monitoring of liver function during this period is recommended.

ILD

Onset of respiratory symptoms is usually within 6 months following start of treatment, but there have been cases where the ILD occurred approximately 18 months after starting pomalidomide. ILD usually resolves with steroid treatment and permanent cessation of pomalidomide. Patients on pomalidomide who present with an acute onset or unexplained worsening of pulmonary symptoms should be carefully assessed to exclude ILD and pomalidomide should be interrupted pending investigation of these symptoms. If ILD is confirmed, appropriate treatment should be initiated. Pomalidomide should only be resumed after a thorough evaluation of the benefits and the risks.

Cardiac failure

Cases of cardiac failure and related events, which include congestive cardiac failure, acute cardiac failure and acute pulmonary oedema, were observed mainly in patients with existing cardiac disease or risk factors such as hypertension. The majority of these events occurred within 6 months of starting treatment with pomalidomide. Patients with cardiac disease or risk factors should be monitored for signs and symptoms of cardiac failure. The safety review also concluded that pomalidomide can cause atrial fibrillation, which may precipitate cardiac failure.

Call for reporting

Pomalidomide is a new active substance that is subject to additional monitoring to facilitate quick identification of new safety information.

Suspected adverse reactions should be reported to the HPRA using a Yellow Card obtained either from the HPRA, or electronically via the website at www.hpra.ie. Adverse reactions can also be reported to the HPRA by calling (01) 676 4971.
When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset and treatment dates.

Adverse reactions associated with the use of pomalidomide may also be reported to Celgene:

Celgene Drug Safety
Celgene Ltd
1 Longwalk Road
Stockley Park
Uxbridg, UB11 1DB

Telephone: 1800 936 217
Fax: 1800 936 477
Email: drugsafetyuk@celgene.com

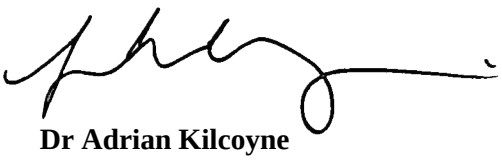
Company Contact Point

If you have any further questions or require further medical information on pomalidomide, please contact your local Celgene representative at:

Celgene Medical Information
Celgene Ltd
1 Longwalk Road
Stockley Park
Uxbridge, UB11 1DB

Telephone: 1800 333 111
Fax: 1800 333 112
E-mail: medinfo.uk.ire@celgene.com

Yours faithfully,



Dr Adrian Kilcoyne
Medical Director, UK and Ireland
Celgene Limited