



Drug Information Bulletin

Drug Information Centre (DIC)

Indian Pharmaceutical Association

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Editorial

Recently Government of India created a mandate of Pharmacovigilance system for reporting ADR to licensing authority by every manufacturer or market authorization holder. They are required to have a pharmacovigilance system in place for collecting, processing and forwarding the report to the licensing authority for information on adverse drug reactions emerging from the use of the drugs manufactured or marketed by the applicant in the country. The entire exercise should be managed by a Medical officer or trained Pharmacist. They are also required to submit Periodic Safety Update Reports (PSURs) as per the regulation.

Pharmacovigilance Programme of India (PvPI), working since 2010 is now a matured one having strong infrastructure and manpower. Presently more than 200 AMCs are working successfully and generating a good number of ICSRs. On the basis of data collected through this system, PvPI contributed several data to the WHO-UMC collaborating centre. They have also provided several alert notices to the stake holders and made several recommendations to the CDSCO. CDSCO has already instructed Marketing Authorization Holders (MAH) to comply the same and also made suitable amendment of Drugs and Cosmetics Act & Rules.

Now the Indian regulatory agencies are taking action on the basis of data generated in our country instead of depending entirely on the data generated in other countries. Being a stake holder Indian Pharmaceutical Association (IPA) is trying its best to support the programme in several ways to ensure safe medicine to the general mass.



Dr. Subhash C. Mandal
Editor

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New Drug: Pomalidomide

Approved indication: multiple myeloma

Pomalyst (Celgene)

1 mg, 2 mg, 3 mg and 4 mg capsules

Australian Medicines Handbook section

14.2.4

Multiple myeloma is characterised by abnormal plasma cells in the bone marrow. The disease is generally considered incurable and most patients eventually become refractory to treatment. Pomalidomide is indicated for those who have already received at least two treatments, including bortezomib (Aust Prescr 2006;29:84-7) and lenalidomide (Aust Prescr 2008;31:49-55). Median overall survival in this group is around nine months with treatment and three months without treatment.

Pomalidomide is structurally related to thalidomide and lenalidomide. Its exact mechanism of action is unknown, but like other drugs in the class, it is thought to have antimyeloma, anti-angiogenic, immunomodulatory and stromal cell effects. In a phase II trial, the efficacy of pomalidomide was enhanced when given with low-dose dexamethasone (see [Table](#)).¹

The approval of pomalidomide is mainly based on an open-label phase III trial which enrolled patients who had relapsed or progressed despite a median of five previous treatments. Participants were randomised to 28-day cycles of pomalidomide with low-dose dexamethasone (302 patients), or to high-dose dexamethasone alone (153 patients). Treatment was continued until disease progressed or patients developed unacceptable toxicity. After 10 months, pomalidomide and low-dose dexamethasone was found to significantly improve response rates, progression-free and overall survival compared to high-dose dexamethasone.²

After a median follow-up of 10 months, most people had discontinued treatment (80% of the pomalidomide group, 93% of the comparator group). Progressive disease was the most common reason for stopping, but

approximately 10% of people discontinued because of an adverse event.²

Serious adverse events, defined as resulting in hospitalisation, disability or incapacity, occurred in 61% of patients in the pomalidomide group and 53% of those in the comparator group. The most common adverse events of any grade with pomalidomide were infections (68% of people), anaemia (52%), neutropenia (51%), fatigue (34%), thrombocytopenia (30%), fever (27%), diarrhoea (22%) and constipation (22%).² Peripheral neuropathy occurred in 12% of patients. Adverse events were more likely to occur during the first two cycles of treatment. There were 11 treatment-related deaths with pomalidomide – eight cases of infections, two cases of multi-organ failure or sudden death, and one nervous system disorder.²

Because of its structural similarity to thalidomide, pomalidomide is contraindicated in pregnancy. It is available under a restricted distribution program, which includes measures to prevent pregnancy. Women should be using a recommended form of contraception and have a negative pregnancy test before starting pomalidomide and men must use a condom throughout treatment, even if they have had a vasectomy.

Regular monitoring of blood counts is recommended with pomalidomide because anaemia, neutropenia and thrombocytopenia are so common and patients often need their dose reduced or interrupted. Dizziness and confusion have been reported and patients should be warned not to drive or operate machinery if this occurs.

Deep vein thrombosis occurs with pomalidomide so prophylaxis is recommended in patients with a high risk. There is no experience of this drug in patients with significant heart problems such as congestive heart failure, recent myocardial infarction or poorly controlled angina, as they were excluded from trials. Close monitoring is recommended in patients with an

increased risk of tumour lysis syndrome (those with a high tumour burden or renal impairment).

Following oral administration, maximum plasma concentrations are reached after 2-3 hours. Pomalidomide's plasma half-life is 7.5 hours in patients with multiple myeloma. After metabolism in the liver, the drug is eliminated in the urine (73%) and faeces (15%). It is unclear if the dose needs to be reduced in renal disease as patients with moderate to severe impairment were excluded from the trials. Patients with hepatic impairment (serum bilirubin >34.2 micromol/L) and elevated transaminases (>3 x upper limit of normal) were also excluded. Pomalidomide is predominantly metabolised by cytochrome P450 (CYP) 1A2 and 3A4 and is also a substrate of P-glycoprotein. Co-administration of strong CYP1A2 inhibitors, such as fluvoxamine, may increase pomalidomide exposure and monitoring is recommended. Close monitoring is also advised in patients taking concomitant warfarin as there is a potential drug interaction with dexamethasone.

For patients with few options left, pomalidomide with low-dose dexamethasone may offer longer progression-free and overall survival compared to treatment with high-dose dexamethasone. However, haematological toxicity and infections are very common and may limit treatment.

References:

1. Richardson PG, Siegel DS, Vij R, Hofmeister CC, Baz R, Jagannath S, et al. Pomalidomide alone or in combination with low-dose dexamethasone in relapsed and refractory multiple myeloma: a randomized phase 2 study. *Blood* 2014;123:1826-32.
2. San Miguel J, Weisel K, Moreau P, Lacy M, Song K, Delforge M, et al. Pomalidomide plus low-dose dexamethasone versus high-dose dexamethasone alone for

patients with relapsed and refractory multiple myeloma (MM-003): a randomised, open-label, phase 3 trial. *Lancet Oncol* 2013;14:1055-66.

Source: Australian Prescriber

Status in India:

Pomalidomide 1mg/2mg/3mg/4mg Capsules approved by the CDSCO on 01.05.2017 for use "In combination with dexamethasone, for patient with patient multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor and have demonstrated disease progression on or within 60 days of completion of the last therapy".

Source: www.cdsc.nic.in

Ministry of Health and Family Welfare-Government of India reported three laboratory-confirmed cases of Zika virus disease in India

On 15 May 2017, the Ministry of Health and Family Welfare-Government of India (MoHFW) reported three laboratory-confirmed cases of Zika virus disease in Bapunagar area, Ahmedabad District, Gujarat, State, India.

The routine laboratory surveillance detected a laboratory-confirmed case of Zika virus disease through RT-PCR test at B.J. Medical College, Ahmedabad, Gujarat. The etiology of this case has been further confirmed through a positive RT-PCR test and sequencing at the national reference laboratory, National Institute of Virology (NIV), Pune on 4 January 2017 (case 2, below). Two additional cases (case 1 and case 3), have then been identified through the Acute Febrile Illness (AFI) and the Antenatal clinic (ANC) surveillance. The cases are reported below in chronological order:

Key facts

- Zika virus disease is caused by a virus transmitted primarily by *Aedes* mosquitoes.
- People with Zika virus disease can have symptoms including mild fever, skin rash, conjunctivitis, muscle and joint pain, malaise or headache. These symptoms normally last for 2-7 days.
- There is scientific consensus that Zika virus is a cause of microcephaly and Guillain-Barré syndrome. Links to other neurological complications are also being investigated.

Treatment

Zika virus disease is usually mild and requires no specific treatment. People sick with Zika virus should get plenty of rest, drink enough fluids, and treat pain and fever with common medicines. If symptoms worsen, they should seek medical care and advice. There is currently no vaccine available.

Prevention

Mosquito bites

Protection against mosquito bites is a key measure to prevent Zika virus infection. This can be done by wearing clothes

(preferably light-coloured) that cover as much of the body as possible; using physical barriers such as window screens or closing doors and windows; sleeping under mosquito nets; and using insect repellent containing DEET, IR3535 or icaridin according to the product label instructions. Special attention and help should be given to those who may not be able to protect themselves adequately, such as young children, the sick or elderly. Travellers and those living in affected areas should take the basic precautions described above to protect themselves from mosquito bites.

It is important to cover, empty or clean potential mosquito breeding sites in and around houses such as buckets, drums, pots, gutters, and used tyres. Communities should support local government efforts to reduce mosquitoes in their locality. Health authorities may also advise that spraying of insecticides be carried out.

Source:

<http://www.who.int/mediacentre/factsheets/zika/en/>

Reader Speak.....

Dear Dr Mandal,

I much appreciate your service to pharma professionals. Most importantly maintaining bi-weekly rhythm, punctuality, diligent and speed at which you keep pace with worldwide latest alerts about drugs & interaction with patients.

Best wishes,

Dr Vijay Bambulkar,

M. Pharm., Ph.D., FIPA

Director, Asia Pacific Regulatory Affairs: External Growth, Johnson & Johnson, Mumbai

Forthcoming Event

IPA Bengal Branch organizes
Seminar on "Impact of GST in Pharma Industry and Trade"

Date: 10.06.2017

Time: 6.30 pm

Venue: IPA Auditorium, 22 B Panchanantola Road, Kolkata-700029

Speaker:

Mr. Ashok Das, Superintendent, National Academy of Customs, Excise & Narcotics (NACEN), RTI, Kolkata

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