Drug Information Bulletin

Drug Information Centre (DIC)
Indian Pharmaceutical Association
Bengal Branch
Tele fax: 033 24612776, E-mail: ipabengal.dic@gmail.com
Web Site: http://www.ipabengal.org
Contact: 09830136291
&
Regulatory Affairs Division (RAD), IPA

Volume: 09 ***Number: 21*** ***16th January 2016***

Content

Editorial

Union Minister, Ministry of Chemicals & Fertilizers -Mr. Ananth Kumar has shown deep concern about Public Health & Pharmaceutical Industry of India during the Inauguration of 67th Indian Pharmaceutical Congress at Mysuru on 19th December 2015. He invited Pharmaceutical Manufacturers to spend more on Research & Development for discovering new molecules, as he felt that reverse engineering is no longer help pharma industry grow. He also expressed deep concern about lack of sufficient manufacturing facilities for Medical Devices in India and appealed entrepreneurs for investment in Medical Devices Industry to reduce dependency on import. Mr. Anant Kumar said that the Government has already framed separate set of legislations for Medical Devices and is going to implement it soon. He informed that his dept. is pushing for a separate Ministry of Pharmaceuticals & Medical Devices and is expecting it to materialize within one year. He also expressed that 106 more drugs will be included in DPCO. Recently a new version of NLEM has been published which contains 376 drugs. Seventy drugs , which are no longer in use or are sparingly used have been deleted and 106 more new drugs under the category of anticancer, cardiac, antidiabetics etc. have been included.

On the second day of the IPC, Mr. J.P.Nadda, Union Health Minister released "The Vision" document "expressing that Indian Pharmacists will realize the vision expressed in the caption by partnering with Government of India initiatives for developing a Healthy India (Swasth Bharat)".

Mr. J.P.Nadda has said that they are considering for extending greater role of pharmacists in health care system. He also expressed that his Govt. is seriously considering to allow pharmacists for prescribing a few drugs in the rural areas.

Pharmaceutical professionals are extremely happy about those decisions and are expecting proper implementation of the same.

Dr. Subhash C. Mandal
Editor

New Drug: Ruxolitinib

Approved indication in Australia: myelofibrosis
Australian Medicines Handbook section 14.2.3

Myelofibrosis can present as a primary disease or develop from polycythaemia vera or essential thrombocythaemia. It is characterised by fibrosis of the bone marrow, progressive anaemia and hepatosplenomegaly from overproduction of abnormal, immature blood cells. Survival of patients after diagnosis ranges from 2 to 11 years. Apart from stem cell transplant, current treatment is usually supportive and directed at symptoms.

Myelofibrosis is associated with overactivation of the Janus kinase pathway. In many patients, this is associated with a mutation in the Janus kinase 2 gene (V617F mutation). Overactivity of the pathway results in increased signalling of a number of cytokines and growth factors involved in haematopoiesis and immune functions.

Ruxolitinib is a selective inhibitor of Janus kinase 1 and 2. Its safety and efficacy has been assessed in two phase III trials – COMFORT-I and COMFORT-II.[1,2] COMFORT-I compared ruxolitinib to placebo for 24 weeks whereas COMFORT-II compared it to best available therapy (usually hydroxyurea or glucocorticoids) for 48 weeks. Approximately half of the patients in the trials had primary myelofibrosis, a third had post-polycythaemia vera myelofibrosis and the rest had post-essential thrombocythaemia myelofibrosis.

In both studies, more patients receiving ruxolitinib (15–25 mg twice daily) had at least a 35% reduction in spleen size compared to patients receiving the control treatments. Spleen size increased in patients who did not receive ruxolitinib. In COMFORT-I, more patients taking ruxolitinib reported a 50% or more improvement in disease-associated symptoms (such as night sweats, itching and abdominal discomfort) than those taking placebo (45.9% vs 5.3%). Similarly in COMFORT-II, more patients taking ruxolitinib reported an improved quality of life and better functioning than those taking best available treatment. In both trials, patients with the V617F mutation seemed to have a better response to ruxolitinib than those without the mutation.

After a median follow-up of 12–14 months, there appeared to be a survival advantage for ruxolitinib over placebo in COMFORT-I (8.4% vs 15.6% of patients had died). However, this was not the case for ruxolitinib over best available treatment in COMFORT-II (7.6% vs 5.6% of patients had died).

Haematological effects with ruxolitinib are common. Anaemia (81.7%), thrombocytopenia (67.4%) and neutropenia (15.3%) were the most frequently reported in the trials. These were generally managed by dose interruption or adjustment but some patients required a blood or platelet transfusion. Three cases of bleeding were fatal in patients receiving ruxolitinib, but only one was attributed to the treatment. The dose should be reduced if platelets fall below 100 x 10^9/L and interrupted if they fall below 50 x 10^9/L.

Overall, infections were common with ruxolitinib and control treatments (38.1% vs 41.7% in COMFORT-I and 63.7% vs 42.5% in COMFORT-II) and were fatal in some cases. Urinary tract infections, herpes zoster, tuberculosis and progressive multifocal leukoencephalopathy[3] have been reported. Ruxolitinib should not be started until serious infections have resolved and patients should be monitored for signs and symptoms of infection.

Diarrhoea[1,2], headache, dizziness, fever and bruising frequently occurred with ruxolitinib, as did hypercholesterolaemia. Elevations in alanine aminotransferase and aspartate aminotransferase were very common during treatment so monitoring of liver function should be considered.

Ruxolitinib is a pregnancy category C drug and is not recommended in pregnancy or lactation. Animal studies found that it crosses the placenta and is excreted in breast milk.

Following oral administration, ruxolitinib is rapidly absorbed with maximum plasma

concentrations reached after an hour. The drug is mainly metabolised by cytochrome P450 (CYP) 3A4 and metabolites are excreted in the urine (74%) and faeces (22%). Its elimination half-life is approximately three hours.

Blood counts should be measured before starting ruxolitinib as the initial dose is determined by the patient's platelet count. Blood monitoring every 2–4 weeks is required to initially titrate the dose (maximum is 25 mg twice daily). A lower starting dose should be used in hepatic impairment, moderate to severe renal impairment (creatinine clearance <60 mL/minute) and in people taking concomitant strong CYP3A4 inhibitors (such as boceprevir, clarithromycin and ketoconazole).

After stopping treatment, myelofibrosis symptoms return to baseline after seven days. Serious withdrawal symptoms have been reported and tapering the dose has been recommended.4

Ruxolitinib reduces spleen volume and disease-associated symptoms in patients with myelofibrosis and offers another option for symptom control. However, its long-term efficacy and tolerability are still to be determined.

REFERENCES:

1. Vertovsek S, Mesa RA, Gotlib J, Levy RS, Gupta V, DiPersio JF, et al. A double-blind, placebo-controlled trial of ruxolitinib for myelofibrosis. N Engl J Med 2012;366:799-807.
2. Harrison C, Kiladjian JJ, Al-Ali HK, Gisslinger H, Waltzman R, Stalbovskaya V, et al. JAK inhibition with ruxolitinib versus best available therapy for myelofibrosis. N Engl J Med 2012;366:787-98.
3. Wathes R, Moule S, Milojkovic D. Progressive multifocal leukoencephalopathy associated with ruxolitinib [letter]. N Engl J Med 2013;369:197-8.
4. Tefferi A, Pardanani A. Serious adverse events during ruxolitinib treatment discontinuation in patients with myelofibrosis. Mayo Clin Proc 2011;86:1188-91.

Ref.: Aust Prescr 2013;36:212-8

(CDSCO has approved Ruxolitinib Tablet for the treatment of patients with polycythemia vera who are resistant to or intolerant of hydroxyl urea on 23.02.2015).

DCGI Launched on line portal- "SUGAM"

This portal is intended for those who desire to file application for various services rendered by CDSCO For security purposes and to avoid spam they have decided that the applicants pre-register themselves on the portal (www.cdscoonline.gov.in). The account will be enabled by the IT team at CDSCO after verification of the information submitted at the time of pre-registration. This is one time process after which the applicant can continuous access subject to the terms and conditions of the web portal. CDSCO has decided that hard copies will be accepted from 15th January 2016 only from those applicants who have registered on the portal. Subsequently, with effect from 15th February 2016 all the registered applicants should submit their application online along with submission of hard copies.

Which drugs are going off-patent in 2016?

This year will be a doozy in terms of drugs going off-patent – undoubtedly a point of contention. Dickson Data put together an excellent infographic that illustrates the various drugs that will be prey for generics makers this year.

Drugs aimed at mitigating heart disease will be most impacted: AstraZeneca cholesterol drug Crestor will be the biggest big pharma blow, as it brings in some $6.4 billion in annual revenue. Other major hits will be Daiichi Sankyo's high blood pressure drug Benicor and Merck's cholesterol drug Zetia.

AstraZeneca, in particular, has been extremely cautious in guarding its patents – for example, it tried to crush potential generic competition from Actavis in a 2013 suit. Apotex has worked to mimic Benicor, and Glenmark has worked on a version of Zetia.

Indeed, it'll be worth watching what AstraZeneca and Merck, in particular, will say at the upcoming conference, in terms of how they'll mitigate these losses this year. But 2016 will represent a shift in market dynamics.

Ref. MedCityNews.com

Union Government launches four mobile health services

Aiming to enhance access and make schemes more cost effective and robust, the government on Friday launched four mobile health services, including M-Cessation which reaches out to those who want to quit tobacco through text messages on mobile phones.

Union Health Minister JP Nadda while launching the four services (m-Health) - Kilkari, Mobile Academy, M-Cessation and TB Missed Call initiative, said that these are part of the government's Digital India programme and are in line with the commitment to prioritise public health.

"The m-Health initiatives launched today will enhance access, make our services cost effective and our systems more robust. We are on our way to realise the vision of our Prime Minister by going digital."

"These four mobile health services will be a game changer in health communication. I am confident that these initiatives will bring us closer to people who need our services the most," Nadda said after launching the services.

The Health Minister said that in keeping with the vision of Digital India based on harnessing technology for the benefit of people, the OPD registration at AIIMS in the national capital has been made online which has resulted in cutting down waiting time of a large section of people from about six hours to nearly one hour.

Under 'Kilkari', which means 'a baby's gurgle', delivery of free and weekly 72 audio messages about pregnancy, child birth and child care will be given directly to mobile phones of the families from the second trimester of pregnancy until the child is one year old.

Kilakri is being launched in Jharkhand, Odisha, Uttar Pradesh, Uttarakhand and High Priority Districts (HPDs) of Madhya Pradesh and Rajasthan in the first phase.

Similarly, Mobile Academy is a free audio training course designed to expand and refresh the knowledge base of Accredited Social Health Activists (ASHAs) and improve their communication skills.

Mobile Academy offers ASHAs a training opportunity via their mobile phones which is both cost-effective and efficient. It reduces the need to travel, sometimes great distances, and provides them the flexibility they need to learn at their own pace and at times they find convenient, an official statement said.

This service is being launched in Jharkhand, Madhya Pradesh, Rajasthan and Uttarakhand.

"M-Cessation aims at reaching out to those willing to quit tobacco use and support them towards successful quitting through text messages sent via mobile phones.

"When offered along with traditional services, M-Cessation has been found to be cost-effective in comparison to traditional options for cessation support. This is first time in the world that such a two-way service is being provided as part of any mHealth initiative," the statement said.

Health Ministry officials said that under the TB Missed Call initiative, a helpline with a toll free number will provide information, counselling and treatment support services for TB.

Under this campaign the callers can give a missed call or call for free to get information related to TB symptoms, treatment services available, address and contact details of the nearest treatment facility amongst others.

Initially, the service will be available to people in Punjab, Haryana, Chandigarh and Delhi.

Nadda also appreciated the efforts of Gates Foundation, UNICEF, USAID and other development partners in complimenting the efforts of the government and invited suggestions from the stakeholders to strengthen the programme further.