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: 10 ***Number: 04*** ***22nd May 2016***

Content

Editorial

A critical survey conducted in USA in 2013, revealed 70% of consumers said they wanting go to a pharmacist for health services if their insurance covered them. Twenty one percent out of these said they would still go to a pharmacist, despite having to pay $75 out of pocket. These percentages suggest that patients would both trust and engage pharmacists for medical care. On a broader context this becomes important, particularly in rural areas where access to physicians is limited. A central point is that pharmacists can play a valuable role working with physicians and other providers to optimize medication therapy, deliver patient-centered care, and assist in managing acute and chronic conditions.

A crucial role a pharmacist can play is, he/she can have a huge influence in improving medication adherence. Medical care costs of people with chronic diseases account for more than 75% of the nation's $2 trillion medical bill. Interestingly almost 50% of people prescribed medications for chronic diseases do not take their medications correctly. Compliance or adherence plays a great role in a patient's management of chronic conditions and providing a value to the cost of medications. This relationship actually costs the United States 300 billion annually in issues involving medication use. The data suggest that the pharmacist can play a critical role in adherence and a systematic review of the adherence literature found that five of six pharmacist-directed interventions in community pharmacies were effective in improving adherence by 7% to 27%.
Currently pharmacists can provide many services to their patients–from information to specific medicines. In fact, the pharmacy is often a first source of medical information for many, since the pharmacists are the first contact point of the patients and medications. Pharmacy services have evolved from strictly dispensing medications to offering services such as medication therapy management, medication education, improving medication adherence, administering immunizations, and promoting health care. In addition, pharmacists can now be found in specialty areas such as oncology, organ transplant and even psychiatry.
This development is gradually transmitting throughout the globe improving scope of pharmacists in health care system. Recently introduced Pharmacy Practice Regulation Act 2015 in India is one of them.

Dr. Subhash C. Mandal
Editor
E mail: subhash.mandaldr@gmail.com
Mob. 9830136291

New Drug: Nintedanib for idiopathic pulmonary fibrosis, non-small cell lung cancer

Approved indication: idiopathic pulmonary fibrosis, non-small cell lung cancer

Ofev 100 mg and 150 mg capsules

Australian Medicines Handbook section 14.2.3

Growth factors contribute to the proliferation of cells in cancers and conditions such as pulmonary fibrosis. This proliferation involves tyrosine kinases such as fibroblast growth factor, vascular endothelial growth factor and platelet-derived growth factor. Nintedanib inhibits these growth factors by binding to their receptors intracellularly. This disrupts the signalling needed for cell proliferation.

Nintedanib capsules are taken twice daily with food. There is extensive first-pass metabolism so the bioavailability is under 5%. The drug is also mainly cleared by metabolism with most of the metabolites being excreted in the faeces. The terminal half-life is 10–15 hours. As nintedanib is a substrate of P-glycoprotein, inducers of this transporter, such as phenytoin and St John's wort, will reduce the concentration of nintedanib. Its plasma concentration will be increased by inhibitors of P-glycoprotein such as ketoconazole.

Idiopathic pulmonary fibrosis

Idiopathic pulmonary fibrosis is one of the interstitial lung diseases. A proliferation of fibroblasts leads to progressive breathlessness. The median survival is 3–5 years.

The main clinical trials of nintedanib in pulmonary fibrosis were INPULSIS-1 and -2.1 In these trials a total of 638 patients were randomised to take 150 mg nintedanib twice daily for 52 weeks and 423 were given a placebo. These patients all had a forced vital capacity (FVC) that was at least 50% of the predicted value. In INPULSIS-1 the FVC fell by 239.9 mL/year with placebo and by 114.7 mL/year with nintedanib. The respective figures in INPULSIS-2 were reductions of 207.3 mL/year and 113.6 mL/year. The smaller decline in lung function with nintedanib was statistically significant.

In INPULSIS-1, 21% of the patients had to discontinue nintedanib because of adverse events. In both trials more than 60% of the patients taking nintedanib developed diarrhoea compared with about 18% of the placebo group. Other adverse events that were more common with nintedanib than with placebo included nausea, vomiting, weight loss and elevated liver enzymes.1

Lung cancer

The inhibition of growth factors by nintedanib has been studied in patients with non-small cell lung cancer of different histological types. The LUME-Lung 1 trial involved 1314 patients with locally advanced, metastatic or recurrent disease that had not responded to first-line chemotherapy. All the patients were given an infusion of docetaxel every 21 days and 652 also took 200 mg nintedanib twice daily on days 2–21 of the cycle. The median duration of treatment was 2.8 months with docetaxel alone and 3.4 months with the combination. After a median follow-up of 7.1 months, progression-free survival was 2.7 months in the control group and 3.4 months in the combination group. This difference is statistically significant.2

Adverse events led to 21.7% of the patients taking docetaxel and 22.7% of those taking docetaxel and nintedanib withdrawing from the trial. Deaths from adverse events were more frequent with the combination treatment. Nausea, vomiting, diarrhoea, altered liver function and febrile neutropenia were also more frequent.2

Precautions

The adverse effects of nintedanib may require treatment to be interrupted or reduced. Blood counts and liver function should be regularly monitored. Nintedanib is not recommended for patients with moderate or severe liver disease. In addition to the common adverse effects, there may also be an increased risk of

gastrointestinal perforation, impaired wound healing, bleeding and thromboembolism. Although patients with a history of myocardial infarction or stroke were excluded from the INPULSIS trials, myocardial infarctions were more frequent with nintedanib than placebo (1.6 vs 0.5%).

Conclusion

Idiopathic pulmonary fibrosis has a poor prognosis, so reducing the decline in lung function is a benefit. However, in a pooled analysis of the INPULSIS trials, nintedanib had no significant advantage over placebo in preventing acute exacerbations in pulmonary fibrosis or in health-related quality of life.1

In non-small cell lung cancer adding nintedanib to docetaxel increases progression-free survival, but the median overall survival is not significantly increased unless the cancer is an adenocarcinoma. The median overall survival for patients with an adenocarcinoma given the combination was 12.6 months compared with 10.3 months for patients treated with docetaxel alone. Pemetrexed is another drug that can be used to treat non-small cell lung cancer. In March 2015 the Pharmaceutical Benefits Advisory Committee concluded that an indirect comparison did not show that the effectiveness of nintedanib and docetaxel was non-inferior to pemetrexed.3

REFERENCES:

1. Richeldi L, du Bois RM, Raghu G, Azuma A, Brown KK, Costabel U, et al.; INPULSIS Trial Investigators. Efficacy and safety of nintedanib in idiopathic pulmonary fibrosis. N Engl J Med 2014;370:2071-82. http://dx.doi.org/10.1056/NEJMoa1402584
2. Reck M, Kaiser R, Mellemgaard A, Douillard JY, Orlov S, Krzakowski M, et al.; LUME-Lung 1 Study Group. Docetaxel plus nintedanib versus docetaxel plus placebo in patients with previously treated non-small-cell lung cancer (LUME-Lung 1): a phase 3, double-blind, randomised controlled trial. Lancet Oncol 2014;15:143-55. http://dx.doi.org/10.1016/ S1470-2045(13)70586-2
3. Pharmaceutical Benefits Advisory Committee. Public Summary Document – March 2015 PBAC meeting. Nintedanib, 100 mg capsule, 60; 150 mg capsule, 60; Ofev®. Canberra: Australian Government Department of Health; 2015.www.pbs.gov.au/info/industry/listing/elements/pbac meetings/psd/2015-03/nintedanib-caps-ofev-psd1-2015-03 [cited 2016 Feb 12]

Ref.: Aust Prescr 2016;39:62-3 | 22 February 2016

Status in India:

Nintedanib soft Gelatin Capsule 100/150mg has been approved by CDSCO for the treatment of Idiopathic Pulmonary Fibrosis (IPF) on 11.03.2016.

Instruction of DCGI regarding 344 FDCs prohibited by the Government of India

DCGI instructed all State & UT Drugs Controllers to take necessary action as per the order of the Delhi High court dated 04.04.2016 & 28.04.2016 regarding 344 FDCs prohibited by the Central Government. Details are available at-www.http://cdsco.nic.in/writereaddata/fdccourtcase17_5_2016.pdf

India begins historical documentation of sickle cell disease

The Indian Council of Medical Research, collaborating with the National Institute of Immunohaematology, has begun gathering blood samples from tribal populations to learn more about sickle cell disease, which is endemic among many tribes in India. Researchers have partnered with a nongovernmental organization to collect dry blood samples

from 8,517 newborn babies, of whom 1,341 had sickle traits and 104 exhibited sickle cell disease.
Ref.: Business Standard (India)

Dr Reddy's recalls anti-nausea medication in US

Dr Reddy's is voluntarily recalling 50,280 bottles of 4-milligram tablets of Ondansetron due to impurities and stability issues, according to a US FDA enforcement report. The drug is used to treat nausea and vomiting following chemotherapy and other treatments.
Ref.: The Economic Times (India)

Early-stage trial finds malaria vaccine provides year-long protection

Researchers from the National Institute of Allergy and Infectious Diseases' Vaccine Research Center found that the PfSPZ vaccine, when given in multiple doses, was able to protect 55% of trial participants against malaria for a year, according to a study in the journal Nature Medicine. Scientists also found that administration of the vaccine intravenously was more effective than intramuscular injection.
Ref.: Medical News Today

Government's patent grant to Gilead challenged in Delhi High Court

The Initiative for Medicines, Access & Knowledge and the DELHI Network of Positive People filed an appeal with the Delhi High Court against the patent awarded by the government to Gilead's hepatitis C drug Sovaldi, saying the firm's patent claims were "unmerited" because the base compound for the drug had already been developed and used in other medications. The groups argue the government disregarded key patent policy and judicial precedents and failed to examine evidence for granting the patent, and that the patent was against public interest.
Ref.: The Economic Times (India)

Forthcoming Event:

WHA69 side event on snakebite outcomes: Challenges & solutions

Every year, snakebite kills 125,000 people around the world and gravely injures 2.7 million more. For the first time at a World Health Assembly (WHA) side event, leading venom and snakebite experts, government representatives and medicine policy experts will discuss global challenges, initiatives and strategies to reduce death and disability from snakebite envenoming—one of the world's most tragic and neglected tropical diseases. Delegates and journalists attending the WHA69 are very welcome to attend. Interpretation will be available in English, Spanish and French.
Refreshments will be served.
Date: Wednesday, 25 May, 2016
Time: 18.00–19.30
Location: World Health Assembly Room VII (7), Palais des Nations Geneva, Switzerland
Panellists are as follows:

David Reddy, CEO, Medicines for Malaria Venture
Christopher Elias, President, Global Development Program, Bill and Melinda Gates Foundation
Herbert Barnard, Director, International Affairs, Ministry of Health, Government of The Netherlands
Suerie Moon, Co-director, Project on Innovation and Access to Technologies for Sustainable Development, Harvard Kennedy School of Public Health
The event will be moderated by Dr Anban Pillay, Deputy Director General, Health Regulation and Compliance, National Department of Health, Government of South Africa.

For more information, please go to http://haiweb.org/what-we-do/global-snakebite-initiative/wha-69-member-state-side-event-snakebite/