Drug Information Bulletin

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&
Regulatory Affairs Division (RAD), IPA

10th Year

Content

Editorial

Recent non availability of Penicillamine in several parts of the country has made concerns among the doctors and the patients, who need this drug urgently.

D-Penicillamine is a medication of chelator group, used for the treatment of Wilson's disease, crystinuria, scleroderma. It is also used as a disease-modifying antirheumatic drug (DMARD) to treat severe active rheumatoid arthritis in patients who have failed to respond to an adequate trial of conventional therapy. For the treatment of Wilson's disease, Penicillamine binds to copper and helps it to be removed from the body. Decreasing copper levels helps to improve liver function.

It is on the World Health Organization's List of Essential Medicines, the most important medication needed in a basic health system. This drug is also included in the National Essential Medicines List of our country. The price of these drugs is under control as per the Drugs Price Control Order in India.

Recently this drug is not easily available in different parts of our country, resulting in severe consequences for those who needed it.

Presently a handful of manufacturers are manufacturing these products in India. Reasons for non availability of these drugs are yet to be confirmed, but experts are of the opinion that due to less volume requirement and low profit margin of the drug, the manufacturers may not be interested to manufacture these essential drugs.

Some experts opined that supply of this essential medicine could be streamlined by ensuring manufacture by the existing manufacturers enforcing the existing legislation and the other option may be manufacturing this essential drug by existing Government undertakings.

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New Drug: Everolimus

Prescribing information of Afinitor (Brand of Everolimus)

Indications and Usage: Advanced Hormone Receptor-Positive, HER2- Negative Breast Cancer (1.1), Dosage and Administration (2.1, 2.2), Warnings and Precautions (5.1, 5.3, 5.5, 5.10) 07/2012 Indications and Usage (1.4, 1.5), Dosage and Administration (2.1, 2.2), Warnings and Precautions (5.1, 5.3, 5.8) 04/2012 Dosage and Administration (2.2, 2.4), Warnings and Precautions (5.7, 5.8) 03/2012

INDICATIONS AND USAGE: AFINITOR is a kinase inhibitor indicated for the treatment of: • postmenopausal women with advanced hormone receptor-positive, HER2- negative breast cancer (advanced HR+ BC) in combination with exemestane after failure of treatment with letrozole or anastrozole. (1.1) • adults with progressive neuroendocrine tumors of pancreatic origin (PNET) that is unresectable, locally advanced or metastatic. The safety and effectiveness of AFINITOR in the treatment of patients with carcinoid tumors have not been established. (1.2) • adults with advanced renal cell carcinoma (RCC) after failure of treatment with sunitinib or sorafenib. (1.3) • adults with renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery. The effectiveness of AFINITOR in treatment of renal angiomyolipoma is based on an analysis of durable objective responses in patients treated for a median of 8.3 months. Further follow-up of patients is required to determine long-term outcomes. (1.4) • adults and children ≥ 3 years of age with subependymal giant cell astrocytoma (SEGA) associated with tuberous sclerosis (TSC) who require therapeutic intervention but are not candidates for curative surgical resection. The effectiveness of AFINITOR is based on an analysis of change in SEGA volume. Clinical benefit such as improvement in diseaserelated symptoms or increase in overall survival has not been demonstrated. (1.5)

DOSAGE AND ADMINISTRATION: Advanced HR+ BC, advanced PNET, advanced RCC, or renal angiomyolipoma with TSC: • 10 mg once daily with or without food. (2.1) • For patients with hepatic impairment, reduce the AFINITOR dose. (2.2) • If moderate inhibitors of CYP3A4 and/or P-glycoprotein (PgP) are required, reduce the AFINITOR dose to 2.5 mg once daily; if tolerated, consider increasing to 5 mg once daily. (2.2) • If strong inducers of CYP3A4 are required, increase AFINITOR dose in 5 mg increments to a maximum of 20 mg once daily. (2.2) SEGA: • Initial dose based on body surface area with subsequent titration to attain trough concentrations of 5-10 ng/mL. (2.3) • If moderate inhibitors of CYP3A4 and/or PgP are required, reduce the AFINITOR dose by approximately 50%. Subsequent dosing should be based on therapeutic drug monitoring (TDM). (2.4) • If strong inducers of CYP3A4 are required, double the AFINITOR dose. Subsequent dosing should be based on TDM. (2.4) Dose reduction or treatment interruption may be needed to manage adverse drug reactions. (2.2, 2.4)

DOSAGE FORMS AND STRENGTHS: 2.5 mg, 5 mg, 7.5 mg, and 10 mg tablets with no score (3)

CONTRAINDICATIONS: Hypersensitivity to everolimus, to other rapamycin derivatives, or to any of the excipients (4)

WARNINGS AND PRECAUTIONS: • Non-infectious pneumonitis: Monitor for clinical symptoms or radiological changes; fatal cases have occurred. Manage by dose reduction or discontinuation until symptoms resolve, and consider use of corticosteroids. (5.1) • Infections: Increased risk of infections, some fatal. Monitor for signs and symptoms, and treat promptly. (5.2) • Oral ulceration: Mouth ulcers, stomatitis, and oral mucositis are common. Management includes mouthwashes (without alcohol or peroxide) and topical treatments. (5.3) • Renal failure: Cases of renal failure (including acute renal failure), some with a fatal outcome, have been observed in patients treated with AFINITOR. (5.4) • Laboratory test alterations:

Elevations of serum creatinine, blood glucose, and lipids may occur. Decreases in hemoglobin, neutrophils, and platelets may also occur. Monitor renal function, blood glucose, lipids, and hematologic parameters prior to treatment and periodically thereafter. (5.6) • Vaccinations: Avoid live vaccines and close contact with those who have received live vaccines. (5.9) • Embryo-fetal toxicity: Fetal harm can occur when administered to a pregnant woman. Apprise women of potential harm to the fetus. (5.10, 8.1)

ADVERSE REACTIONS: Advanced HR+ BC, Advanced PNET, Advanced RCC: Most common adverse reactions (incidence ≥30%) include stomatitis, infections, rash, fatigue, diarrhea, edema, abdominal pain, nausea, fever, asthenia, cough, headache and decreased appetite. (6.1, 6.2, 6.3) Renal angiomyolipoma with TSC: Most common adverse reaction (incidence ≥ 30%) is stomatitis. (6.4) SEGA: Most common adverse reactions (incidence ≥ 30%) are stomatitis, upper respiratory tract infection, sinusitis, otitis media, and pyrexia. (6.5) To report SUSPECTED ADVERSE REACTIONS, contact Novartis Pharmaceuticals Corporation at 1-888-669-6682 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS: • Strong CYP3A4 inhibitors: Avoid concomitant use. (2.2, 2.4, 5.7, 7.1) • Moderate CYP3A4 and/or PgP inhibitors: If combination is required, use caution and reduce dose of AFINITOR. (2.2, 2.4, 5.7, 7.1) • Strong CYP3A4 inducers: Avoid concomitant use. If combination cannot be avoided, increase dose of AFINITOR. (2,2, 2.4, 5.7, 7.2)

USE IN SPECIFIC POPULATIONS: • Nursing mothers: Discontinue drug or nursing, taking into consideration the importance of drug to the mother. (8.3) • Hepatic impairment: For advanced HR+ BC, advanced PNET, advanced RCC, and renal angiomyolipoma with TSC patients with hepatic impairment, reduce AFINITOR dose. For SEGA patients with Child-Pugh class A or Child-Pugh class B hepatic impairment, adjustment to the starting dose may not be needed; however, subsequent dosing should be based on TDM. AFINITOR should not be used in SEGA patients with Child-Pugh class C hepatic impairment. (2.2, 2.4, 5.8, 8.7) See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling Revised: 07/2012.

For details: http://www.accessdata.fda.gov/drugsatfda_docs/label/2012/022334s016lbl.pdf

Indian status:

Everolimus tablets 2.5mg. 5mg and 10 mg has been approved by CDSCO on 08.06.2016 with an indication "Treatments of adults patients with progressive, well differentiated, non-functional neuroendrocrine tumors (NET) of gastrointestinal (GT) or lungs origin with unresectable, locally advanced or metastatic disease"

With Condition:

1. "Warning: To be sold by retail on the prescription of Oncologist only."

Delhi Government caps Chikungunya test cost

After a cap on cost of dengue test last month, Delhi government today announced a similar ceiling for chikungunya, even as the city continues to grapple with rising cases of the two vector-borne diseases.

The government in a statement said, it has decided to cap the price for "chikungunya serology IgM at Rs 600 and for RT PCR for chikungunya at Rs 1,500".

It also warned private hospitals and laboratories and nursing homes against overcharging.

With spurt in dengue cases, Delhi government last month capped at Rs 600 the cost of test to diagnose the vector-borne disease and Rs 50 for ascertaining the platelet count in private hospitals in the national capital.

"This is continuation of the previous office order... wherein ceiling price has been fixed in all private sector at Rs 600 for each NS1-Ag (ELISA based) and MAC ELISA test for antibodies and Rs 50 for platelets," the statement said.

Last year also, the AAP government had capped the dengue test charges following complaints that many private hospitals and

laboratories were overcharging, sensing an opportunity to make profit.

Chikungunya cases in Delhi have shot up to 432 a massive rise in the figure released by civic authorities, who had reported just 20 cases till last week.

For details:
http://economictimes.indiatimes.com/industry/healthcare/biotech/healthcare/delhi-govt-caps-chikungunya-test-cost/articleshow/53933971.cms

3 Drugs identified to potentially fight Zika virus

Three already existing drugs may offer pregnant women and their developing fetuses protection against the damaging effects of Zika virus, a new multicenter study reports.

Researchers identified these three potential Zika treatments in the laboratory by screening 6,000 different compounds that included already-approved drugs and clinical trial drug candidates.

"We specifically in this screen tried to take advantage of compounds that are already FDA-approved or in some stage of clinical development," said study co-author Emily Lee. She's a graduate student of molecular biology at Florida State University in Tallahassee.

One of the drugs, sold as Niclosamide, is already on the market as a treatment for tapeworm. But it appears to also have antiviral properties that inhibit Zika from replicating, the researchers reported.

Another antiviral drug potentially effective against Zika is PHA-690509. This is a medication that is currently in development that works by interfering with gene expression, the study authors said.

And finally, investigators identified a third medication awaiting U.S. Food and Drug Administration approval that doesn't directly viral damage. The drug, Emricasan, inhibits a natural process that causes programmed cell death.

For details: Healthday

Forthcoming Events:

National workshop on "Ensuring Data Integrity: Need of the hour in Pharma Industry"
18th September 2016
Organized Jointly by:
Indian Pharmaceutical Association, Bengal Branch &
Regulatory Affairs Division (RAD), IPA
Venue:
Floatel, Kolkata
For Registration contact:
9433202089 & 9830136291

Celebration of "Pharmacists Day"
25th September 2016
Organizer: IPA, Bengal Branch

- **Health Camps on detection & counseling on Diabetes at different Metro Railway Stations**
- **Seminar jointly with PAWB at R.G.Kar Medical College & Hospital, Kolkata**

3rd Convention: SFE India
National Seminar on "Analytical Techniques for Drug Discovery & Development from Natural Products"
24th September 2016
Organized by:
School of Natural Product Studies, JU
In association with-
Society for Ethnopharmacology, India
Venue:
K.P.Basu Memorial Hall, Jadavpur University, Kolkata
For Details:
www.jaduniv.edu.in;
www.ethnopharmacology.in