Drug Information Bulletin

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Regulatory Affairs Division (RAD), IPA

World Hemophilia Day 17th April 2019

Volume: 13 ***Number: 02*** ***21st April 2019***

Content

Editorial

Presently more than 250 Adverse Drug Monitoring Centers (AMC) are collecting ADR data regularly and collected about 3 lacks of ADR under the Pharmacovigilance Programme of India (PvPI). PvPI is now contributing considerable amount of ADR data to the Uppsala Monitoring Centers (UMC)-a WHO collaborating centre.

3rd version of Pharmacovigilance system in India started in the year of 2010 operating from Indian Pharmacopoeia Commission (IPC) and growing with a steady pace. In order to collect the data from specialized areas two more wings have been developed, which are Haemovigilance Programme (HvPI) and Materiovigilance Programme (MvPI). Haemovigilance Programme (MvPI) started since 10th Dec. 2012 in collaboration with National Institute of Biologicals (NIB) and Materiovigilance programme started since 6th July 2015, Indian Pharmacopoeia Commission (IPC) as National Coordinating Centre & Sree Chitra Tirunal Institute of Medical Sciences & Technology (SCTIMST) will be function as National Collaborating Centre.

Now Adverse Events Following Immunization (AEFI) is also integrated with PvPI. PvPI, CDSCO and Pharmaceutical Industries working to Harmonize PSUR reporting.

AMCs have also started in focused therapeutic areas like Anti-tubercular drugs. ADRs are being collected from six centers spread over the country on newly introduced anti-tubercular Drug-Bedaquiline.

PvPI is also collaborating with Medical Council of India (MCI), Indian Medical Association (IMA) and some other organizations for more intensive Pharmacovigilance. It is felt by the experts that the system is working well and will serve the society continuously.

Recently DCGI instructed all manufacturers of seven drugs like-Ofloxacin, Cefotaxime injection, Cefixime, Sulfasalazine, Sodium Valproate, Tranexamine acid, Quetiapine to mention ADRs in the Package inserts. This action is one of the outcome of the PvPI.

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New Drug: Fingolimod hydrochloride

Gilenya (Novartis) 0.5 mg capsules

Approved indication: multiple sclerosis

Multiple sclerosis is thought to be an autoimmune disease. Some patients have therefore been treated with drugs such as glatiramer, interferon and natalizumab. A problem with these drugs is that they have to be injected. Fingolimod is an oral immunomodulator which has been approved for the treatment of relapsing–remitting multiple sclerosis, and secondary progressive multiple sclerosis with superimposed relapses. Patients take fingolimod once a day. It is metabolised to its active form, fingolimod phosphate. This reduces the release of lymphocytes from lymphoid tissues which may prevent the cells from attacking the myelin sheaths of the nervous system. Fingolimod is eliminated by metabolism with most of the metabolites being excreted in the urine. The terminal half-life is 6–9 days so it takes several weeks for a steady state to be reached. In a phase II study, 281 patients with relapsing multiple sclerosis were randomised to take fingolimod 1.25 mg, 5 mg or placebo. After six months the mean cumulative number of lesions seen on MRI was 8.4, 5.7 and 14.8 respectively. The volume of the lesions was also significantly less in the patients given fingolimod. Although the study lacked the statistical power to confirm a treatment effect, there were more patients in the fingolimod group who were free of relapses than there were in the placebo group.1 The patients who completed the study could continue treatment. Those who had taken placebo were randomised to one of the fingolimod groups. After a further six months the number of lesions seen in the patients who had switched from placebo reduced, and remained low in those who continued fingolimod. At 12 months 65–67% of those who switched were free of relapse compared with 79% of those who took fingolimod continuously.1 A total of 189 patients completed a further extension of the study. After 24 months the number of lesions seen on MRI remained low. Between 12 months and 24 months the mean number of new lesions was less than one in all groups. Most (75–77%) of the patients who had been treated continuously remained relapse free.2 A larger placebo-controlled trial studied the effect of fingolimod 0.5 mg or 1.25 mg on disability and the rate of relapse. After 24 months, the annualised relapse rate was 0.16 in the 429 patients taking 1.25 mg, 0.18 in those taking 0.5 mg and 0.4 in those taking placebo. Approximately 70–75% of the fingolimod groups were relapse free for two years compared with 46% of the placebo group. The patients' disabilities did not progress in 82–83% of the fingolimod groups and 76% of the placebo group. These differences and the changes seen on MRI were statistically significant.3 Adverse events are more frequent with higher doses of fingolimod. In the large placebo-controlled trial 14.2% of patients taking 1.25 mg discontinued treatment because of adverse events compared with 7.5% of the 0.5 mg group and 7.7% of the placebo group.3 As fingolimod reduces the peripheral lymphocyte count there is a potential increased risk of infection. The overall rate of infection is similar, but in one study lower respiratory tract infections were more common with fingolimod than with placebo.3 As fingolimod is slowly excreted, it may take up to two months for lymphocyte counts to return to normal. The patient's immunity to organisms such as varicella should be checked before treatment begins. Liver function should also be checked as it is more frequently altered by fingolimod than by placebo.3 The risk of adverse reactions may be greater in patients with hepatic impairment. Blood pressure should be monitored as hypertension can occur during treatment. Fingolimod also reduces the heart rate and can cause atrioventricular block.3 Patients need to be observed for six hours after taking the first dose. Macular oedema may occur so patients also need ophthalmological assessments.3 To help establish its place in therapy, oral fingolimod has been compared to intramuscular interferon beta-1a. A total of 1292 patients with relapsing-remitting multiple sclerosis were randomised to receive daily fingolimod 0.5 mg or 1.25 mg, or weekly injections of interferon 30 microgram. After a year the rate of relapse was significantly lower in the fingolimod groups. Approximately 80–83% of these patients had no relapse compared with 69% of the interferon group. Although there were fewer new or enlarged lesions seen on MRI with

fingolimod, there were no significant differences from interferon in the time to progression of disability. Fingolimod 1.25 mg and interferon had similar rates of adverse events, but fewer of the patients taking interferon discontinued treatments. The rates of infection were similar, but atrioventricular block and macular oedema only occurred in patients taking fingolimod. Skin cancers and hypertension were also more frequently found in the fingolimod groups.4 Fingolimod appears to have greater efficacy than interferon over a year, but multiple sclerosis is a long-term disease. Postmarketing studies will be needed to assess not only effectiveness, but also the emergence of any long-term adverse effects. manufacturer provided the product information

References

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Source: Australian Prescriber

Status in India:

Fingolimod Capsules 0.5mg and Fingolimod hydrochloridebulk approved by CDSCO on 25.03.2019 for the treatment of patients with relapsing forms of multiple sclerosis (MS) to reduce the frequency of clinical exacerbations and to delay the accumulation of physical disability.

Hemophilia a treatment drug launched recently in India

Drug firm Roche Wednesday said it has launched Emicizumab under the brand name Hemlibra in India for preventive treatment of Hemophilia A, an inherited disorder in which a person's blood does not clot properly. Hemlibra is the first weekly subcutaneous prophylaxis injection shown to prevent or reduce the frequency of bleeding episodes and improve the quality of life, Roche said in a statement.

All current prophylactic treatment options for people with Hemophilia A with factor VIII inhibitors require intravenous infusions several times a week, it added.

"The introduction of Emicizumab (Hemlibra) is a significant milestone in the treatment of Hemophilia A in India and reaffirms our commitment to bring Roche's ground breaking medicines to patients in India as early as possible," Roche PharmaIndia's Chief Purpose Officer Lara Bezerra said.

This breakthrough medicine represents a completely new way to manage Hemophilia A and redefines the standard of care, she added.

The company, however, did not disclose the price at which it would be selling the drug in the country.

Hemlibra is approved by multiple regulatory authorities across the world and is now also approved and available in India, the statement said.

Source: Healthworld

Drugs Controller General of India directed all manufacturers of the following drugs to mention ADR in the Package inserts

Sl. No.	Name of the Drug	ADRs
1	Ofloxacin	Stevens- Johnson Syndrome, Toxic epidermal necrolysis
2	Cefotaxime Injection	Angioedema
3	Cefixime	Acute generalized exanthematous pustulosis
4	Sulfasalazine	DRESS Syndrome
5	Sodium Valproate	Gum hyperplasia
6	Tranexamic acid	Seizure
7	Quetiapine	Urinary incontinence

Many essential drugs priced much higher than manufacturing cost

Around 40% of the essential medicines in India with lowest MRP are priced significantly higher than estimated production costs, an assessment by the World Health Organisation (WHO) shows highlighting the "exorbitant" profiteering by pharmaceutical companies and the scope for lowering prices of drugs.

While innovative and newer drugs for cancer, hepatitis C and rare diseases are out of reach of many due to their unaffordable prices, even off patent drugs which are in the market for long and commonly used for diseases like HIV, tuberculosis and malaria are priced very high with huge margins over their cost of production.

This results in high expenditure pushing people into poverty. In India over 75% of health expenditure is out-of-pocket, of which the major chunk is spent on medicines. This is despite India being a manufacturing hub and the biggest supplier of low cost generic medicines to the world.

The study shows while Indian prices were below WHO's estimated generic pri- ce in many cases, they were mostly government tender prices, which are likely to be significantly lower than the private market prices more often experienced by those needing medicines in India.

Moreover, most of the high-priced medicines in India were found only in the private market, suggesting a lack of availability in public facilities, the study said.

Findings of the report were discussed by the global health community at an international forum hosted by the UN agency on fair pricing and access to medicines last week in Johannesburg.

For details: IndianPharma.in

Nearly half of the asthma patient not taking inhaler correctly

A recent study in US finds that preponderance number of asthma patients demonstrated improper inhaler use. This means they consistently were not taking in the full dose of medication.

The details were published in the Journal of Hospital Medicine.

These critical errors have been found common in children - the group which remains at highest risk for complications and death from asthma. They also often skipped using a spacer. A device that is recommended for use with an inhaler to help the right amount of asthma medication reaches the lungs.

"We know that asthma can be well managed in the majority of patients and using your inhaler correctly is key factor to managing asthma. Improper inhaler technique can contribute to children having uncontrolled asthma and needing to come to the hospital for their asthma. Our study suggests that as healthcare providers we can do a better job showing patients and families the correct inhaler and spacer technique, and checking it frequently to ensure they master it.," says lead author Waheeda Samady.

Out of 113 study participants, 42 percent missed at least one critical step in their inhaler technique. Researchers found that 18 percent did not use a spacer device with their inhaler and that these patients were mostly older.

For details: Journal of Hospital Medicine

Forthcoming Event

ISPOR Annual Meeting 2019

May 18-22, 2019 | New Orleans, LA, USA

Theme: Rapid. Disruptive. Innovative: A New Era in HEOR

For details:https://www.ispor.org/conferences-education/conferences/upcoming-conferences/ispor-2019/about