Drug Information Bulletin

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Content

Editorial

Pharmacovigilance Programme of India (PvPI) has taken a mature shape with more than 200 Adverse Drug Monitoring Centers (AMC) are collecting ADR data regularly and collected about 1.4 lacks of ADR . PvPI is now contributing considerable amount of ADR data to the Uppsala Monitoring Centers (UMC)-a WHO collaborating centre and CDSCO. Recently PvPI has circulated a list of 24 ADRs requesting all concerned to be more vigilant about the drug-ADR combinations mentioned below and report them on priority basis to NCC-PvPI.

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 pharmaceutical industries for more intensive Pharmacovigilance. It is felt by the experts that the system is working well and will serve the society continuously. On the basis of ADR identified by PvPI, DCGI has taken some steps.

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Deflazacort Tablet and Oral suspension has been approved by USFDA recently for the treatment of Duchenne muscular dystrophy (DMD) in patients 5 years of age and older

HIGHLIGHTS OF PRESCRIBING INFORMATION
INDICATIONS AND USAGE:
EMFLAZA is a corticosteroid indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients 5 years of age and older (1)
DOSAGE AND ADMINISTRATION: The recommended once-daily dosage is approximately 0.9 mg/kg/day• administered orally (2.1) Discontinue gradually when administered for more than a few days (2.2)
DOSAGE FORMS AND STRENGTHS: Tablets: 6 mg, 18 mg, 30 mg, and 36 mg (3)• Oral Suspension: 22.75 mg/mL (3)
CONTRAINDICATIONS: Hypersensitivity to deflazacort or any of the inactive ingredients in EMFLAZA (4) -WARNINGS AND PRECAUTIONS: • Alterations in Endocrine Function: Hypothalamic-pituitary-adrenal axis suppression, Cushing's syndrome, and hyperglycemia can occur; Monitor patients for these conditions with chronic use of EMFLAZA (2.2, 5.1) • Immunosuppression and Increased Risk of Infection: Increased risk of new, exacerbation, dissemination, or reactivation of latent infections, which can be severe and at times fatal; Signs and symptoms of infection may be masked (5.2) Alterations in Cardiovascular/Renal Function: Monitor for elevated blood• pressure and sodium, and for decreased potassium levels (5.3) Gastrointestinal Perforation: Increased risk in patients with certain GI• disorders; Signs and symptoms may be masked (5.4) Behavioral and Mood Disturbances: May include euphoria, insomnia,• mood swings, personality changes, severe depression, and psychosis (5.5) Effects on Bones: Monitor for decreases in bone mineral density with• chronic use of EMFLAZA (5.6) • Ophthalmic Effects: May include cataracts, infections, and glaucoma; Monitor intraocular pressure if EMFLAZA is continued for more than 6 weeks (5.7) Vaccination: Do not administer live or live attenuated vaccines to patients• receiving immunosuppressive doses of corticosteroids (5.8) Serious Skin Rashes: Discontinue at the first sign of rash, unless the rash is• clearly not drug related (5.9)
ADVERSE REACTIONS: The most common adverse reactions (≥ 10% for EMFLAZA and greater than placebo) are Cushingoid appearance, weight increased, increased appetite, upper respiratory tract infection, cough, pollakiuria, hirsutism, central obesity, and nasopharyngitis (6.1)
DRUG INTERACTIONS: Moderate or strong CYP3A4 inhibitors: Give one third of the• recommended dosage of EMFLAZA (7.1) Avoid use of moderate or strong CYP3A4 inducers with EMFLAZA, as• they may reduce efficacy (7.1) To report SUSPECTED ADVERSE REACTIONS, contact Marathon Pharmaceuticals, LLC at 1-866-562-4620 or DrugSafety@propharmagroup.com or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. See 17 for PATIENT COUNSELING INFORMATION and FDAapproved patient labeling. Revised: 02/2017.
For details:
https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208684s000,208685s000lbl.pdf

Fluoroquinolones Potential risk of persistent and disabling side effects

Health Canada has recommended updating the safety information for all fluoroquinolone products to include information about the risk of persistent and disabling side effects including tendonitis/tendinopathy, peripheral neuropathy and central nervous system disorders. Fluoroquinolones (ciprofloxacin, levofloxacin, moxifloxacin, norfloxacin and ofloxacin) are antibiotics which are authorized to treat many types of bacterial infections including urinary tract and respiratory infections. Health Canada started a safety review following a review done by

the US FDA on systemic fluoroquinolone drugs. The Health Canada safety review focussed on serious known side effects that included: tendonitis/tendinopathy, peripheral neuropathy, worsening of myasthenia gravis, hypersensitivity and serious skin reactions, mental disorders, depression and suicide/self-injury, convulsions, cardiovascular disorders, phototoxicity and vision disorders. At the time of the review, Health Canada identified 115 reports of persistent and disabling side effects associated with the use of fluoroquinolones. In 78 of these reports, a probable (29 reports) or possible (49 reports) causal link could bemade between the use of fluoroquinolones and persistent disability. In the remaining cases, there was either not enough information available or it was unlikely that the reports of persistent disability were related to the use of fluoroquinolones. Most of the side effects that were reported in the 115 reports and linked to persistent disability included tendonitis/ tendinopathy, peripheral neuropathy and central nervous system disorders. The side effects of tendinopathy, peripheral neuropathy and central nervous system disorders are included in the current safety information. However, the possibility of persistent duration of these events was not included in the safety information for all fluoroquinolone products. There was little information in the scientific and medical literature on persistent and disabling nature of side effects reported with fluoroquinolone use. Health Canada's review concluded that some of the known side effects, specifically tendonitis/tendinopathy, peripheral neuropathy and central nervous system disorders, already linked to the use of fluoroquinolones, may be persistent and/or disabling.

Reference: Summary Safety Review, Health Canada, 23 January 2017 (www.hc-sc.gc.ca) (See WHO Pharmaceuticals Newsletters No.5, 2016: Disabling and potentially permanent adverse effects of the tendons, muscles, joints, nerves, and central nervous system in the US and No.3, 2016: Restricting use in the US)

Furosemide Risk of dermatitis lichenoid

The Pharmacovigilance Program of India-Indian Pharmacopoeia Commission (PvPI-IPC) has recommended that the Central Drugs Standard Control Organisation(CDSCO) revise the drug safety label of furosemide to include dermatitis lichenoid as potential adverse drug reaction. Furosemide is a diuretic used to treat oedema and mild to moderate hypertension. Between 2011 and November 2016, the PvPI received four furosemide-dermatitis lichenoid ICSRs. The cases were reviewed by the Signal Review Panel (SRP)-PvPI-IPC and it was concluded that there was a strong causal relationship between furosemide and dermatitis lichenoid in these cases. The PvPI-IPC has reminded health-care professionals that dermatitis lichenoid is a potential adverse drug reaction with furosemide use. Reference: Based on the communication from IPC, NCC-PvPI, India (www.ipc.gov.in)

Itraconazole Risk of acute generalized exanthematous pustulosis

The PvPI-IPC has recommended that the CDSCO revise the drug safety label of itraconazole to include acute generalized exanthematous pustulosis as a potential adverse drug reaction. Itraconazole is used for systemic infections of aspergillosis and candidosis, cryptococcosis, histoplasmosis, sportrichosis, paracoccidioidomycossis, blastomycosis and other rare systemic or tropical mycosis. Between 2011 and November 2016, PvPI received two itraconazole-acute generalized exanthematous pustulosis ICSRs. The cases were reviewed by the SRP-PvPI-IPC and it was concluded that there is a strong causal relationship between itraconazole and acute generalized exanthematous pustulosis in

these cases. The PVPI-IPC has reminded healthcare professionals that acute generalized exanthematous pustulosis is a potential adverse drug reaction with itraconazole use. Reference: Based on the communication from IPC, NCC-PvPI, India (www.ipc.gov.in)

Menthol containing OTC topical pain relievers Risk of serious skin burns

Health Canada has updated the labelling standard for OTC topical pain relievers containing menthol alone or in combination, to inform about this risk. OTC topical pain relievers are applied on the skin to relieve pain in muscles or joints. These products, which may contain menthol, methyl salicylate or capsaicin, either alone or in combination, relieve pain by slightly irritating the skin surface. This irritation reduces the feeling of pain in the underlying joints and muscles. Health Canada has carried out a follow-up safety review, following the safety review in 2013 and based on the additional safety information gathered by Health Canada or obtained by certain manufactures on these products. At the time of the review, Health Canada had received a total of 29 reports of serious skin burns related to the use of OTC topical pain relievers containing menthol, methyl salicylate or capsaicin in Canada. The products were used as directed in 28 reports; in some reports, other factors may have played a role in the development of burns. In the remaining reports, the product was not used as directed. Of these 29 reports, there were seven reports involving products containing only menthol, two reports involving products containing only methyl salicylate, and one report involving a product containing only capsaicin. There were 19 reports involving products containing multiple ingredients, and most of these contained menthol and methyl salicylate together. The review of the safety information provided by manufacturers identified over 100 additional international reports of serious burns linked to the use of topical painrelievers. The majority of these cases contained menthol, alone or in combination with methyl salicylate. There were no cases of serious burns linked to the use of topical muscle and joint pain relievers containing methyl salicylate or capsaicin alone. In the medical literature, there is only one case of serious skin burns linked to the use of a topical pain reliever product containing menthol and methyl salicylate; however, the product was used inappropriately. Health Canada's current review has established a link between the use of topical pain relievers containing menthol and the risk of rare but serious skin burns; however, there was not enough information to draw the same conclusions for the products containing methyl salicylate or capsaicin alone.

Reference: Summary Safety Review, Health Canada, 13 February 2017 (www.hc-sc.gc.ca) (See WHO Pharmaceuticals Newsletter No.5, 2012: Rare cases of serious burns with Over-The-Counter Topical Muscle and Joint Pain Relievers in the US)