DEPARTMENT OF PHARMACOLOGY
ARMED FORCES MEDICAL COLLEGE, PUNE-40

Drug Safety Bulletin: Be Aware

Issue: Third; Jan-Mar 2022

Dear Readers,
The purpose of this bulletin is to disseminate important safety information related to drugs and medical devices from drug regulatory agencies like CDSCO, US FDA, European Union. This will help clinicians to be aware of latest safety issues with drugs. The current issue highlights recent safety updates on piperacillin, labetalol, ertapenem, olmesaretan, warfarin and alerts from PvPI database. Feedback and suggestions, if any, may be sent at email Id: pvpiafmc@gmail.com.

Piperacillin; piperacillin, tazobactam – Haemophagocytic lymphohistiocytosis (HLH)[1]

The Pharmacovigilance Risk Assessment Committee (PRAC) recommended to update Summary of Product Characteristics (SPC) of piperacillin / piperacillin plus tazobactam with addition of following text in Special Warning and Precaution section "Cases of HLH have been reported in patients treated with piperacillin / piperacillin plus tazobactum, often following treatment longer than 10 days. HLH is a life-threatening syndrome of pathologic immune activation characterised by clinical signs and symptoms of an excessive systemic inflammation (e.g. fever, hepatosplenomegaly, hypertriglyceridaemia, hypofibrinogenaemia, high serum ferritin, cytopenias and haemophagocytosis). Patients who develop early manifestations of pathologic immune activation should be evaluated immediately. If diagnosis of HLH is established, treatment should be discontinued."

Labetalol – Nipple pain and suppressed lactation[1]

The PRAC has considered the available evidence in databases including EudraVigilance, the literature, and the data submitted by Pharma Company regarding the risk of nipple pain and suppressed lactation associated with labetalol. The SPC will be updated with following text in Fertility, pregnancy and lactation section. "Breast-feeding: Nipple pain and Raynaud's phenomenon of the nipple have been reported."

Ertapenem – Toxic encephalopathy in patients with renal impairment[1]

PRAC recommended to update SPC of ertapenem with addition of following text in Special Warning and Precaution section. "Encephalopathy has been reported with the use of ertapenem. If ertapenem-induced encephalopathy is suspected (e.g. myoclonus, seizures, altered mental status, depressed level of consciousness), discontinuation of ertapenem should be considered. Patients with renal impairment are at higher risk of ertapenem-induced encephalopathy and the resolution may be prolonged."

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Olmesartan – Autoimmune hepatitis[1]

Cases of autoimmune hepatitis with a latency of few months to years have been reported in post-marketing, that were reversible after the withdrawal of olmesartan. The 'Undesirable effects' section of Summary of Product Characteristics (SPC) of Olmesartan and olmesartan containing FDC will be updated with following text. "Hepatobiliary disorders - Autoimmune hepatitis: Frequency not known"

Warfarin – Anticoagulant-related nephropathy[1]

A few cases of anticoagulant-related nephropathy have been reported in patients with no pre-existing kidney disease. Close monitoring including renal function evaluation is advised in patients with a supratherapeutic INR and hematuria (including microscopic). The 'Undesirable effects' section of SPC of warfarin will be updated with following text. "Renal and urinary disorders - anticoagulant-related nephropathy: Frequency not known"

Source

Drug Safety Alerts by PvPI Database[2] from Oct to Dec 21

Suspected Drug	Indications	ADRs
Diclofenac	Inflammatory conditions, migraine attack	Skin hyperpigmentation
Remdesivir	Emergency use for treatment of patients with severe COVID-19.	Sinus Bradycardia

1. Pharmacovigilance Risk Assessment Committee (PRAC). European Medicines Agency. Last accessed on 10 Jan 2022 (https://www.ema.europa.eu/en/human-regulatory/post-authorisation/pharmacovigilance/signal-management/prac-recommendations-safety-signals)
2. Pharmacovigilance Programme of India (PvPI) Updates. Last accessed on 07 Oct 2021 (https://www.ipc.gov.in/mandates/pvpi/pvpi-updates/8-category-en/416-drug-safety-alerts.html)

You are requested to report any observed ADRs to Dept of Pharmacology, ADR monitoring centre with following mode of communication:

1. **ADR form (Version 1.4) can be downloaded from IPC website. Link: https://www.ipc.gov.in/PvPI/adr.html**
2. **Contact Number: 7385666876 / 9923693597**
3. **Email-ID: pvpiafmc@gmail.com**
4. **Google Form Link: https://docs.google.com/forms/d/e/1FAIpQLSfFWfSHemNQ56a3Pz5rfKe-jfZ2oumA0Xs_3kO4iYcs0-mr5Q/viewform**
5.

Any Person ADR Any Time
Any Drug