

Drug Safety Bulletin: Be Aware

Issue: Fourth; Apr-Jun 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 donepezil, pregabalin, buprenorphine, calcineurin and mTOR inhibitors and alerts from PvPI database. Feedback and suggestions, if any, may be sent at email Id: pvpiafmc@gmail.com.

Donepezil– QT Prolongation/Torsades de Pointes¹

Cardiac conduction disorders have been reported in patients receiving donepezil. The Product Information (PI) documents of Therapeutic Goods Administration (TGA) Australia for this medicine are being updated to advise caution in patients with known QTc prolongation or a family history of this condition. The following warning has been added to 'Cardiovascular conditions' in the 'Special warnings and precautions for use' section (4.4) of the donepezil PI. 'Cases of QTc interval prolongation and Torsades de Pointes have been reported for donepezil. Caution is advised when donepezil is used in combination with other medicinal products known to prolong the QTc interval and clinical monitoring may be required.'

Pregabalin– Toxic Epidermal Necrolysis (TEN)²

The Pharmacovigilance Risk Assessment Committee (PRAC) has considered the available evidence in databases preclinical and clinical studies, EudraVigilance, the literature, regarding the risk of TEN associated with pregabalin. The SPC will be updated with following text in Warning and precaution section. "Severe cutaneous adverse reactions (SCARs) including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), which can be life-threatening or fatal, have been reported rarely in association with pregabalin treatment. At the time of prescription patients should be advised of the signs and symptoms and monitored closely for skin reactions. If signs and symptoms suggestive of these reactions appear, pregabalin should be withdrawn immediately and an alternative treatment considered (as appropriate) "

Calcineurin inhibitors & mTOR inhibitors - Drug interaction with Cannabidiol leading to toxicity²

The PRAC has considered the responses from Pharma companies, available data from EudraVigilance and the literature regarding the risk of interaction of cannabidiol with calcineurin inhibitors (tacrolimus, ciclosporin) or mTOR inhibitors (everolimus, sirolimus, temsirolimus). The PRAC agrees that there is sufficient evidence to recommend the inclusion of information regarding the risk of interaction with cannabidiol (P-gp inhibitor) in the product information of calcineurin inhibitors and mTOR inhibitors.



Buprenorphine– Dental problems³

The US-FDA is warning that dental problems have been reported with medicines containing buprenorphine that are dissolved in the mouth. The dental problems, including tooth decay, cavities, oral infections, and loss of teeth, can be serious and have been reported even in patients with no history of dental issues. Prescribers should refer patients to dental care services and encourage them to have regular check-ups while taking buprenorphine tablet/sublingual films. Patients should tell the dentist about all medicines they take, including buprenorphine.

Drug Safety Alerts by PvPI Database⁴ from Jan to Mar 22

Suspected Drug	Indications	ADRs
Ibuprofen	Chronic arthritic disorders, painful musculoskeletal conditions	Fixed drug eruption
Losartan	Hypertension	Muscle spasm
Cephalosporin class	Wide range of infections from Gram-positive & Gram-negative bacteria	Fixed drug eruption

Source

1. Therapeutic Goods Administration (TGA) Australia. Last accessed on 17 Apr 2022 (<https://www.tga.gov.au/publication-issue/donepezil-and-cardiac-conduction-disorders>)
2. Pharmacovigilance Risk Assessment Committee (PRAC). European Medicines Agency. Last accessed on 17 Apr 2022 (<https://www.ema.europa.eu/en/human-regulatory/post-authorisation/pharmacovigilance/signal-management/prac-recommendations-safety-signals>)
3. US FDA Drug Safety, Last accessed on 17 Apr 2022 (<https://www.fda.gov/drugs/drug-safety-and-availability>)
4. Pharmacovigilance Programme of India (PvPI) Updates. Last accessed on 07 Oct 2021 (<https://www.ipc.gov.in/PvPI/das.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/1FAIpQLSfFWfSHemNQ56a3Pz5rfKejfZ2oumA0Xs_3kO4iYcs0-mr5Q/viewform

Any Person  Any Time
Any Drug

