



# Drug Information Bulletin

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## *Editorial*

Disposal of Bio-hazardous waste and drugs-that have expired / confiscated under law, pose a huge problem with respect to environmental pollution. The environment today is overloaded with myriad hazardous chemicals, drugs, excipients and biohazardous waste from different institutions pose a serious threat to the environment. It is a serious concern to the responsible citizens. Strict guidelines need to be framed and enforced with proper vigilance, so that they do not contaminate soil, water bodies / air and through these contaminate / damage human or animal bodies, crops, cattle, fishes etc. It is imperative to note that packaging materials used in the pharmaceutical industry is also another area, whose disposal poses a serious problem. Antimicrobial waste is creating resistance against several several diseases including tuberculosis.

Guidelines for "Safe Disposal of unwanted pharmaceuticals in and after emergencies" have been framed by international agencies, but no such guidelines have been framed in India under any legislation. It is high time to prepare and enforce strict legislation for disposal of Pharmaceuticals and packaging materials to save the environment.

As pharmacists, we should be more conscious and cautious about disposal of drugs and other pharmaceutical and medical substances / aids, so as to reduce environmental hazards.



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## New Drug: Brivaracetam

Approved indication: epilepsy

Briviact (UCB)

25 mg, 50 mg film-coated tablets, oral solution containing 10 mg/mL

Australian Medicines Handbook section 16.1.3

Temporal lobe epilepsy is the most common of the partial epilepsies. Carbamazepine is generally considered the first-line drug for managing partial epilepsy, but it may not completely control seizures. There are many antiepileptic drugs which can be added such as gabapentin, lamotrigine and levetiracetam. Brivaracetam is another add-on therapy for adults with partial-onset seizures, with or without secondary generalised seizures.

Brivaracetam is thought to act on a protein (SV2A) in the synaptic vesicles. By binding to this protein the drug is thought to alter the release of neurotransmitters into the synapse. The reduction in seizures is proportional to the concentration of brivaracetam in plasma.

It is recommended to begin treatment with 100 mg doses (50 mg twice daily) then adjust the dose according to the response. The tablets are completely absorbed and brivaracetam rapidly enters the brain. Its half-life is about nine hours with most of the dose being metabolised and excreted in the urine. Dose adjustments may be necessary for patients with hepatic impairment and the drug should be avoided in patients with end-stage renal disease on dialysis due to a lack of data. Plasma concentrations of brivaracetam are reduced if it is taken with carbamazepine, phenobarbital (phenobarbitone) or phenytoin.

The approval of brivaracetam is based on the results of three main trials.<sup>1-3</sup> The patients in these trials had partial epilepsy that was not controlled by one or two drugs. Different doses of brivaracetam were compared with placebo over 12 weeks.

One trial studied total daily doses of 5 mg, 20 mg or 50 mg in 396 patients. Only the 50 mg dose was significantly better than adding a placebo. This dose reduced weekly seizure frequency by 12.8% more than placebo.<sup>1</sup>

A similar trial involving 398 patients studied total daily doses of 20 mg, 50 mg and 100 mg. Respectively, these reduced weekly seizure

frequency by 6.8%, 6.5% and 11.7% more than placebo. Only the 100 mg dose made a statistically significant difference.<sup>2</sup>

The third main trial of brivaracetam involved 768 patients and studied total daily doses of 100 mg and 200 mg. Based on the reduction in seizure frequency during the treatment period, the proportion of patients having a response of 50% or more was significantly higher with brivaracetam. This responder rate was achieved by 38.9% of the patients taking 100 mg, 37.8% of those taking 200 mg and 21.6% of the placebo group. Averaged over a 28-day period, the reduction in seizure frequency was 22.8% greater than placebo for 100 mg and 23.2% greater with 200 mg.<sup>3</sup>

Across the clinical trials, 6.7% of the patients taking brivaracetam discontinued it because of adverse events. Only 3.9% of the patients given a placebo discontinued. The main reasons for stopping treatment included dizziness, headache and fatigue. Other adverse events caused by brivaracetam include nausea, irritability and somnolence. Some patients become depressed and a few may develop suicidal thoughts. Pooled data suggest the incidence of suicide and suicide attempts is 3.2 per 1000 patient-years.

The clinical trials show that the percentage reduction in seizures is greater than the reduction with placebo. Based on the trial of higher doses, in which patients were having a median of 10 seizures every month, the difference between brivaracetam and placebo is probably two or three seizures per month. Few patients will stop having seizures. In the same trial 5.2% of the patients taking a total daily dose of brivaracetam 100 mg became seizure free.<sup>3</sup>

An attempt has been made to compare brivaracetam with levetiracetam. This indirect comparison was based on a systematic review of 13 placebo-controlled trials. There were 1919 patients in the brivaracetam trials and 1765 in the levetiracetam trials. For all doses of brivaracetam, there were no statistically significant differences in efficacy.<sup>4</sup> Some patients who have previously been treated with levetiracetam may respond to brivaracetam, but there is no benefit in using the drugs together.<sup>1-3</sup> The systematic review found that levetiracetam was less likely to cause

dizziness than higher total daily doses (150 mg, 200 mg) of brivaracetam.<sup>4</sup>

#### References

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3. Klein P, Schiemann J, Sperling MR, Whitesides J, Liang W, Stalvey T, et al. A randomized, double-blind, placebo controlled, multicenter, parallel-group study to evaluate the efficacy and safety of adjunctive brivaracetam in adult patients with uncontrolled partial-onset seizures. *Epilepsia* 2015;56:1890-8.
4. Zhang L, Li S, Li H, Zou X. Levetiracetam vs. brivaracetam for adults with refractory focal seizures: a meta-analysis and indirect comparison. *Seizure* 2016;39:28-33.

Ref. Australian Prescriber

#### **Cipla introduces new drug for pediatric malaria**

Mumbai-based Cipla teamed with the Medicines for Malaria Venture to promote 100 milligram artesunate suppositories for treatment of severe malaria in children from six months to six years of age. The objective is to make the medication available in rural Africa and to national community health programs, said Cipla CEO Umang Vohra.

Ref.: The Economic Times (India)/Press Trust of India

#### **Study finds HIV vaccine candidate safe to use in adults**

Researchers from Harvard Medical School found that a novel investigative HIV vaccine regimen was well-tolerated and produced immune responses in healthy adult participants, according to data presented at the ninth International AIDS Society Conference on HIV Science in Paris. Researchers look to clinical trials possibly later this year.

Ref.: MedPage Today (free registration)

#### **36 drugs added to China's insurance list with price cuts**

China's Ministry of Human Resources and Social Security is adding 36 drugs to those covered by basic insurance plans after pharma companies said they would provide an average 44% decrease -- and up to 70% -- from last year's prices. Additions include Celgene's Revlimid; Johnson & Johnson's Zytiga; Roche Holding's Herceptin, Avastin and MabThera; Novartis' Afinitor; Brilinta, from AstraZeneca; and Victoza, from Novo Nordisk.

Ref.: Reuters (7/19)

#### **Essential drugs not available in 24 states: CAG**

Essential drugs for patients were not available in 24 states and medicines were issued without prescribed quality checks or observing their expiry dates, exposing patients to health risks, the country's audit watchdog CAG has found.

The Report of the Comptroller and Auditor General (CAG) of India on Performance Audit of the Reproductive and Child Health under National Rural Health Mission which was tabled in Parliament today also found shortage of doctors and paramedical staff in almost all selected facilities.

The performance audit covered the period from 2011-12 to 2015-16.

As per the report, instances of non-availability of essential drugs were observed in 24 states, including Assam, Bihar, Chhattisgarh, Gujarat, Haryana, Karnataka, Madhya Pradesh, Maharashtra, Rajasthan, Sikkim, Tamil Nadu, Telangana, Tripura and Uttar Pradesh.

In eight states, essential medicines and consumables such as Vitamin A, contraceptive pills, ORS packets, RTI/STI drugs, essential obstetric kits etc were not available in selected health facilities.

Non-maintenance of administration records of antenatal checkups (ANCs) of pregnant women was noticed in 20 out of 28 states.

"Shortfalls in administration of iron and folic acid tablets were noticed in all the 28 states.

"Similarly, in four states (Arunachal Pradesh, Jammu and Kashmir, Manipur and Meghalaya), less than 50 per cent of pregnant women were

immunised with both doses of Tetanus Toxoid vaccine (TT1 and TT2)," the report said.

The CAG report further said that against the target of Infant Mortality Rate (27 per 1,000 live births) to be achieved by 2015 as per the Millennium Development Goals, the achievement was 39.

"IMR was higher than 40 in the six states of Assam (49), Bihar (42), Chhattisgarh (43), Madhya Pradesh (52). Odisha (49) and Uttar Pradesh (48)," it said.

Besides, against the target of Maternal Mortality Ratio (109 per 1,00,000 live births) to be achieved by 2015 as per the Millennium Development Goals, the achievement was 167.

"MMR was higher than 200 in the nine states of Assam (300), Bihar (208), Chhattisgarh (221), Jharkhand (208), Madhya Pradesh (221), Odisha (222), Rajasthan (244), Uttar Pradesh (285) and Uttarakhand (285)," it said.

Deficiencies were noticed in the implementation of Janani Suraksha Yojana, such as non-payment of incentives to beneficiaries, delayed payment to beneficiaries, payment to 12,723 excess number of beneficiaries among others.

The report further stated that in 17 states, including Chhattisgarh, Gujarat, Haryana, Karnataka, Rajasthan, Tamil Nadu, Uttarakhand and West Bengal, 428 equipment (ultrasound, X-ray, ECG, cardiac monitors, blood storage units) costing Rs 30.39 crore were lying unutilised due to non-availability of doctors and trained manpower to operate them and lack of adequate space for their installation.

"Shortage of doctors and paramedical staff was observed in almost all selected facilities, compromising the quality of healthcare being administered to the intended beneficiaries," the report stated.

In the selected CHCs of 27 states, the average shortfall of five types of specialists (general surgeon, general physician, obstetrician/gynaecologist, paediatrician and anaesthetist) ranged between 77 to 87 per cent.

The report further highlighted that 67 primary health centres were functioning without any doctor in 13 states.

Mobile medical units were not operational in four states of Chhattisgarh, Himachal Pradesh, Mizoram and Uttar Pradesh while these were partially operational in 10 states including Gujarat, Haryana, Kerala, Madhya Pradesh and Maharashtra.

Around 3,588 accredited social health activists (ASHAs) surveyed did not have disposable delivery kits and blood pressure monitors, the report said.

The report pointed out that financial management at both central and state levels was not satisfactory with substantial amounts persistently remaining unspent with the state health societies at the end of each year.

In 27 states, the unspent amount increased from Rs 7,375 crore in 2011-12 to Rs 9,509 crore in 2015-16.

### Forthcoming Event

**9<sup>th</sup> NATIONAL IPA STUDENTS CONGRESS 2017**  
1st - 2nd, September 2017 (Friday-Saturday)  
Venue : VIKAS INSTITUTE OF PHARMACEUTICAL SCIENCES, Rajahmundry, A.P., INDIA

Theme: Empowering Future Pharmacists

Experience pharmacy with innovative learning  
Join us to ... Connect Catalyse Innovate

Indian Pharmaceutical Association - Students' Forum (IPA-SF)  
IPA-SF is a national forum for pharmacy students under the Indian Pharmaceutical Association. IPA-SF was formed on August 16, 2008 in Mumbai in the presence of former president of India, late Dr. A. P. J. Abdul Kalam. This body has brought Pharmacy students under one umbrella, where their energies have been synergized towards activities pertaining to the pharmaceutical world. It enables students to become better future pharmacists while abiding to the highest ethical and professional standards and thus contribute to the overall development of their personality.

IMPORTANT DATES	
Registration Fee	: Rs. 1200/- Only
Last Date for Registration	: 20 <sup>th</sup> August 2017
Last date for Abstract Submission	: 10 <sup>th</sup> August 2017
Announcement of Abstract Acceptance	: 16 <sup>th</sup> August 2017

IMPORTANT EVENTS	
Prize Money for Each Event - Rs. 1 Lac.	
Poster & Oral Presentation	Dance Competition
Patient Counseling Competition	Clinical Skills Competition
Compounding Competition	Interaction & Work Shop

Organised by: IPA Students Forum  
Host: IPA Rajahmundry Local Branch  
Supported by: IPA AP State Branch, APTI AP State Branch

VIKAS INSTITUTE OF PHARMACEUTICAL SCIENCES

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