



Drug Information Bulletin

Drug Information Centre (DIC)

Indian Pharmaceutical Association

Bengal Branch

Tele fax: 033 24612776, [E-mail: ipabengal.dic@gmail.com](mailto:ipabengal.dic@gmail.com)

Web Site: <http://www.ipabengal.org>

Contact: 09830136291

&

Regulatory Affairs Division (RAD), IPA

Volume: 11

Number: 12

10th September 2017

Content

- **Editorial**
- **New Drug: Brivaracetam**
- **WHO pilot program aims to expedite biosimilar approvals**
- **India proposes government support for APIs made in-country**
- **Mylan will distribute Japanese TB drug in India**
- **Drug Safety Alerts by PvPI during July & August 2017**
- **Recommendation for Acharya P.C.Ray Memorial Gold Medal Award 2017 invited**

Editorial

Death due to Tuberculosis is a global problem and this problem is aggravated by development of Multidrug Resistant TB (MDR-TB) and Extremely Drug Resistant TB (XDR-TB). In 2014 about 480000 people developed MDR-TB globally and about 9.7% of these cases were XDR-TB.

Govt. of India has started Revised National Tuberculosis Control Programme in 1997 to eradicate TB. RNTCP followed the WHO recommendation of Directly Observed Short Course (DOTS) strategy and reaches over a billion people in 632 districts.

One of the shortfalls of this programme is discontinuation of treatment because of several reasons. Now Govt. of India recognizes that services of private facilities and are taking help of NGOs under this RNTCP Programme.

Indian Pharmaceutical Association (IPA) is working for TB care and control utilizing services of the community pharmacists as they are more accessible to the TB patient. In 2011 World Health Organization (WHO) has signed a MOU with FIP at Hyderabad during FIP congress in 2011. Thereafter TBC, Govt. of India has signed a MOU with IPA, PCI, SEARPharm Forum & AIOCD for care & control of tuberculosis. As per this agreement IPA has started working in different states involving Pharmacists working in community Pharmacy and found extremely positive outcome.

RNTCP of CTD has given direction to all state TB officers to involve community pharmacists in this programme. Along with all other states State TB officer of West Bengal has given direction to the Chief Municipal Health Officer and CMOH of all districts for involving community Pharmacist in RNTCP for early detection, referral of TB suspects for treatment, DOT provision for TB treatment and generating awareness about TB and MDR-TB. This is a golden opportunity for the community pharmacists to serve the community and am requesting them to extend all sorts of help for success of this programme.



Dr. Subhash C. Mandal
Editor

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.¹⁻³ 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.¹

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.²

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.³

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.³

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.⁴ Some patients who have previously been treated with levetiracetam may respond to brivaracetam, but there is no benefit in using the drugs together.¹⁻³ The systematic review found that levetiracetam was less likely to cause

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

References

1. Biton V, Berkovic SF, Abou-Khalil B, Sperling MR, Johnson ME, Lu S. Brivaracetam as adjunctive treatment for uncontrolled partial epilepsy in adults: a phase III randomized, double-blind, placebo-controlled trial. *Epilepsia* 2014;55:57-66.
2. Ryvlin P, Werhahn KJ, Blaszczyk B, Johnson ME, Lu S. Adjunctive brivaracetam in adults with uncontrolled focal epilepsy: results from a double-blind, randomized, placebo controlled trial. *Epilepsia* 2014;55:47-56.
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.

Source: Australian Prescriber

Status in India:

Brivaracetam Film Coated Tablets 50mg/75mg/100mg has been approved by the Central Drugs Standard Control Organization (CDSCO) as adjunctive therapy in the treatment of partial -onset seizures in patients 16 years of age and older with epilepsy on 07.09.2017.

WHO pilot program aims to expedite biosimilar approvals

The World Health Organization will begin a pilot in October to prequalify biosimilars to make cancer treatments available in middle- and lower-income countries. The first biosimilar applications will cover the Roche Holding drugs Rituxan, or rituximab, and Herceptin, or trastuzumab.

Ref. Regulatory Focus

India proposes government support for APIs made in-country

India's Department of Pharmaceuticals proposed in a draft policy released last week to reduce the country's dependence on imported active pharmaceutical ingredients by favoring purchases of locally produced APIs. The draft report also suggested exempting locally made APIs from price caps for five years.

Ref. In-Pharma Technologist

Mylan will distribute Japanese TB drug in India

Japan's Otsuka Pharmaceutical licensed its multidrug-resistant tuberculosis medicine delamanid to a subsidiary of Mylan in India. Initially, Mylan will provide 400 courses of treatment with delamanid for free over the next six months; after that, a six-month treatment course would cost \$1,700.

Ref. The Economic Times (India)

Drug Safety Alerts by PvPI during July & August 2017

Health care professionals, Patients/Consumers has been advised to closely monitor the possibility of the below mentioned adverse events associated with the use of the mentioned drugs. If such events are encountered they are requested to report to the NCC-PvPI either by filling of Suspected Adverse Drug Reactions Reporting Form/ Medicines Side Effect Reporting Form for Consumer (<http://www.ipc.gov.in>) or by PvPI Helpline No. 1800-180-3024.

The preliminary analysis of ADRs from the PvPI database reveals that the following drugs are associated with the risks as given below.

Sl. No	Suspected Drugs	Indication	Adverse Reactions
1.	Clindamycin	Respiratory tract infections, penicillin resistant staphylococcal infections and many anaerobes such as bacteroides, skin, soft tissue and dental infections	Acute Generalised Exanthematous Pustulosis
2.	Triamcinolone	Corticosteroid	Skin Peeling

3.	Polymyxin B	Antibiotic	Mottled Skin
4.	Diclofenac	Acute musculo-skeletal pain; arthritis; gout; spondylitis; migraine; post-operative pain	Nicolau Syndrome
5.	Inactivated Influenza Vaccine	Active immunisation against influenza in individuals at risk	Papulovascular Exanthema
6.	Measles Rubella Vaccine	Active immunisation against Measles and Rubella in individuals at risk	Arthritis/Joint Pain
7.	Terbinafine	Treatment of fungal infections	Acute Generalised Exanthematous Pustulosis (AGEP)
8.	Nitrofurantoin	Urinary tract infections; cystitis	Vasculitis

Recommendations for Acharya P. C. Ray Memorial Gold Medal Award, 2017 invited

The Indian Pharmaceutical Association, Bengal Branch gives annually gold medal on the occasion of celebration of National Pharmacy Week during 3rd week of November of each year to perpetuate the memory of great national figure Acharya P.C.Ray, the pioneer designer of Pharmaceutical Industry in our country since 1962.

IPA, Bengal Branch Council select the awardee amongst the Pharmaceutical Scientists, Teachers, Pharma Regulators, Hospital Pharmacists, Community Pharmacist, Administrators, etc. for outstanding contribution in their respective field and for overall development of the profession of pharmacy.

Any member of IPA can recommend name of the person with their detailed Bio-data & Two Page summary of the Bio data for 2017 award, which may be sent by 15th October 2017 to:

The Hony. Secretary,

Indian Pharmaceutical Association, Bengal Branch, 22 B Panchanontola Road, Kolkata – 700029

e-mail: ipabengal@gmail.com

N.B.: Biodata should include the following points-

1. Date of Birth.
2. Qualification.
3. Experiences in the selected field.
4. Achievements in advancement of sciences/Administration/relevant field.
5.
 - a. Whether member of IPA? If yes, how many years?
 - b. Whether member of allied pharmaceutical profession other than IPA? If yes, how many years?
6. Services rendered (in years) on the executive Council of IPA Centre or any of its Branches in the capacity as:
 - a. President/Vice President / Hony. Secretary/Treasurer/Editor of Official Publication of IPA.
 - b. Executive Council Member.
7. Recognition/Award received from other professional organizations including industry/trade associations.
8. Award/Recognition/Honour received from international/national Govt. authorities or prestigious institution/organization by way of award or membership of their constituted body/committee other than sl. No. 6 above.
9. Performance in growth/ improvement of any of the field of pharmacy and shown creditable leadership in the chosen field.
10. Involvement and outstanding achievements in professional development in national/international arena.
11. Notable achievements in any other field or profession excluding pharmacy for which the nominee is nominated for the award including social welfare activities with Govt. and Non Govt. organizations.

DISCLAIMER:

The Newsletter intends to provide updated and reliable information on medicines and other related issues in an attempt to equip healthcare professionals to take informed decision in recommending medicines to the patients. However, they are encouraged to validate the contents. None of the people associated with the publication of the Newsletter nor the organization shall be responsible for any liability for any damage incurred as a result of use of contents of this publication. The brand names of medicines, if mentioned, are for illustration only and the Newsletter