Supplementary material

Title: Efficacy and safety of Pregabalin prolonged release-Etoricoxib combination compared to Etoricoxib for chronic low back pain: Phase 3, randomized study

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1. **Subject Eligibility Criteria**

**Inclusion Criteria**

Subjects eligible for Randomization in the study were required to meet all the following criteria.

1. Male or female patients of 18 to 65 years of age (both inclusive)
2. Patients with chronic low back pain (symptoms duration: ≥ 3 months) and at least one of the following features on the side corresponding to leg pain:
   a. Sharp and shooting pain below the knee;
   b. Pain evoked by straight leg raising to 60 degrees or less;
   c. Decreased or absent ankle reflex;
   d. Weakness of muscles below the knee.
   e. Sensory loss in L5/S1 distribution
3. Patient who have pain score at least 4 on a Numeric Rating Scale (11-point)
4. Patients who agree not to use any other approved or experimental pharmacological treatments for low back pain, other than mentioned in the protocol, at any time during the study
5. Patient or his/her legally accepted representative is willing to give informed consent
6. Female participants of childbearing potential must be willing to use acceptable method of contraception (female of childbearing potential is defined as one who has not been postmenopausal for at least one year, or has not been surgically sterilised, or has not had a hysterectomy at least three months prior to the start of this study. Acceptable method of contraception includes (e.g., barrier method with spermicide). The "calendar method," withdrawal, or an IUD is NOT an acceptable method.
7. Patients willing to follow the study protocol.

**Exclusion Criteria**

Subjects who met any of the following criteria were not be enrolled in the study:

1. Breast feeding or pregnant females
2. History of hepatitis B, hepatitis C or HIV infection
3. Anticonvulsants, antidepressants (eg. tricyclic, tetracyclic, atypical), aspirin at doses >81 mg/day, benzodiazepines, opioids, herbal medications, mexiletine HCl, epidural injection procedure (eg.acupuncture) performed within 6 weeks prior to screening or planning to use during the study or taken more than recommended doses of any dosage form NSAIDs analgesics in last 15 days prior to screening and any treatment for low back pain within 2 days prior to enrolment
4. Patients who, in the opinion of the investigator, have history of clinically significant cardiovascular disease (ex. MI), psychiatric disorders as per DSM-5 (Bipolar disorder, generalized anxiety disorder, depression, psychosis or post-traumatic stress disorder), epilepsy or seizure disorder requiring treatment with anti-epileptic drugs, severe hepatic and renal impairment (defined as either creatinine clearance <60 mL/min or renal dysfunction requiring hemodialysis), neoplastic disease, suicidal behavior, underlying conditions that may precipitate encephalopathy (ex. Liver failure), lactose intolerance, angle closure glaucoma, angioedema, urinary retention, thyroid disorder, uncontrolled hypertension and diabetes or abnormal ECG or the participant has any other abnormal laboratory value or MRI lumbosacral spine finding (e.g., neoplasia) of clinical significance for this study during screening visit

5. Medical condition or disorder that would interfere with the action, absorption, distribution, metabolism, or excretion of Pregabalin Prolonged Release or Etoricoxib in the investigator's judgment

6. Patients with known alcohol or other substance abuse within last one year as per DSM-5 criteria

7. Participant has hypersensitivity, intolerance, or contraindication to the use of Etoricoxib and Pregabalin, or any of its components.

8. HbA1c > 8% at screening.

9. Patient received treatment with an investigational device or compound within 6 months prior of the screening.

10. Patients with clinically significant disorder that, in the opinion of the investigator, would result in the participant’s inability to understand and comply with the requirements of the study.

11. Patients operating heavy complex machinery or who intend to drive
### 2. Ethics committee details

| SN | Ethics committee                                                                 | Registration number |
|----|----------------------------------------------------------------------------------|---------------------|
| 1  | Supe Hospital Ethics Committee  
Address: Supe Heart & Diabetes Hospital & Research Centre, Opposite Adharashram, Gharpure Ghat, Near Rungtha High School, Gharpure Ghat, Ashok Stambh, Nasik-422002, Maharashtra, India. | ECR/272/INST/MH/2013/RR-16 |
| 2  | Institutional Ethics Committee  
Address: Osmania Medical College, Koti Hyderabad-500095, Telangana State, India | ECR/300/Inst/AP/2013/RR-16 |
| 3  | Institutional Ethics Committee of Kovai Diabetes Speciality Centre & Hospital  
Address: 15, Vivekanand Road, Ramnagar, Coimbatore – 641009, Tamil Nadu, India | ECR/233/Inst/TN/2013/RR-16 |
| 4  | Institutional Ethics Committee, Post Graduate Institute of Medical Education & Research, Room No. 6006, 6th floor, P N Chuttani Block, Chandigarh 160012, India | ECR/25/Inst/CH/2013/RR-16 |
| 5  | The Ethics Committee, S.M.S. Medical College and Attached Hospitals, Jaipur  
Address: First Floor, Dhanvantari OPD Block, S.M.S Hospital, J.L.N. Marg, Jaipur-302004, Rajasthan, India | ECR/26/Inst/Raj/2013 |
| 6  | Institutional Ethics Committee  
Address: Gandhi Medical College/Gandhi Hospital, Musheerabad, Secunderabad-500003, Telangana, India | ECR/180/Inst/AP/2013/RR-16 |
| 7  | Hi-Tech Ethics Committee (HEC)  
Address: Hi-Tech Multispeciality Hospital, Sector-3-D, Plot No. 1180, GH-11/2 Bus stand, Gandhinagar-382003, Gujarat, India | ECR/1057/Inst/GJ/2018 |
| 8  | Kanoria Ethics Committee  
Address: Kanoria Hospital and Research Centre, Airport-Gandhinagar Highway, Village-Bhat, Gandhinagar-382428, Gujarat, India | ECR/620/Inst/GJ/2014/RR-17 |
| 9  | Institutional Ethics Committee, Grant Government Medical College and Sir J J Group of Hospital, Byculla, Mumbai-400008, Maharashtra, India | ECR/382/Inst/MH/2013/RR-16 |
| 10 | Institutional Ethics Committee  
Address: Sparsh Hospital and Critical Care Pvt. Ltd, Plot No. A/407, Saheed Nagar, Bhubaneswar Khordha Orissa 751007, India | ECR/68/Inst/OR/2013/RR-19 |
| 11 | Institutional Ethics Committee, Office of Research Cell, Administrative block, King George’s Medical University, Lucknow (UP)-226003, India | ECR/262/Inst/UP/2013/RR-16 |
| 12 | Institutional Ethics Committee of B. J. Govt. Medical College & Sassoon General Hospital, Dept of Pharmacology, B J Government Medical college, Sassoon Road, Pune 411001, Maharashtra, India | ECR/280/Inst/Maha/2013/RR-16 |