

Sodium valproate injection (6 vials) and Levetiracetam injection (8 vials) enclosed with all drug information sheets to serve information which health care provider need before drug administration.

**Conclusion:** SE BOX may be suitable for resolve the problems of SE service to reduce the waiting time and improve effectiveness of SE treatment; however the benefit of SE BOX need more study.

**Keywords:** status epilepticus; SE, AED

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### Intranasal midazolam as initial in-hospital treatment for status epilepticus: A pharmaco-EEG cohort study

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**Background:** To evaluate the efficacy and tolerability of intranasal midazolam (in-MDZ) as first line in-hospital therapy in patients with status epilepticus (SE) during continuous EEG recording.

**Methods:** Medical records of all patients treated with in-MDZ during EEG recording between August 2015 and April 2018 were retrospectively reviewed. Data on medical history, etiology and semiology of SE, as well as anticonvulsive medication, efficacy, and safety of in-MDZ was collected. Time to end of SE regarding administration of in-MDZ and beta-band effects were independently analysed by two board certified epileptologists on EEG and with frequency analysis.

**Results:** In total, 42 patients (mean age  $52.7 \pm 22.7$  years; 23 female) were treated with a median dose of 5 mg in-MDZ (range 2.5-15 mg, mean 6.4 mg, SD 2.6) for SE. Most of the patients suffered from non-convulsive status epilepticus ( $n=24$ ; 55.8%). In total, 24 (57.1%) patients were responders as SE stopped after administering in-MDZ without any other drug being given in-between. On average, SE ceased on EEG five minutes and five seconds after application of in-MDZ (median 04:56 mins; range 00:29 mins -14:53 mins; SD 03:13mins). Frequency analysis showed an increased beta-band on EEG after application of in-MDZ at four minutes and seven seconds on average (median 03:50; range 02:20 - 05:40; SD 01:09 mins). Adverse events were recorded in six patients (14.3%) with nasal irritations in five (11.9%) and prolonged sedation in one (2.6%) patient.

**Conclusions:** This pharmaco-EEG based study showed that in-MDZ is effective and well-tolerated for initial treatment of SE. EEG and clinical effects occur within 04:07 and 5:05 mins on average. Intranasal administration of midazolam appears to be an easily applicable and rapidly effective alternative to buccal and intramuscular application as first line treatment if an intravenous route is not available.

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### Effect of ZX008 (Fenfluramine HCl Oral Solution) on Total Seizures in Dravet Syndrome

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**Objective:** Assess ZX008 (fenfluramine) effect on total seizure frequency in patients with Dravet syndrome.

**Background:** Dravet syndrome (DS) is a rare, severe, treatment-resistant, developmental epileptic encephalopathy. In a Phase 3, randomised, double-blind, placebo-controlled trial, ZX008 significantly reduced convulsive seizure (CS) frequency (defined as tonic-clonic, hemiclonic, tonic, atonic, clonic, and focal motor seizures). We present secondary analyses of total seizure (TS) frequency (defined as CS plus absence or atypical absence, myoclonic, atonic, and focal seizures without clear observable motor signs).

**Methods:** Patients (2-18y) with DS, and CSs not controlled by current anti-epileptic drug regimen were enrolled. Following a 6-week baseline period, patients were randomised 1:1:1 to placebo, ZX008 0.2 mg/kg/day (ZX008/0.2), or ZX008 0.8 mg/kg/day (ZX008/0.8; maximum 30 mg/day), and treated for 14 weeks, including 2-week titration. Caregivers recorded seizure number and type daily via electronic diary.

**Results:** A total 119 patients were randomised (10.1% UK, mean age  $9 \pm 4.7$ y). Baseline median monthly TS frequency ranged from 40.7-53.9 across groups. ZX008 significantly reduced TS frequency in a dose-related manner during 14 weeks' treatment. Median TS frequency reductions were 13.1% with placebo, 34.3% with ZX008/0.2 ( $p=0.031$ ), and 70.1% with ZX008/0.8 ( $p<0.001$ ). Median non-CS seizure subtype reductions (combined) were 55.6% with placebo and 75.1% with ZX008/0.8 ( $p<0.035$ ), including a 54.8 and 78.6% reduction in absence and 34.8 and 64.0% reduction in myoclonic seizures, respectively. Seizure freedom was experienced by 3 (7.5%) subjects with ZX008/0.8, 3 (7.7%) with ZX008/0.2, and none with placebo. Median longest seizure-free interval was significantly longer in ZX008 groups vs placebo. ZX008 was generally well-tolerated, and no cases of FDA-defined cardiac valvulopathy were observed; neither were there echocardiographic findings or clinical symptoms suggesting pulmonary hypertension.

**Conclusions:** In addition to significantly reducing convulsive seizures, ZX008/0.8 mg/kg/day also significantly reduced other