PDL NEW DRUG REVIEW

Proprietary Name: Potiga®
Common Name: ezogabine
PDL Category: Anticonvulsants

Comparable Products	Preferred Drug List Status
Lamotrigine	Preferred
Oxcarbazepine	Preferred
Topiramate	Preferred

Summary

Indications and Usage: Adjunctive treatment of partial-onset seizures in adults. This is a pregnancy category C medication. The safety and efficacy of use in children under the age of 18 have not been established.

Dosage Forms: Film-coated tablets: 50mg, 200mg, 300mg, and 400mg

Drug Interactions: It is recommended that the dose of Potiga® be increased if used concomitantly with carbamazepine and phenytoin.

Potiga® may increase digoxin serum levels. It is recommended that digoxin levels be monitored if this combination is used.

Counseling should be done to warn of the potential worsening of Potiga's® dose-related adverse reactions if used concomitantly with alcohol.

As Potiga® can have an effect on the QT-interval, it is recommended that the QT interval be monitored if using Potiga® concomitantly with medicines known to increase QT interval.

Recommended Dosage: The recommended initial dose is 100mg TID, titrated on a weekly basis to a maintenance dose of 200-400mg TID (600-1,200mg per day). Dosage adjustment is not required in those with mild renal or hepatic impairment. In those with moderate, severe, and ESRD, the initial recommended dose is 50mg TID to a max of 200mg TID. In those with moderate or severe hepatic impairment, the recommended initial dose is 50mg TID; however, the recommended max dose with moderate hepatic impairment is 250mg TID and with severe impairment is 200mg TID.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions = reported % incidence for drug minus reported % incidence for placebo.* The most commonly reported adverse events includes diplopia (5%), blurred vision (3%), nausea (2%), constipation (2%), fatigue (9%), asthenia (3%), weight increase (2%), dizziness (14%), somnolence (10%), memory impairment (3%), tremor (5%), vertigo (6%), abnormal coordination (4), gait disturbance (3%), balance disorder (3%),

disturbance in attention (5%), amnesia (1%), confusional state (6%), anxiety (1%), dysuria (1%), urinary hesitation (1%), hematuria (1%), and chromaturia (1%).

Contraindications: There are currently no contraindications listed in the prescribing information.

Manufacturer: GlaxoSmithKline

Analysis: Ezogabine, the active ingredient of Potiga®, is thought to be effective as an anticonvulsant by way of enhancing the transmembrane potassium currents mediated by the KCNQ family of ion channels. With enhancement of these KCNQ channels, it is thought that Potiga® stabilizes the resting membrane potential and reduces brain excitability. Potiga® is classified as a Schedule V controlled substance; therefore, there is a potential risk for abuse and dependence.

A warning exists with Potiga and the QT interval. As Potiga® can have an effect on the QT-interval, it is recommended that the QT interval be monitored in those with known prolonged QT interval, CHF, ventricular hypertrophy, hypokalemia, or hypomagnesemia. Another warning exists regarding suicidal behavior and ideation, which is a listed warning for all antiepileptic drugs (AED). It is recommended that those being treated with an AED be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or unusual changes in mood or behavior.

Three multicenter, randomized, double-blind, placebo-controlled trials were performed to assess the safety and efficacy of Potiga® in a population who had partial onset seizures with or without secondary generalization and who were not adequately controlled with 1-3 concomitant AEDs (N=1,239). The primary outcome was the % change in seizure frequency from baseline in the double-blind treatment phase. Results suggest that there were statistically significant differences seen with all 3 doses of Potiga® (3 doses of 600mg, 900mg, and 1200mg) as compared with placebo in regards to the median % reduction from baseline in seizure frequency. In study 1, the approximate values were 40% (Potiga® 900mg) and 28% (600mg dose) vs 16% with placebo ($p<0.05$ for both vs placebo). In study 2, the approximate values were 44% (1200mg dose) vs 18% placebo ($p<0.05$). In study 3, the approximate values were 35% (1200mg dose), 29% (900mg dose), and 23% (600mg dose) vs 13% placebo ($p<0.05$ for all comparisons vs placebo).

There is no evidence at this time to support that Potiga® is more efficacious or safer than the currently available, more cost effective medications. Therefore, it is recommended that Potiga® remain non-preferred and be available to those who fail on or are unable to tolerate any preferred medications.

PDL Placement:

- ☐ **Preferred**
- ☒ **Non-Preferred**
- ☐ **Preferred with Conditions**

References

[1] Potiga [package insert]. Research Triangle Park, NC: GlaxoSmithKline; 2012.