ATTACHMENT A – Dear Healthcare Professional Letter – Physicians

IMPORTANT DRUG WARNING

Subject: Risk of Urinary Retention with POTIGA

Dear Healthcare Professional

The purpose of this letter is to inform you of important safety information for POTIGA™ (ezogabine) Tablets®, approved by the Food and Drug Administration (FDA) for adjunctive treatment of partial onset seizures in patients 18 years of age and older. As a potassium channel opener, POTIGA can reduce the contractility of urinary bladder smooth muscle which can cause urinary retention.

FDA has determined that a Risk Evaluation and Mitigation Strategy (REMS) is necessary for POTIGA to ensure the benefits of the drug outweigh the risk of urinary retention and its associated morbidities. As one element of the REMS, we are providing this letter to further communicate this risk.

Risk of Urinary Retention

POTIGA caused urinary retention in clinical trials. Urinary retention was reported in 29 of 1365 (approximately 2%) patients receiving POTIGA in open-label and placebo controlled epilepsy trials with 5 (17%) of these patients requiring catheterization for urinary retention. POTIGA was discontinued in 4 patients who required catheterization. Following discontinuation, these 4 patients were able to void spontaneously; however, 1 of the 4 patients continued intermittent self-catheterization. A fifth patient continued treatment with POTIGA and was able to void spontaneously after catheter removal. Hydronephrosis occurred in 2 patients, one of whom had associated renal function impairment that resolved upon discontinuation of POTIGA. Hydronephrosis was not reported in placebo patients. An assessment of a patient’s risk of urinary retention, including medical history and concomitant medication use, should be made for all patients before initiating treatment with POTIGA.

The Prescribing Information for POTIGA states in the Warnings and Precautions section that because of the increased risk of urinary retention on POTIGA, urologic symptoms should be carefully monitored. Closer monitoring is recommended for patients who have other risk factors for urinary retention (e.g., benign prostatic hyperplasia [BPH]), patients who are unable to communicate clinical symptoms (e.g., cognitively impaired patients), or patients who use concomitant medications that may affect voiding (e.g., anticholinergics). In these patients, a comprehensive evaluation of urologic symptoms prior to and during treatment with POTIGA may be appropriate.
Prescribers should inform all patients that:

- POTIGA may cause urinary retention, including urinary hesitation and dysuria
- Patients should seek immediate medical attention if they experience any symptoms of urinary retention, are unable to urinate and/or have urinary pain

Urologists and Emergency Room Physicians may be asked to evaluate patients with respect to suitability for treatment with POTIGA or to evaluate and/or treat patients with potential urinary retention.

Medication Guide

A Medication Guide is available for POTIGA and contains important safety information for patients. Specifically, the Medication Guide includes information on symptoms of urinary retention described as being unable to start urinating, having trouble emptying the bladder, having a weak urine stream, or having pain with urination. The Medication Guide instructs patients to call their healthcare provider right away if they experience any of these symptoms.

Additional copies of the Medication Guide for POTIGA are available from:

- the toll-free medical information line at 1-888-825-5249
- an informational website for POTIGA: www.potiga.com

Reporting Adverse Events

If you become aware of an adverse event involving POTIGA please contact:

- GlaxoSmithKline at 1-800-334-4153 and/or
- FDA MedWatch program by phone at 1-800-FDA-1088 or online at www.fda.gov/medwatch/report.htm

This letter is not a comprehensive description of the risks with the use of POTIGA. Please read the accompanying full Prescribing Information and Medication Guide for a complete description of these risks.