Sunovion Announces Health Canada Approval of Aptiom® (eslicarbazepine acetate) as Adjunctive Therapy for the Treatment of Partial-Onset Seizures in Adolescents and Children Above Six Years of Age

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- APTIOM provides an important new treatment option for adolescents and children above six years of age with partial-onset seizures -

MARLBOROUGH, Mass.--(BUSINESS WIRE)--Sunovion Pharmaceuticals Inc. today announced that Health Canada approved the Supplemental New Drug Submission (SNDS) to expand the indication for its antiepileptic drug (AED) APTIOM® (eslicarbazepine acetate) to include use as an adjunctive therapy for the treatment of partial-onset seizures (POS) in adolescents and children above six years of age who are not satisfactorily controlled with conventional therapy.

APTIOM is also approved in Canada as monotherapy and adjunctive therapy for the treatment of POS in adults living with epilepsy. APTIOM is a once-daily, immediate release AED that can be taken whole or crushed, with or without food.

“The unpredictability of partial-onset seizures is one of the most challenging aspects of this condition – for children and their families,” said Anne Lortie, M.D., FRCPC, Associate Professor of Neurology, CHU Sainte Justine, Montreal, Quebec. “This expanded indication for APTIOM in Canada helps to bring an important treatment option to children and adolescents for whom previous treatments have not been able to control their partial-onset seizures.”

The safety and efficacy of APTIOM as an adjunctive therapy in the treatment of POS in adolescents and children above six years of age have been established using data from clinical studies in pediatric patients and a population pharmacokinetic study, which was used to support the recommended dosing regimen in the pediatric population. The safety and efficacy in pediatric patients six years of age and below have not been established.

“We are proud of this milestone approval by Health Canada for the use of APTIOM, as an adjunctive therapy, for children and adolescents,” said David Frawley, Executive Vice President and Chief Commercial Officer at Sunovion. “This approval strengthens our commitment to advancing therapies for people living with neurological conditions like epilepsy.”

About APTIOM® (eslicarbazepine acetate)

APTIOM is a member of the dibenzazepine carboxamide family of antiepileptic drugs (AEDs), an established class of medicines. APTIOM is approved in Canada as monotherapy for the treatment of POS in adults, as adjunctive therapy for the treatment of partial-onset seizures (POS) in adults with epilepsy that are not satisfactorily controlled with conventional therapy and as adjunctive therapy for the treatment of POS in adolescents and children above six years of age. The precise mechanism(s) by which eslicarbazepine, the primary active metabolite of APTIOM, exerts anticonvulsant activity is unknown but is thought to involve inhibition of voltage-gated sodium channels. APTIOM can be taken whole or crushed, with or without food.

The initial research and development of eslicarbazepine acetate was performed by BIAL, a privately held Portuguese research-based pharmaceutical company. Sunovion acquired the rights to eslicarbazepine acetate in the United States and Canada markets under an exclusive license from BIAL. APTIOM is approved in the U.S. for the treatment of partial-onset seizures in adults, adolescents and children (four years of age and older). APTIOM is not classified as a controlled substance by the U.S. Food and Drug Administration (FDA). BIAL gained approval for eslicarbazepine acetate from the European Medicines Agency (EMA) in April 2009, as adjunctive therapy in adult patients with partial-onset seizures with or without secondary generalization; in December 2016, as adjunctive treatment for patient's above six years of age with partial-onset seizures with or without secondary generalization; and in March 2017, as monotherapy in the treatment of partial-onset seizures, with or without secondary generalization, in adults with newly diagnosed epilepsy. In Europe, the product is marketed under the trade name Zebinix®.

About Epilepsy and Partial-Onset Seizures
Epilepsy is a neurological condition that manifests as unprovoked seizures, which are caused by abnormal firing of impulses from nerve cells in the brain.\(^1\) Epilepsy is one of the most common neurological diseases globally, affecting approximately 50 million people worldwide.\(^2\) An estimated 300,000 Canadians live with epilepsy.\(^3\) Each year in Canada, an average of 15,500 people learn they have epilepsy; 75-85 percent are diagnosed before age 18.\(^4\)

Partial-onset seizures are characterized by bursts of electrical activity that are initially focused in specific areas of the brain and may become more widespread, with symptoms varying according to the affected areas.\(^5\) The unpredictable nature of seizures may have a significant impact on those with epilepsy. Reducing the frequency of seizures may lessen the burden of epilepsy. With approximately one-third of people living with epilepsy still unable to control seizures, there continues to be a need for new therapies.\(^6\) Up to 40 percent of people living with epilepsy do not respond to the first or second monotherapy,\(^7\) and approximately 36 percent fail to achieve adequate control of seizures despite the use of two or more antiepileptic medications.\(^8\)

**About Sunovion Pharmaceuticals Inc. (Sunovion)**

Sunovion is a global biopharmaceutical company focused on the innovative application of science and medicine to help people with serious medical conditions. Sunovion’s vision is to lead the way to a healthier world. The company’s spirit of innovation is driven by the conviction that scientific excellence paired with meaningful advocacy and relevant education can improve lives. With patients at the center of everything it does, Sunovion has charted new paths to life-transforming treatments that reflect ongoing investments in research and development and an unwavering commitment to support people with psychiatric, neurological and respiratory conditions.

Headquartered in Marlborough, Mass., Sunovion is an indirect, wholly-owned subsidiary of Sumitomo Dainippon Pharma Co., Ltd. Sunovion Pharmaceuticals Europe Ltd., based in London, England, and Sunovion Pharmaceuticals Canada Inc., based in Mississauga, Ontario, are wholly-owned direct subsidiaries of Sunovion Pharmaceuticals Inc. Additional information can be found on the company’s web sites: www.sunovion.com \(^{[3]}\), www.sunovion.eu \(^{[4]}\) and www.sunovion.ca \(^{[5]}\). Connect with Sunovion on Twitter \(^{[6]}\), LinkedIn \(^{[7]}\), Facebook \(^{[8]}\) and YouTube \(^{[9]}\).

**About Sumitomo Dainippon Pharma Co., Ltd.**

Sumitomo Dainippon Pharma is among the top-ten listed pharmaceutical companies in Japan, operating globally in major pharmaceutical markets, including Japan, the U.S., China and the European Union. Sumitomo Dainippon Pharma aims to create innovative pharmaceutical products in the Psychiatry & Neurology area, the Oncology area and Regenerative medicine/Cell therapy field, which have been designated as the focus therapeutic areas. Sumitomo Dainippon Pharma is based on the merger in 2005 between Dainippon Pharmaceutical Co., Ltd., and Sumitomo Pharmaceuticals Co., Ltd. Today, Sumitomo Dainippon Pharma has more than 6,000 employees worldwide. Additional information about Sumitomo Dainippon Pharma is available through its corporate website at www.ds-pharma.com \(^{[10]}\).

**(U.S.) Important Safety Information for APTIOM**

**INDICATION:**

Aptiom\(^TM\) (eslicarbazepine acetate) is a prescription medicine to treat partial-onset seizures in patients 4 years of age and older.

**IMPORTANT SAFETY INFORMATION:**

It is not known if APTIOM is safe and effective in children under 4 years of age.

Do not take APTIOM if you are allergic to eslicarbazepine acetate, any of the other ingredients in APTIOM, or oxcarbazepine.

**Suicidal behavior and ideation:** Antiepileptic drugs, including APTIOM, may cause suicidal thoughts or actions in a very small number of people, about 1 in 500. Call your doctor right away if you have any of the following symptoms, especially if they are new, worse, or worry you: thoughts about suicide or dying; attempting to commit suicide; new or worse depression, anxiety, or irritability; feeling agitated or restless; panic attacks; trouble sleeping (insomnia); acting aggressive; being angry or violent; acting on dangerous impulses; an extreme increase in activity and talking (mania); or other unusual changes in behavior or mood.

**Allergic reactions:** APTIOM may cause serious skin rash or other serious allergic reactions that may affect organs or other parts of your body like the liver or blood cells. You may or may not have a rash with these types of reactions. Call your doctor right away if you experience any of the following symptoms: swelling of the face, eyes, lips, or tongue; trouble swallowing or breathing; hives; fever, swollen glands, or sore throat that do not go away or come and go; painful sores in the mouth or around your eyes; yellowing of the skin or eyes; unusual bruising or bleeding; severe fatigue or weakness; severe muscle pain; or frequent infections or infections that do not go away.

**Low salt (sodium) levels in the blood:** APTIOM may cause the level of sodium in your blood to be low. Symptoms may include nausea, tiredness, lack of energy, irritability, confusion, muscle weakness or muscle spasms, or more frequent or more severe seizures. Some medicines can also cause low sodium in your blood. Be sure to tell your health care provider about all the other medicines that you are taking.

**Nervous system problems:** APTIOM may cause problems that can affect your nervous system, including dizziness, sleepiness, vision problems, trouble concentrating, and difficulties with coordination and balance. APTIOM may slow your thinking or motor skills. Do not drive or operate heavy machinery until you know how APTIOM affects you.

**Liver problems:** APTIOM may cause problems that can affect your liver. Symptoms of liver problems include yellowing of your skin or the whites of your eyes, nausea or vomiting, loss of appetite, stomach pain, or dark urine.

**Most common adverse reactions:** The most common side effects in adult patients taking APTIOM include dizziness,
sleepiness, nausea, headache, double vision, vomiting, feeling tired, problems with coordination, blurred vision, and shakiness. Side effects seen in pediatric patients are similar to those seen in adult patients.

**Drug interactions:** Tell your health care provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Taking APTIOM with certain other medicines may cause side effects or affect how well they work. **Do not start or stop other medicines without talking to your health care provider.** Especially tell your health care provider if you take oxcarbazepine, carbamazepine, phenobarbital, phenytoin, primidone, clobazam, omeprazole, simvastatin, rosuvastatin, or birth control medicine.

**Discontinuation:** Do not stop taking APTIOM without first talking to your health care provider. Stopping APTIOM suddenly can cause serious problems.

**Pregnancy and lactation:** APTIOM may cause your birth control medicine to be less effective. Talk to your health care provider about the best birth control method to use. APTIOM may harm your unborn baby. APTIOM passes into breast milk. Tell your health care provider if you are pregnant or plan to become pregnant, or are breastfeeding or plan to breastfeed. You and your health care provider will decide if you should take APTIOM. If you become pregnant while taking APTIOM, talk to your health care provider about registering with the North American Antiepileptic Drug (NAAED) Pregnancy Registry. The purpose of this registry is to collect information about the safety of antiepileptic medicine during pregnancy. You can enroll in this registry by calling 1-888-233-2334.

**Get medical help right away if you have any of the symptoms listed above.**

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

For more information, please see the APTIOM Medication Guide and Full Prescribing Information.

**INDICATIONS AND CLINICAL USE**

APTIOM (eslicarbazepine acetate) is indicated as:

- Monotherapy in the management of partial-onset seizures in adult patients with epilepsy. All patients who participated in the monotherapy trial were newly or recently diagnosed with epilepsy.
- Adjunctive therapy in the management of adults, and children above 6 years of age, with partial-onset seizures who are not satisfactorily controlled with conventional therapy.

**Geriatrics (>65 years of age)**

There were insufficient numbers of elderly patients who completed partial-onset seizure controlled trials (N=39) to determine the safety and efficacy of APTIOM in this patient population. Caution should be exercised during dose titration, and age-associated decrease in renal clearance should be considered in elderly patients.

**Pediatrics (<18 years of age)**

The safety and efficacy of APTIOM has not been established in children under 6 years of age. APTIOM is not indicated for use in this patient population.

**CONTRAINDICATIONS**

Patients with a known hypersensitivity to APTIOM (eslicarbazepine acetate) or other carboxamide derivatives (e.g., carbamazepine, oxcarbazepine) or any of its components. For a complete listing, see the Dosage Forms, Composition and Packaging section of the product monograph.

Patients with a history of, or presence of, second- or third-degree atrioventricular (AV) block.

**WARNINGS AND PRECAUTIONS**

**General**

**Withdrawal of Antiepileptic Drugs (AEDs)**

As with all AEDs, APTIOM (eslicarbazepine acetate) should be withdrawn gradually to minimize the potential of increased seizure frequency, but if withdrawal is needed because of a serious adverse event, rapid discontinuation can be considered.

**Cardiac Rhythm and Conduction Abnormalities**

**PR Interval Prolongation**

APTIOM causes PR interval prolongation. Caution should be observed in patients with first degree atrioventricular block, conduction disorders, a history of syncope or arrhythmia, angina, or ischemic heart disease. Such patients should receive careful monitoring, with ECG recordings at baseline and after titration of APTIOM to steady-state. Concomitant medications that result in a PR interval prolongation (e.g., carbamazepine, pregabalin, lamotrigine, beta-blockers) should be carefully considered to determine whether the therapeutic benefit outweighs the potential risk.

In Phase III adult adjunctive epilepsy studies with APTIOM, the mean increase in PR interval at the end of 12 weeks maintenance treatment was 2.4 msec, 1.3 msec, and 2.6 msec in the 400, 800, and 1200 mg/day groups, respectively, and 0.6 msec in the placebo group. The mean maximum increase in PR interval in these controlled trials was 2.4 msec, 1.3 msec and 2.6 msec in the 400, 800, and 1200 mg/day groups, respectively, and 0.6 msec in the placebo group. A total of 9/1021
APTOM patients and 1/426 (0.2%) placebo patients had a PR-interval value >200 msec at study end that was not present at baseline.

Patients with significant electrocardiographic (ECG) abnormalities were systematically excluded from these trials.

In a clinical pharmacology ECG trial of healthy subjects, the maximum mean difference from placebo in PR interval was 4.4 msec at 5 h post-dosing on day 5 in the 1200 mg (maximum recommended daily dose) treatment arm. For the 2400 mg (2 times maximum recommended daily dose) treatment arm, the maximum mean difference from placebo was 8.2 msec at 3 h post-dosing on day 5.

Post-marketing cases of atrioventricular block have also been reported.

**Heart Rate**

In Phase III adult adjunctive epilepsy studies, the mean change in heart rate at the end of 12 weeks maintenance treatment was -0.5 bpm, 0.8 bpm, and -0.3 bpm in the 400, 800, and 1200 mg/day groups, respectively, and -0.6 bpm in the placebo group. In a clinical pharmacology ECG trial of healthy subjects, APTOM was associated with a dose-dependent increase in heart rate. The maximum mean difference from placebo was 3.6 bpm and 6.8 bpm in the 1200 and 2400 mg dose groups, respectively. Caution should be observed in patients with cardiac conditions that could be worsened by an increase in heart rate, such as tachyarrhythmias or ischemic heart disease.

**Atrial Fibrillation and Atrial Flutter**

APTOIM administration may predispose patients to atrial arrhythmias (atrial fibrillation or flutter), especially in patients with cardiovascular disease. Patients should be made aware of the symptoms of atrial fibrillation and flutter (e.g., palpitations, rapid or irregular pulse, shortness of breath) and told to contact their physician should any of these symptoms occur. One case of atrial flutter was reported in open-label epilepsy trials.

**OTHER RELEVANT WARNINGS AND PRECAUTIONS**

- Drug-induced Liver Injury
- Serious Dermatologic Reactions
- Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)
- Anaphylactic Reactions and Angioedema
- Hyponatremia
- Abnormal Thyroid Function Tests
- Dizziness and Disturbance in Gait and Coordination
- Somnolence and Fatigue
- Cognitive Dysfunction
- Ophthalmological Effects
- Bone Disorders
- Hematologic
- Caution with Driving and Use of Machinery
- Suicidal and Ideation and Behaviour
- Abuse
- Dependence/Liability
- Renal
- Women of Childbearing Potential and Hormonal Contraceptives
- Pregnant Women
- Pregnancy Exposure Registry
- Labour and Delivery
- Nursing Women
- Fertility

For more information:

Please consult the product monograph [https://www.sunovion.ca/monographs/aptiom.pdf](https://www.sunovion.ca/monographs/aptiom.pdf) for important information relating to adverse drug reactions, drug interactions, and dosing information which have not been discussed in this piece.

The product monograph is also available by calling 1-866-260-6291.

**Sunovion Pharmaceuticals Canada Inc. contact information:**
Medical Information or to Report an Adverse Drug Reaction  
1-866-260-6291 Phone  
1-866-933-6799 Fax  
sunovionmedinfo@solutionsinhealth.com
Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html[16]) for information on how to report online, by mail or by fax; or calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

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For a copy of this release, visit Sunovion’s web site at www.sunovion.com[3]

References


Language:
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