Sunovion Announces Health Canada Approval of Aptiom® (eslicarbazepine acetate) as Monotherapy to Treat Partial-Onset Seizures in Adults with Epilepsy

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– APTIOM now provides a once-daily monotherapy treatment option for adults with partial-onset seizures –

MARLBOROUGH, Mass.--(BUSINESS WIRE)--Sunovion Pharmaceuticals Inc. (Sunovion) announced today that Health Canada has approved the use of APTIOM® (eslicarbazepine acetate) as monotherapy for partial-onset seizures in adults with epilepsy. All patients who participated in the monotherapy trial were newly or recently diagnosed with epilepsy.

APTIOM is now indicated in Canada as monotherapy and as adjunctive therapy for the treatment of partial-onset seizures (POS) in adults with epilepsy.

"Partial-onset seizures are the most common type of seizures experienced by people living with epilepsy and, given their unpredictable nature, can have a significant impact on their life," said Eduard Bercovici, M.D., Epileptologist, director of the Southern Ontario Epilepsy Clinic. "This new indication for APTIOM in Canada helps to provide an additional treatment option for health care professionals and patients with partial-onset seizures."

The SNDs approval is supported by data from a Phase 3, double-blind, active-controlled, non-inferiority study in which APTIOM met its primary efficacy endpoint of non-inferiority to the active comparator, carbamazepine controlled release (CBZ-CR).

"APTIOM’s approval in Canada as a once-daily, monotherapy treatment option for adults living with partial-onset seizures is a significant milestone in Sunovion’s commitment to the epilepsy community and improving the lives of people affected by neurological conditions," said David Frawley, Executive Vice President and Chief Commercial Officer at Sunovion. "We are pleased to offer APTIOM as a new monotherapy treatment option for even more adults living with epilepsy and partial-onset seizures, which can be challenging to manage."

Phase 3 Study Results
In a double-blind, active-controlled, non-inferiority study, 813 adults with newly or recently diagnosed epilepsy received either APTIOM (800, 1200 or 1600 mg, once-daily) or the active comparator, carbamazepine controlled release (CBZ-CR: 200, 400 or 600 mg, twice-daily). All patients were randomized to the lowest dose level of each drug and only escalated to the next dose level if a seizure occurred. APTIOM met its primary efficacy endpoint of non-inferiority to CBZ-CR. In the primary efficacy analysis, 71.1 percent of the patients were classified as seizure-free in the APTIOM group and 75.6 percent in the CBZ-CR group within the 26-week evaluation period.

APTIOM was generally well-tolerated. The most common treatment-emergent adverse events (TEAEs) reported for APTIOM included dizziness (13.7 percent) and headache (22.9 percent). The study (BIA-2093-311) was conducted by Sunovion’s partner, BIAL, a privately held Portuguese research-based pharmaceutical company.

About APTIOM® (eslicarbazepine acetate)
APTIOM is a member of the dibenzepine carboxamide family of antiepileptic drugs (AEDs), an established class of medicines. APTIOM is approved in Canada 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 monotherapy for the treatment of POS. All patients who participated in the monotherapy trial were newly or recently diagnosed with epilepsy. The precise mechanism(s) by which eslicarbazepine acetate, 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 FDA. BIAL gained approval for eslicarbazepine acetate from the European Medicines Agency 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 patients 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

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.4 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.5 Up to 40 percent of people living with epilepsy do not respond to the first or second monotherapy,6 and approximately 36 percent fail to achieve adequate control of seizures despite the use of two or more antiepileptic medications.7

(U.S.) Important Safety Information for APTIOM

INDICATION:
APTIOM® (eslicarbazepine acetate) is a prescription medicine used alone or with other medicines to treat partial-onset seizures in patients 4 years of age and older.

Related Links:

https://news.sunovion.com
In Phase III epilepsy studies with APTIOM, the mean increase in PR (e.g., carbamazepine, pregabalin, titration of APTIOM to steady-state. Concomitant medications that result disease. Such patients should APTIOM causes PR interval prolongation. Caution should be observed in patients with first degree atrioventricular (AV) block. 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 patients taking APTIOM include dizziness, sleepiness, nausea, headache, double vision, vomiting, feeling tired, problems with coordination, blurred vision, and Shakiness.

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 [3] or call 1-800-FDA-1088.

For more information, please see the APTIOM Medication Guide [4] and Full Prescribing Information [5].

(CANADA) Important Safety Information for APTIOM

INDICATIONS AND CLINICAL USE

**Adults (≥18 years of age)**

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 partial-onset seizures in adult patients with epilepsy 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 in pediatric patients have not been established. APTIOM is not indicated for use in this 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**

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 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 (0.8 percent) APTIOM patients and 1/426 (0.2 percent) 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 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, APTIOM was associated with a dose-dependent increase in heart rate. The maximum mean difference from placebo was 3.6 bpm and 8.8 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
APTIOM 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
- Withdrawal of Antiepileptic Drugs (AEDs)
- 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
- Hematological
- 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
- Labour and Delivery
- Nursing Women
- Fertility

For more information:

Please consult the product monograph http://www.sunovion.com/manufactures/aptiom.pdf [6] 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 [7]

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 (http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) [8] 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.

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.


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 Chemical 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 [16].

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