RECORDATI RARE DISEASES GROUP

IMPORTANT PRESCRIBING INFORMATION

November 23, 2020

Subject: **Discontinuation of US-labeled PEGANONE 250 mg Tablets (ethotoin tablets, USP)**

Dear Health Care Provider,

Recordati Rare Diseases Inc. is discontinuing the manufacture, distribution and sale of PEGANONE 250 mg tablets (ethotoin tablets, USP) indicated for the control of tonic-clonic (grand mal) and complex partial (psychomotor) seizures. This decision was made due to the combination of low product demand and complex manufacturing difficulties. This discontinuation for PEGANONE 250 mg tablets (ethotoin tablets, USP) is effective immediately.

U.S. FDA-approved Indication

PEGANONE (ethotoin tablets, USP) is an oral antiepileptic of the hydantoin series. PEGANONE is indicated for the control of tonic-clonic (grand mal) and complex partial (psychomotor) seizures.

For reporting of adverse events and more information

Any adverse effects or medication issues resulting from the use of this drug or quality issues should be reported to Recordati Rare Diseases Inc. at 1-888-575-8344.

Adverse reactions or quality problems experienced with the use of this product may also be reported to the FDA's MedWatch Adverse Event Reporting program either online, by regular mail or by fax:

- Complete and submit the report **Online**: www.fda.gov/medwatch/report.htm
- **Regular mail or Fax**: Download form www.fda.gov/MedWatch/getforms.htm or call 1-800-332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178.

Important Safety Information

Antiepileptic drugs (AEDs), including PEGANONE, increase the risk of suicidal thoughts or behavior in patients taking these drugs for any indication. Patients treated with any AED for any indication should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.

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Anyone considering prescribing PEGANONE or any other AED must balance the risk of suicidal thoughts or behavior with the risk of untreated illness. Epilepsy and many other illnesses for which AEDs are prescribed are themselves associated with morbidity and mortality and an increased risk of suicidal thoughts and behavior. Should suicidal thoughts and behavior emerge during treatment, the prescriber needs to consider whether the emergence of these symptoms in any given patient may be related to the illness being treated.

Advise both patients and caregivers that AEDs, including PEGANONE, may increase the risk of suicidal thoughts and behavior and also about the need to be alert for the emergence or worsening of symptoms of depression, any unusual changes in mood or behavior, or the emergence of suicidal thoughts, behavior, or thoughts of self-harm. Advise both patients and caregivers to report behaviors of concern immediately to healthcare providers.

PEGANONE can cause fetal harm when administered to a pregnant woman. There are multiple reports in the clinical literature which indicate that the use of antiepileptic drugs during pregnancy results in an increased incidence of birth defects in the offspring. Therefore, antiepileptic drugs should be administered to women of child- bearing potential only if they are clearly shown to be essential in the management of their seizures.

Antiepileptic drugs should not be discontinued in patients in whom the drug is administered to prevent major seizures because of the strong possibility of precipitating status epilepticus with attendant hypoxia and risk to both mother and the unborn child. Consideration should, however, be given to discontinuation of antiepileptics prior to and during pregnancy when the nature, frequency and severity of the seizures do not pose a serious threat to the patient.
If PEGANONE is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus.

PEGANONE is contraindicated in patients with hepatic abnormalities or hematologic disorders.

Blood dyscrasias have been reported in patients receiving PEGANONE. Advise both patients and caregivers to report immediately such signs and symptoms as sore throat, fever, malaise, easy bruising, petechiae, epistaxis, skin rash or others that may be indicative of an infection or bleeding tendency.

Adverse reactions associated with PEGANONE, in decreasing order of severity, are:

Isolated cases of lymphadenopathy and systemic lupus erythematosus have been reported in patients taking hydantoin compounds, and lymphadenopathy has occurred with PEGANONE. Withdrawal of therapy has resulted in remission of the clinical and pathological findings. Therefore, if a lymphoma-like syndrome develops, the drug should be withdrawn and the patient should be closely observed for regression of signs and symptoms before treatment is resumed.

Ataxia and gum hypertrophy have occurred only rarely—usually only in patients receiving an additional hydantoin derivative. It is of interest to note that ataxia and gum hypertrophy have

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subsided in patients receiving other hydantoins when PEGANONE (ethotoin tablets, USP) was given as a substitute antiepileptic.

Occasionally, vomiting or nausea after ingestion of PEGANONE has been reported, but if the drug is administered after meals, the incidence of gastric distress is reduced. Other side effects have included chest pain, nystagmus, diplopia, fever, dizziness, diarrhea, headache, insomnia, fatigue, numbness, skin rash, and Stevens-Johnson syndrome.

Prescribers or other health professionals should inform patients, their families, and their caregivers about the benefits and risks associated with treatment with ethotoin and should counsel them in its appropriate use.

We are committed to helping address patients' unmet needs through our corporate mission. If you have questions or concerns regarding this product, please call Recordati Rare Diseases Medical Information at 1-888-575-8344.

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