RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOALS
The goal of the MYALEPT REMS is to mitigate (1) the risks of serious adverse sequelae (such as severe infections, excessive weight gain, glucose intolerance, diabetes mellitus) due to the development of anti-metreleptin antibodies that neutralize endogenous leptin and/or MYALEPT, and (2) the risk of lymphoma by:

- Educating prescribers about the development of neutralizing anti-metreleptin antibodies, the serious adverse sequelae that may result from these antibodies, and the risk for lymphoma associated with MYALEPT
- Limiting the population exposed to MYALEPT by requiring prescriber certification, pharmacy certification, and prescriber attestation that each patient has a diagnosis consistent with the approved indication
II. REMS ELEMENTS

A. Elements to Assure Safe Use (ETASU)

1. Healthcare Providers (HCPs) who prescribe MYALEPT are specially certified.
   a. Aegerion will ensure that HCPs who prescribe MYALEPT are specially certified.
   b. To become specially certified to prescribe MYALEPT, prescribers must enroll in the MYALEPT REMS Program. Prescribers must complete the following requirements:
      i. review the Prescribing Information
      ii. complete the Prescriber Training Module
      iii. complete and sign the Prescriber Enrollment Form and submit it to the MYALEPT REMS Program.
   c. Aegerion will:
      i. Ensure that the Prescriber Training Module and the Prescriber Enrollment Form are available on the MYALEPT REMS Program website (www.MYALEPTREMS.com) or can be obtained by contacting the MYALEPT REMS Program by phone at 1-855-6MYALEPT (1-855-699-2537).
      ii. Ensure that prescribers complete the Prescriber Training Module and the Prescriber Enrollment Form before activating prescribers’ certification in the MYALEPT REMS Program.
      iii. Ensure that prescribers are notified when they have been successfully certified by the MYALEPT REMS Program.
      iv. Inform certified prescribers following substantial changes to the MYALEPT REMS or MYALEPT REMS Program; substantial changes include significant changes to the operation of the MYALEPT REMS Program or changes to the Prescribing Information that affect the risk-benefit profile of MYALEPT.
      v. Communicate information about the risks and MYALEPT REMS Program requirements to prescribers through the MYALEPT REMS Program website and MYALEPT REMS introductory information sheet titled MYALEPT REMS Program: An Introduction. Aegerion will provide the REMS Program: An Introduction, Prescriber Training Module, Prescriber Enrollment Form, and the Prescribing Information to prescribers who (1) attempt to prescribe MYALEPT and are not yet certified, or (2) inquire about how to become certified.

The following materials are part of the REMS and are appended:

- Prescriber Training Module
- Prescriber Enrollment Form
- MYALEPT REMS Program: An Introduction
2. Pharmacies that dispense MYALEPT are specially certified.

a. Aegerion will ensure that MYALEPT is dispensed only by specially certified pharmacies.

To become certified to dispense MYALEPT, each pharmacy representative must agree to the following:

i. to educate all pharmacy staff involved in the dispensing of MYALEPT on the MYALEPT REMS Program requirements

ii. to put processes and procedures in place to verify, prior to dispensing MYALEPT, that:

1) the prescriber is certified in the MYALEPT REMS Program

2) the MYALEPT REMS Prescription Authorization Form is received for each new prescription

iii. to be audited to ensure that all processes and procedures are in place and are being followed for the MYALEPT REMS Program

iv. to provide prescription data to the MYALEPT REMS Program, and

v. to refrain from reselling or transferring MYALEPT to other pharmacies or distributors.

The following material is part of the REMS and appended:

• MYALEPT REMS Prescription Authorization Form
3. **MYALEPT is dispensed only to patients with evidence or other documentation of safe-use conditions.**

   a. MYALEPT is dispensed only to patients whose prescribers are specially certified in the MYALEPT REMS Program and attest on the MYALEPT REMS Prescription Authorization Form that:

      i. They understand that MYALEPT is indicated as an adjunct to diet as replacement therapy to treat the complications of leptin deficiency in patients with congenital or acquired generalized lipodystrophy.

      ii. They affirm that their patient has a clinical diagnosis consistent with the approved indication, and that the patient (or caregiver) has been properly informed of the benefits and risks of MYALEPT therapy.

      iii. They understand that MYALEPT is not indicated for the treatment of complications of partial lipodystrophy.

      iv. They understand that MYALEPT is not indicated for the treatment of liver disease, including non-alcoholic steatohepatitis (NASH).

      v. They understand that MYALEPT is not indicated for use in patients with HIV-related lipodystrophy.

      vi. They understand that MYALEPT is not indicated for use in patients with metabolic disease, including diabetes mellitus and hypertriglyceridemia, without concurrent evidence of congenital or acquired generalized lipodystrophy.

      vii. They understand that MYALEPT is contraindicated in patients with general obesity not associated with congenital leptin deficiency.

      viii. They understand that MYALEPT is associated with serious adverse events due to the development of anti-metreleptin antibodies that neutralize endogenous leptin and/or MYALEPT.

      ix. They agree to test for neutralizing antibodies to MYALEPT if a patient experiences severe infections or if they suspect MYALEPT treatment is no longer working (e.g., loss of glycemic control, increased triglycerides).

      x. They understand that MYALEPT is associated with a risk of lymphoma.
xi. They understand it is important to carefully consider treatment with MYALEPT in patients with significant hematologic abnormalities and/or acquired generalized lipodystrophy

B. Implementation System

1. Aegerion will ensure that MYALEPT is distributed to and dispensed only by certified pharmacies.

2. Aegerion will maintain, monitor, and evaluate the implementation of the MYALEPT REMS Program.
   a. Aegerion will maintain a secure, validated database of certified prescribers and pharmacies in the MYALEPT REMS Program. Amylin Pharmaceuticals will send confirmation of certification to each certified pharmacy.
   b. Aegerion will maintain a MYALEPT REMS Program Call Center to support patients, prescribers, and pharmacies interfacing with the MYALEPT REMS.
   c. Aegerion will ensure that all materials listed in or appended to the MYALEPT REMS Program will be available through the MYALEPT REMS Program website (www.MYALEPTREMS.com) or by calling the MYALEPT REMS Program Call Center at 1-855-6MYALEPT (1-855-699-2537).
   d. If there are substantive changes to the MYALEPT REMS or MYALEPT REMS Program, Aegerion will update all affected materials, and notify enrolled prescribers and certified pharmacies, as applicable. Substantive changes are defined as significant changes to the operation of the MYALEPT REMS Program or changes to the Prescribing Information that affect the risk-benefit profile of MYALEPT.
   e. Aegerion will monitor and audit the certified pharmacies within 180 days after the pharmacy is certified to ensure that all processes and procedures are in place and functioning to support the requirements of the MYALEPT REMS Program. Thereafter, Aegerion will include the certified pharmacies in the company’s annual audit plan. Corrective action will be instituted by Aegerion if noncompliance is found.
   f. Based on monitoring and evaluation of the MYALEPT REMS elements to assure safe use, Aegerion will take reasonable steps to improve implementation of these elements and to maintain compliance with the MYALEPT REMS Program requirements, as applicable.

C. Timetable for Submission of Assessments

Aegerion will submit REMS Assessments to the FDA 6 months, 12 months, and annually thereafter from the date of the initial REMS approval. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the
submission date for that assessment. Aegerion will submit each assessment so that it will be received by the FDA on or before the due date.