myalept®

(metreleptin) for injection 11.3 mg per vial

Risk Evaluation and Mitigation Strategy (REMS) Program

Prescriber Training Module

Reference ID: 3811882

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Introduction

Introduction

MYALEPT® (metreleptin) for injection is available only through a restricted program called the MYALEPT REMS Program.

- Prescribers must complete this training module and enroll in the MYALEPT REMS Program prior to prescribing MYALEPT.

The purpose of this training module is to educate prescribers about

- the development of anti-metreleptin antibodies that neutralize endogenous leptin and/or MYALEPT and the serious adverse events that may result from these antibodies,
- the risk of lymphoma, and
- appropriate patient selection

Because of these risks, appropriate patient selection consistent with the approved indication for MYALEPT is very important.

MYALEPT® (metreleptin) for injection Product Information

Indication

MYALEPT® (metreleptin) for injection 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**

Serious Risks Associated with MYALEPT

Serious Risks Associated with MYALEPT

1. Development of anti-metreleptin antibodies that neutralize endogenous leptin and MYALEPT
2. Lymphoma

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Boxed Warning: Anti-metreleptin Antibodies with Neutralizing Activity - Serious Adverse Events

- Anti-metreleptin antibodies with neutralizing activity associated with adverse events consistent with loss of endogenous leptin activity and/or loss of efficacy have been identified among patients with generalized lipodystrophy
  - 2 of 33 patients who underwent antibody testing
    1. tested positive for anti-metreleptin antibodies with neutralizing activity

    and

    2. reported adverse events consistent with neutralizing activity, including severe infections, loss of glycemic control, and increases in triglycerides

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Boxed Warning: Anti-metreleptin Antibodies with Neutralizing Activity - Serious Adverse Events (continued)

- In other populations
  - 3 of 563 patients who underwent antibody testing
    1. tested positive for anti-metreleptin antibodies with neutralizing activity

    and

    2. reported adverse events consistent with neutralizing activity, including excessive weight gain and development of glucose intolerance or diabetes mellitus

The clinical implications associated with development of anti-metreleptin antibodies with neutralizing activity are not well-characterized at this time due to the small number of reports.

Antibody Testing in MYALEPT Trials - Data

- Anti-metreleptin antibodies were detected in 84% (36/43) of patients with generalized lipodystrophy studied in the MYALEPT trials
- Total anti-metreleptin antibody titers ranged between 1:5 and 1:1,953,125
- Anti-metreleptin antibodies with neutralizing activity associated with adverse events consistent with loss of endogenous leptin activity and/or loss of MYALEPT efficacy were observed in 6% (2/33) of the patients tested

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Antibody Testing in MYALEPT Trials - Limitations

- The immunogenicity assays utilized in clinical trials lacked sensitivity, resulting in potential underestimation of the number of samples positive for anti-metreleptin antibodies with neutralizing activity
  - The observed incidence of an antibody assay (including neutralizing antibody assays) positivity may be influenced by several factors including assay sensitivity and specificity, assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease.

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Antibody Testing in MYALEPT Trials – Limitations (continued)

- Antibody testing was not performed uniformly in the MYALEPT trials. The incompleteness of the current immunogenicity database precludes understanding of the magnitude and persistence of the observed anti-metreleptin antibody responses.

- Comparison of the incidence of antibodies to metreleptin with the incidence of antibodies to other products may be misleading.

Neutralizing Activity - What is My Role?

- Test for neutralizing activity in patients who experience severe infections or if you suspect that MYALEPT is no longer working.
- Contact Aegerion Pharmaceuticals, Inc. (Aegerion) at 1-866-216-1526 for instructions on how to submit samples for neutralizing antibody testing. The assay is not commercially available.

Aegerion will ask you to:

1. Obtain written consent from your patient to release the sample and send a copy of the consent to Aegerion.
2. Complete a questionnaire to explain why you are requesting neutralizing activity testing and send it to Aegerion.
3. Send the sample to the designated laboratory for testing.
   - The results are generally available within 60 days
4. Aegerion will contact you to provide and discuss the results.

Boxed Warning: Lymphoma

- Three cases of T-cell lymphoma have been reported in the MYALEPT lipodystrophy program
  - All 3 patients had **acquired generalized lipodystrophy (out of a total of 20 patients with acquired generalized lipodystrophy).**
    - Two of these patients were diagnosed with peripheral T-cell lymphoma while receiving MYALEPT.
    - Both had immunodeficiency and significant hematologic abnormalities, including severe bone marrow abnormalities, before the start of MYALEPT treatment.
    - A separate case of anaplastic large cell lymphoma was reported in a patient receiving MYALEPT <u>who did not have hematological abnormalities before treatment.</u>

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Lymphoma – What is My Role?

- Take a careful medical history for past or current hematologic abnormalities
- Carefully consider the benefits and risks of treatment with MYALEPT in patients with
  - significant hematologic abnormalities, and/or
  - acquired generalized lipodystrophy

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Adverse Reaction Reporting

To report SERIOUS ADVERSE REACTIONS, please call/contact:

- 1-855-669-2537 and/or
- FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

Appropriate Patient Selection

Appropriate Patient Selection

Contraindication – General Obesity

MYALEPT is contraindicated in patients with general obesity not associated with congenital leptin deficiency.

- MYALEPT has not been shown to be effective in treating general obesity, and the development of anti-metreleptin antibodies with neutralizing activity has been reported in obese patients treated with MYALEPT
- Adverse events consistent with loss of endogenous leptin activity have been identified in three patients without lipodystrophy who received metreleptin (excessive weight gain, development of glucose intolerance or diabetes mellitus).

The clinical implications associated with development of anti-metreleptin antibodies with neutralizing activity are not well-characterized at this time due to the small number of reports.

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Appropriate Patient Selection

Important Limitations of Use

- **The safety and effectiveness of MYALEPT for the following conditions have <u>not</u> been established**
  - The treatment of complications of partial lipodystrophy
  - The treatment of liver disease including non-alcoholic steatohepatitis (NASH)

- **MYALEPT <u>is not indicated for use</u> in patients with**
  - HIV-related lipodystrophy
  - Metabolic disease including diabetes mellitus and hypertriglyceridemia, without concurrent evidence of congenital or acquired generalized lipodystrophy.

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MYALEPT® (metreleptin) for injection
REMS PROGRAM INFORMATION

MYALEPT® (metreleptin) for injection REMS Program

Key program elements:

- Certification of Prescribers of MYALEPT
  - Certification consists of training, and enrolling in the MYALEPT REMS Program.
- Completion of a Prescription Authorization Form for each new prescription
- Restricted distribution of MYALEPT through certified pharmacies.

MYALEPT® (metreleptin) for injection REMS Program

Before prescribing MYALEPT, prescribers must complete the following steps:

1. Review the Prescribing Information and this Prescriber Training Module.
2. Complete, sign, and submit the one-time MYALEPT REMS Program Prescriber Enrollment Form.
3. Complete, sign, and submit the MYALEPT REMS Program Prescription Authorization Form for each new prescription.

Note: All Materials can be downloaded from the MYALEPT REMS website at: www.MYALEPTREMS.com

Or request these materials by calling 1-855-669-2537

1. Review Prescriber Education Materials

Review the following Prescriber Education Materials:

a) MYALEPT® (metreleptin) for injection Prescribing Information

b) This Prescriber Training Module

2. Enroll in MYALEPT® (metreleptin) for injection REMS Program

To enroll in the MYALEPT REMS Program:

- Download the MYALEPT REMS Program Prescriber Enrollment Form at www.MYALEPTREMS.com or request a copy by calling 1-855-669-2537
- Complete the enrollment form
- Sign & submit the enrollment form
  - Fax to 1-877-328-9682

3. Submit Prescription Authorization Form

When prescribing MYALEPT® (metreleptin) for injection, a prescriber must complete a Prescription Authorization Form for each new prescription.

As part of completing the Prescription Authorization Form, you attest that:

- I 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.
- I affirm that my patient has a clinical diagnosis consistent with generalized lipodystrophy, and that my patient (or their caregiver) has been properly informed of the benefits and risks of MYALEPT therapy.

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3. Submit Prescription Authorization Form (continued)

- I understand that MYALEPT is not indicated for the treatment of complications of partial lipodystrophy.
- I understand that MYALEPT is not indicated for the treatment of liver disease, including non-alcoholic steatohepatitis (NASH).
- I understand that MYALEPT is not indicated for use in patients with HIV-related lipodystrophy.
- I 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.

3. Submit Prescription Authorization Form (continued)

- I understand that MYALEPT is contraindicated in patients with general obesity not associated with congenital leptin deficiency.
- I understand that MYALEPT is associated with serious adverse events due to the development of anti-metreleptin antibodies that neutralize endogenous leptin and/or MYALEPT.
- I agree to test for neutralizing antibodies in patients who experience severe infections or if I suspect MYALEPT is no longer working (e.g., loss of glycemic control, or increases in triglycerides).
- I understand that MYALEPT is associated with a risk of lymphoma.
- I understand I must carefully consider the risks of treatment with MYALEPT in patients with significant hematologic abnormalities and/or acquired generalized lipodystrophy.

3. Submit Prescription Authorization Form

Each new prescription for MYALEPT must be written using the MYALEPT Prescription Authorization Form.

1. Download the Prescription Authorization Form at www.MYALEPTREMS.com or request a copy by calling 1-855-669-2537
2. Complete the Prescription Authorization Form
3. Sign & submit the Prescription Authorization Form
   - Fax to 1-877-328-9682

Knowledge Assessment

Knowledge Assessment

- The following questions about MYALEPT® (metreleptin) for injection are provided to reinforce learning.
- If you have difficulty answering these questions, review the previous slides and refer to the Prescribing Information.

Knowledge Assessment

1. Which of the following statements is true?
   - ☐ MYALEPT (metreleptin) for injection is indicated for use in patients with HIV-related lipodystrophy.
   - ☐ MYALEPT is indicated for use in patients with metabolic disease, including diabetes mellitus and hypertriglyceridemia, without concurrent evidence of inherited or acquired generalized lipodystrophy.
   - ☐ MYALEPT is a recombinant analog of murine leptin.
   - ☐ 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.

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Knowledge Assessment

1. Which of the following statements is true?
   - ☐ MYALEPT (metreleptin) is indicated for use in patients with HIV-related lipodystrophy.
   - ☐ MYALEPT is indicated for use in patients with metabolic disease, including diabetes mellitus and hypertriglyceridemia, without concurrent evidence of inherited or acquired generalized lipodystrophy.
   - ☐ MYALEPT is a recombinant analog of murine leptin.
   - ✓ **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.

Answer: 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

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- **The safety and effectiveness of MYALEPT for the following conditions have not been established**
  - The treatment of complications of partial lipodystrophy
  - The treatment of liver disease including non-alcoholic steatohepatitis (NASH)

- **MYALEPT <u>is not indicated for use</u> in patients with**
  - HIV-related lipodystrophy
  - Metabolic disease including diabetes mellitus and hypertriglyceridemia, without concurrent evidence of congenital or acquired generalized lipodystrophy.

- **MYALEPT is <u>contraindicated</u> in patients with general obesity not associated with congenital leptin deficiency.**

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Knowledge Assessment

2. The risks and benefits of MYALEPT® (metreleptin) for injection treatment should be carefully considered in patients with significant hematologic abnormalities (for example, leukopenia, neutropenia, bone marrow abnormalities, lymphoma and/or lymphadenopathy) and/or acquired generalized lipodystrophy.

   ☐ True

   ☐ False

Knowledge Assessment

2. The risks and benefits of MYALEPT® (metreleptin) for injection treatment should be carefully considered in patients with significant hematologic abnormalities (for example, leukopenia, neutropenia, bone marrow abnormalities, lymphoma and/or lymphadenopathy) and/or acquired generalized lipodystrophy.

   ✓ True

   ☐ False

Answer:
- Peripheral T-cell lymphoma was diagnosed in two patients with acquired generalized lipodystrophy while receiving MYALEPT.
  - Both had immunodeficiency and significant hematologic abnormalities including severe bone marrow abnormalities before the start of MYALEPT treatment.
- A separate case of anaplastic large cell lymphoma was reported in a patient with acquired generalized lipodystrophy who did not have hematologic abnormalities before MYALEPT treatment.

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Knowledge Assessment

3. Developing neutralizing activity to metreleptin could:
   - ☐ affect endogenous leptin
   - ☐ result in loss of efficacy
   - ☐ both of the above
   - ☐ none of the above

Knowledge Assessment

3. Developing neutralizing activity to metreleptin could:
   - ☐ affect endogenous leptin
   - ☐ result in loss of efficacy
   - ✓ both of the above
   - ☐ none of the above

Answer: Developing neutralizing activity to metreleptin could affect endogenous leptin and could result in loss of efficacy.

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Knowledge Assessment

4. If a patient is experiencing severe infections and/or I suspect Myalept is no longer working, I will contact Aegerion Pharmaceuticals, Inc. for instructions on how to send a blood sample to test for anti-metreleptin antibodies with neutralizing activity.

   - ☐ True
   - ☐ False

Knowledge Assessment

4. If a patient is experiencing severe infections and/or I suspect Myalept is no longer working, I will contact Aegerion Pharmaceuticals, Inc. (Aegerion) for instructions on how to send a blood sample to test for anti-metreleptin antibodies with neutralizing activity.

   ✓ True

   ☐ False

Answer: If you suspect your patient is experiencing complications from the development of anti-metreleptin neutralizing antibodies, you can submit a request and obtain results from Aegerion at no cost.

1. Call 1-866-216-1526
   - Aegerion will provide you information on the requirements for sample collection and shipment.
2. Aegerion will instruct you to:
   a. Obtain written consent from your patient to release the sample and send a copy of the consent to Aegerion.
   b. Complete a questionnaire to explain why you are requesting neutralizing activity testing.
   c. Send the sample and paperwork to the designated laboratory for testing.
   - The results are generally available within 60 days
3. Aegerion will contact you to provide and discuss the results.

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Knowledge Assessment

5. How often should the Prescription Authorization Form be completed?
   - ☐ Each new prescription
   - ☐ Only on the first prescription
   - ☐ Every refill
   - ☐ Once a year

Knowledge Assessment

5. How often should the Prescription Authorization Form be completed?
   - ✓ Each new prescription
   - ☐ Only on the first prescription
   - ☐ Every refill
   - ☐ Once a year

Answer: For each new prescription, the prescriber must submit a Prescription Authorization Form.

Knowledge Assessment

6. MYALEPT® (metreleptin) for injection is available only through certified pharmacies.

   ☐ True

   ☐ False

Knowledge Assessment

6. MYALEPT® (metreleptin) for injection is available only through certified pharmacies.
   - ✓ True
   - ☐ False

Answer: MYALEPT is available only through pharmacies that are specially certified and agree to follow REMS requirements. For a list of certified pharmacies call: 1-855-669-2537.

Completion of Training for the MYALEPT® (metreleptin) for injection REMS Program

You have completed training for the MYALEPT REMS Program.

To enroll in the MYALEPT REMS Program, complete the Enrollment Form and return via fax at 1-877-328-9682.

For more information on the MYALEPT REMS Program, please call 1-855-669-2537 or visit www.MYALEPTREMS.com.

Aegerion Pharmaceuticals

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