

myalept[®]
(metreleptin) for injection 11.3 mg
per vial

Risk Evaluation and Mitigation Strategy (REMS) Program
Prescriber Training Module

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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 the use of MYALEPT:

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

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



- Anti-metresleptin antibodies with neutralizing activity associated with adverse events consistent with loss of endogenous leptin activity, including loss of efficacy and/or severe infections, have been identified among patients with generalized lipodystrophy
 - 2 of 33 patients who underwent antibody testing
 1. tested positive for anti-metresleptin antibodies with neutralizing activity
and
 2. reported adverse events consistent with neutralizing activity, including:
 - Severe infections,
 - Loss of glycemie control, and
 - Increases in triglycerides.

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



■ In other populations

- 3 of 563 patients who underwent antibody testing
 1. tested positive for anti-metresleptin 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-metresleptin 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-metresleptin antibodies were detected in 84% (36/43) of patients with generalized lipodystrophy studied in the MYALEPT trials
- Total anti-metresleptin antibody titers ranged between 1:5 and 1:1,953,125
- Anti-metresleptin 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 with generalized lipodystrophy tested

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-metresreptin 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.

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-metresreptin antibody responses.
- Comparison of the incidence of antibodies to metresreptin 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 Amryt Pharmaceutical DAC (Amryt) at 1-866-216-1526 for instructions on how to submit samples for neutralizing antibody testing. The assay is not commercially available.

Amryt will ask you to:

1. Obtain written consent from your patient to release the sample and send a copy of the consent to Amryt.
2. Complete a questionnaire to explain why you are requesting neutralizing activity testing and send it to Amryt.
3. Send the sample to the designated laboratory for testing.
 - The results are generally available within 60 days
4. Amryt 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 who did not have hematological abnormalities before treatment.

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

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.



Important Limitations of Use

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



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, and the
- 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,
and
- 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

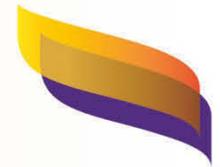


When prescribing MYALEPT® (metreleptin) for injection, a prescriber must complete a Prescription Authorization Form for each new prescription.

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.

3. Submit Prescription Authorization Form (continued)



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

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

(continued on next slide)



(continued from previous slide)

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

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

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.

Knowledge Assessment



3. Developing neutralizing activity to metreleptin could:
- affect endogenous leptin
 - result in loss of efficacy
 - result in increased susceptibility to severe infection
 - all of the above
 - none of the above

Knowledge Assessment



3. Developing neutralizing activity to metreleptin could:
- affect endogenous leptin
 - result in loss of efficacy
 - result in increased susceptibility to severe infection
 - all of the above
 - none of the above

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

Knowledge Assessment



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

True

False

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

1. Call 1-866-216-1526
 - Amryt will provide you information on the requirements for sample collection and shipment.
2. Amryt will instruct you to:
 - a. Obtain written consent from your patient to release the sample and send a copy of the consent to Amryt.
 - 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. Amryt will contact you to provide and discuss the results.

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.



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