Myalepta (metreleptin) 3 mg vial: inconsistency in the Spanish language package leaflet (PL)

Dear Healthcare Professional,

Amryt Pharmaceuticals DAC in agreement with the European Medicines Agency and the National Competent Authority of Spain, Spanish Agency for Medicines and Health Products (AEMPS), would like to inform you of the following:

Summary

- **An inconsistency has been identified in the package leaflet (PL) that accompanies the Myalepta (metreleptin) 3 mg vial distributed for use in Spain.**
- **In the PL Section 7, Step B – Filling the 1 mL syringe with 0.6 mL water for injection, the text mentions that the patient should withdraw 0.6 mL of water for injection (WFI) from the vial. The accompanying picture shows a syringe with 2.2 mL of WFI. The picture is incorrect and should show a syringe with 0.6 mL of WFI.**
- **In Spain the Myalepta 3 mg vial is distributed with a 1 mL syringe for reconstitution. The risk of the patient reconstituting with 2.2 mL WFI is low but nevertheless there is a risk that the patient may use the incorrect volume of WFI. If this did occur the patient would be at risk of administering too low a dose of Myalepta, which may lead to lack of treatment effect.**

Background on the safety concern

Myalepta (metreleptin) is indicated as an adjunct to diet as a replacement therapy to treat the complications of leptin deficiency in lipodystrophy (LD) patients:

- with confirmed congenital generalised LD (*Berardinelli-Seip syndrome*) or acquired generalised LD (*Lawrence syndrome*) in adults and children 2 years of age and above
- with confirmed familial partial LD or acquired partial LD (*Barraquer-Simons syndrome*), in adults and children 12 years of age and above for whom standard treatments have failed to achieve adequate metabolic control.

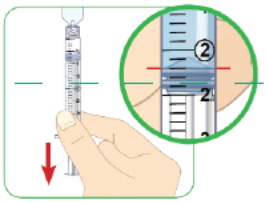
We are writing to inform you of an inconsistency in the package leaflet (PL) that accompanies the Myalepta (metreleptin) 3 mg vial distributed for use in Spain.

In **Section 7, Step B – Filling the 1 mL syringe with 0.6 mL water for injection**, the text mentions that the patient should withdraw 0.6 mL of water for injection (WFI) from the vial. The accompanying picture shows a syringe with 2.2 mL of WFI (please see image 1 below). The picture is incorrect and should show a syringe with 0.6 mL of WFI (please see image 2 below).

Image 1 - Step B – Filling the 1 mL syringe with 0.6 mL water for injection with INCORRECT picture

Mantenga la jeringa dentro de la ampolla y dele la vuelta. La jeringa deberá estar ahora hacia arriba.
Mantenga la jeringa dentro de la ampolla y tire del émbolo con precaución.

- Tire del émbolo hasta que el borde superior de este se alinee con la marca negra de 0,6 ml.
- Debe comprobar que no haya bolsas ni burbujas de aire en la jeringa de 1 ml. Consulte los pasos del 6 al 8 que se muestran a continuación sobre la extracción de bolsas de aire o burbujas de aire de la jeringa.
- Extraiga la jeringa de la ampolla de plástico.



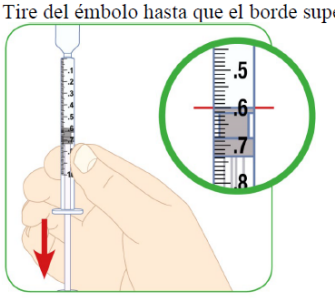
Conecte la aguja a la jeringa.

- No apriete demasiado la aguja.
- No retire el protector de la aguja.
- No toque la aguja.

Image 2 - Step B – Filling the 1 mL syringe with 0.6 mL water for injection with CORRECT picture

Mantenga la jeringa dentro de la ampolla y tire del émbolo con precaución.

- Tire del émbolo hasta que el borde superior de este se alinee con la marca negra de 0,6 ml.



In Spain the Myalepta 3 mg vial is distributed with a 1 mL syringe for reconstitution. The risk of the patient reconstituting with 2.2 mL WFI is low but nevertheless there is a risk that the patient may use the incorrect volume of WFI. If this did occur the patient would be at risk of administering too low a dose of Myalepta, which may lead lack of treatment effect. It is possible that incorrect usage and adverse events could occur, however we assess the risk as low and no reports of adverse events have been received to date. To address this issue, Amryt Pharmaceuticals DAC is correcting this error in the PL artwork.

Further information on recommendations to healthcare professionals

Until the correct artwork is available, we would appreciate your assistance in communicating this error in the PL to patients currently receiving Myalepta 3 mg vial under your care. Please find enclosed a sample letter for you to provide to your patients. In addition, it may be helpful to also provide a completed Patient Dosing Card, either electronically or as a paper copy. To assist with this, we have enclosed a copy of the Patient Dosing Card that can be edited as a pdf document.

Call for reporting

If your patient experiences any adverse reactions please report as usual through the Spanish Pharmacovigilance System for Medicinal Products for Human Use: www.notificaRAM.es.

Please also report to Amryt Pharmaceuticals DAC on email: medinfo@amrytpharma.com or via freephone: 00 800 4447 4447. Please contact us if you have any questions by email: medinfo@amrytpharma.com or via freephone: 00 800 4447 4447.

Attachment:

Dear Patient [ ]

Myalepta (metreleptin) 3mg vial: inconsistency in the Spanish language package leaflet (PL).

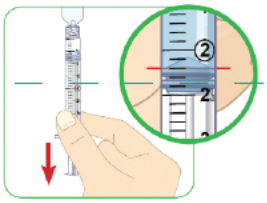
We are writing to inform you of an inconsistency in the package leaflet (PL) that accompanies the Myalepta (metreleptin) 3 mg vial distributed for use in Spain.

In **Section 7 Step B – Filling the 1 mL syringe with 0.6 mL water for injection**, the text mentions that you should withdraw 0.6 mL of water for injection (WFI) from the vial. The accompanying picture shows a syringe with 2.2 mL of WFI (please see image 1 below). The picture is incorrect and should show a syringe with 0.6 mL of WFI (please see image 2 below).

Image 1 - Step B – Filling the 1 mL syringe with 0.6 mL water for injection with INCORRECT picture

Mantenga la jeringa dentro de la ampolla y dele la vuelta. La jeringa deberá estar ahora hacia arriba.
Mantenga la jeringa dentro de la ampolla y tire del émbolo con precaución.

- Tire del émbolo hasta que el borde superior de este se alinee con la marca negra de 0,6 ml.
- Debe comprobar que no haya bolsas ni burbujas de aire en la jeringa de 1 ml. Consulte los pasos del 6 al 8 que se muestran a continuación sobre la extracción de bolsas de aire o burbujas de aire de la jeringa.
- Extraiga la jeringa de la ampolla de plástico.



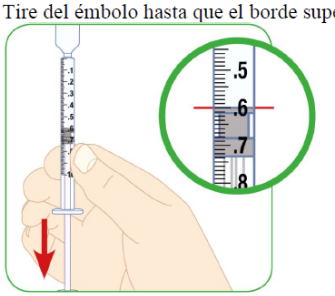
Conecte la aguja a la jeringa.

- No apriete demasiado la aguja.
- No retire el protector de la aguja.
- No toque la aguja.

Image 2 - Step B – Filling the 1 mL syringe with 0.6 mL water for injection with CORRECT picture

Mantenga la jeringa dentro de la ampolla y tire del émbolo con precaución.

- Tire del émbolo hasta que el borde superior de este se alinee con la marca negra de 0,6 ml.



If you did reconstitute Myalepta with more than 0.6 mL WFI, you would be at risk of administering too low a dose of metreleptin, which may lead to lack of treatment effect

[I have also included a completed copy of the Patient Dosing Card to confirm your dose of Myalepta and the volume of WFI that you should use in reconstituting your Myalepta].

If you have any questions about how to reconstitute Myalepta, please contact [me or a member of our department].

Kind regards

[Physician signature]

DHPC COMMUNICATION PLAN	
Medicinal product(s)/active substance(s)	Instance 1: English language presentation: Myalepta (metreleptin) 5.8 mg powder for solution for injection (30 pack) Instance 2: Spanish and Portuguese language presentation: Myalepta (metreleptin) 3 mg and 5.8 mg powder for solution for injection (30 pack)
Marketing authorisation holder(s)	Amryt Pharmaceuticals DAC 90 Harcourt Street Dublin 2 Ireland MAH no: EU/1/18/1276/004 EU/1/18/1276/006
Safety concern and purpose of the communication	Instance 1: Myalepta (metreleptin) 5.8 mg vial: inconsistency in the English language package leaflet (PL) Instance 2: Myalepta (metreleptin) 3 mg and 5.8 mg vials: inconsistency in the Spanish and Portuguese language package leaflet (PL)
DHPC recipients	Instance 1: Hospital Specialists known to prescribe the product Instance 2: Hospital Specialists known to prescribe the product
Member States where the DHPC will be distributed	Instance 1: Germany, Greece, Italy, United Kingdom[1] Instance 2: Portugal, Spain

Timetable	Date
DHPC and communication plan (in English) agreed by CHMP/CMDh	08 June 2020
Submission of translated DHPCs to the national competent authorities for review	10 June 2020
Agreement of translations by national competent authorities	16 June 2020
Dissemination of DHPC	18 June 2020