Myalepta (metreleptin) 5.8 mg vial: inconsistency in the Portuguese-language package leaflet

Dear Healthcare Professional,

Amryt Pharmaceuticals DAC in agreement with the European Medicines Agency and the National Competent Authority <of Portugal, National Authority of Medicines and Health Products (INFARMED)>, would like to inform you of the following:

Summary

- **An inconsistency has been identified in the package leaflet (PL) that accompanies the Myalepta (metreleptin) 5.8 mg vial distributed for use in Portugal.**
- **In Section 7, Step B – Filling the 3 mL syringe with 1.1 mL water for injection, the text mentions that the patient should withdraw 1.1 mL of water for injection (WFI) from the vial. The accompanying picture shows a syringe with 2.2 mL of WFI. This picture is incorrect and should show a syringe with 1.1 mL of WFI.**
- **The risk of the patient reconstituting with 2.2 mL WFI is low; nevertheless, there is a risk that the patient may use the incorrect volume of WFI. Should this occur, the patient would be at risk of administering too low a dose of Myalepta, which may lead to a 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) 5.8 mg vial distributed for use in Portugal.

In **Section 7. Instructions for use**, **Step B – Filling the 3 mL syringe with 1.1 mL water for injection**, the text mentions that the patient should withdraw 1.1 mL of water for injection (WFI) from the vial. However, the accompanying picture shows a syringe with 2.2 mL of WFI (please see Image 1 below). This picture is incorrect and should show a syringe with 1.1 mL of WFI (please see Image 2 below).

Image 1: Step B – Filling the 3 mL syringe with 1.1 mL water for injection with INCORRECT picture

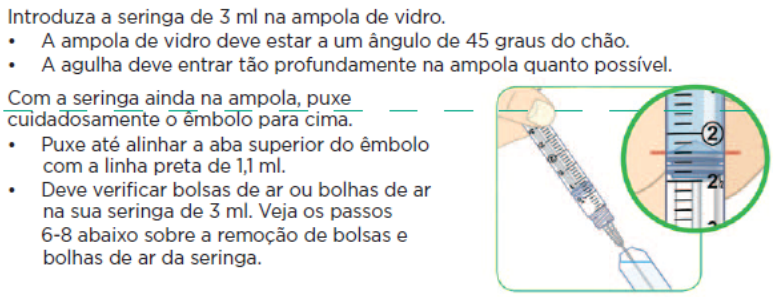
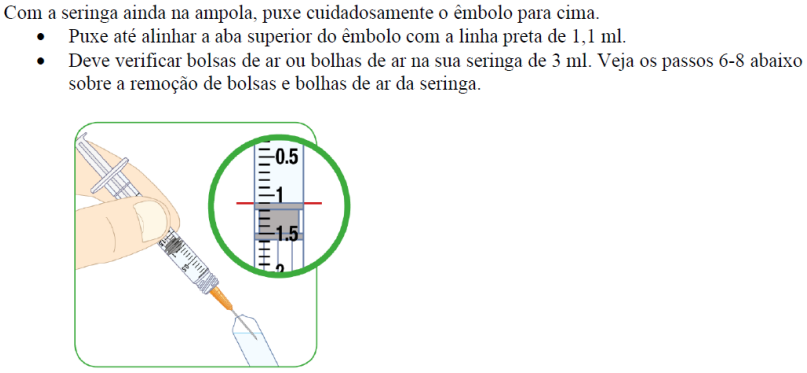


Image 2: Step B – Filling the 3 mL syringe with 1.1 mL water for injection with CORRECT picture



Although the risk of the patient reconstituting with 2.2 mL WFI is low, there nevertheless remains a risk that the patient may use the incorrect volume of WFI. Should this occur, the patient would be at risk of administering too low a dose of Myalepta. This may lead to a lack of treatment effect.

It is possible that incorrect usage and adverse events could occur; however, we assess the risk as low and have received no reports of adverse events to date. To address this issue, Amryt Pharmaceuticals DAC is correcting the error in the PL artwork.

Further information on recommendations to healthcare professionals

Until the corrected artwork is available, we would appreciate your assistance in communicating this error in the PL to patients currently receiving Myalepta 5.8 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 provide a completed English language 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 website: http://www.infarmed.pt/web/infarmed/submissaoram (preferable) or through the following contacts: INFARMED, I.P. Direção de Gestão do Risco de Medicamentos. Parque da Saúde de Lisboa, Av. Brasil 53. 1749-004 Lisboa. Tel.: +351 21 798 73 73. Linha do Medicamento: 800222444 (gratuita).
E-mail: farmacovigilancia@infarmed.pt.

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

Attachment:

Dear [Patient]

Metreleptin (Myalepta) 5.8 mg vial and an inconsistency in the Portuguese language package leaflet

We are writing to inform you of an inconsistency in the package leaflet (PL) that accompanies the Myalepta (metreleptin) 5.8 mg vial in Portugal.

The inconsistency occurs in **Section 7** of the PL, under **Step B – Filling the 3 mL syringe with 1.1 mL water for injection.** Here, the text correctly states that you should withdraw 1.1 mL of water for injection (WFI) from the vial, but the accompanying picture shows a syringe with 2.2 mL of WFI (please see Image 1 below). This picture is incorrect and should show a syringe with 1.1 mL of WFI (please see Image 2 below).

Image 1: Step B – Filling the 3 mL syringe with 1.1 mL water for injection with INCORRECT picture

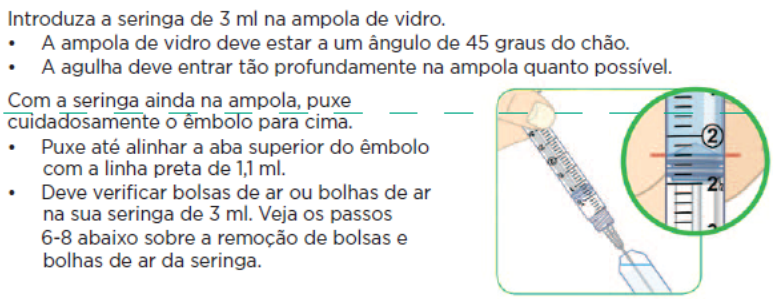
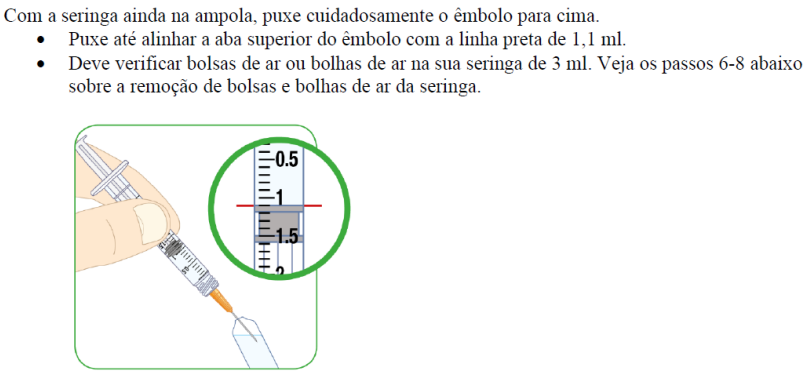


Image 2: Step B – Filling the 3 mL syringe with 1.1 mL water for injection with CORRECT picture



If you were to reconstitute Myalepta with more than 1.1 mL WFI, you would be at risk of administering too low a dose of metreleptin. This may lead to a 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