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

Dear Healthcare Professional,

Amryt Pharmaceuticals DAC in agreement with the European Medicines Agency and the <National Competent Authority> 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 the UK.**
- **In the PL Section 7, Step B – Filling the 3 mL syringe with 1.1 mL water for injection, detailing the method for reconstitution using water for injections (WFI) in the glass vial presentation, the artwork text mentions in only one place that the patient should withdraw 0.6 mL of WFI from the vial. This is incorrect; the patient should draw 1.1 mL of WFI from the vial.**
- **If the patient did reconstitute Myalepta with 0.6 mL WFI, they would be at risk of administering a dose of metreleptin with a concentration higher than 5 mg/mL. This may cause adverse effects, such as injection site reactions. The patient may also administer a higher dose than intended, up to a dose of 5 mg.**

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:

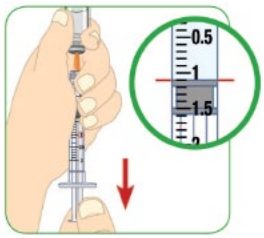
- with confirmed congenital generalised LD (*Berardinelli-Seip syndrome*) or acquired generalised LD (*Lawrence syndrome*) in adults and children 2 years of age and above
- with confirmed familial partial LD or acquired partial LD (*Barraquer-Simons syndrome*), in adults and children 12 years of age 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 UK.

In **Section 7. Instructions for use** of the PL, under **Step B: Filling the 3 mL syringe with 1.1 mL water for injection,** detailing the method for reconstitution using water for injections (WFI) in the **glass vial presentation** under step 5, the text mentions in only one place that the patient should withdraw 0.6mL of WFI from the vial. **This is incorrect**, as shown in the first image below. In the subsequent text (Step 8 of Step B), the information is correct in instructing the patient to check the amount of water for injection, stating "If there is less than 1.1 mL of water for injection in the syringe, draw more water for injection into the syringe and repeat the steps 6 and 7 until you have 1.1 mL in the syringe".

<u>INCORRECT TEXT - Filling the 3 mL syringe with 1.1 mL water for injection from glass vial</u>

Pull the plunger down carefully
- Pull it down until the top rim of the plunger lines up with the black 0.6 mL line.



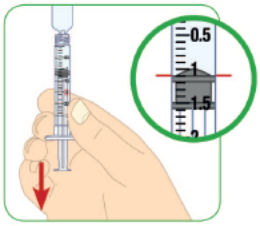
The instructions for the use of WFI in a plastic or glass ampoule are correct and do not carry this error, as shown in the second image below.

CORRECT TEXT - Filling the 3 mL syringe with 1.1 mL water for injection from plastic or glass ampoule

With the syringe still in the ampoule, pull the plunger down carefully,

- Pull down until the top rim of the plunger lines up with the black 1.1 mL line.
- You must check for air pockets or air bubbles in your 3 mL syringe. See steps 6-8 below on removal of air pockets and air bubbles from the syringe.
- Remove the syringe from the plastic ampoule.

Attach the needle to the syringe.



If the patient did use the incorrect volume of WFI, they would be at risk of administering a dose of metreleptin with a concentration higher than 5 mg/mL. This may cause adverse effects such as injection site reactions. In addition, if a patient is prescribed a dose of less than 5 mg a day from the 5.8 mg vial, reconstitution at a higher concentration may also result in administration of a higher than intended dose, up to 5mg. 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 this misstatement in the PL artwork text.

Further information on recommendations to healthcare professionals

Until the new packs of Myalepta 5.8 mg are available with the revised PL, we would appreciate your assistance in communicating this misstatement 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 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 via <*insert details of national reporting system*> 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: inconsistency in the English-language Package Leaflet (PL)

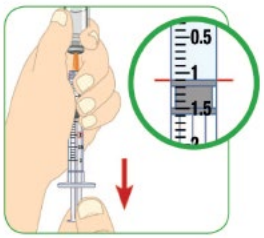
We are writing to inform you of an inconsistency in the Package Leaflet (PL) that accompanies the Myalepta (metreleptin) 5.8 mg vial distributed for use in United Kingdom.

The inconsistency occurs in only one place in the PL, in **Section 7: Instructions for use**, under **Step B: Filling the 3 mL syringe with 1.1 mL water for injection**. Here, the explanation of how to reconstitute the medicine using a **glass vial** of water for injections (WFI) mentions that you should withdraw 0.6mL of WFI from the vial. **This volume is incorrect**, as highlighted in the first image below. In the text following this step (step 8 of Step B), the information is correct in instructing that you check the amount of water for injection and states "If there is less than 1.1 mL of water for injection in the syringe, draw more water for injection into the syringe and repeat the steps 6 and 7 until you have 1.1 mL in the syringe".

INCORRECT TEXT - Filling the 3 mL syringe with 1.1 mL water for injection from glass vial

Pull the plunger down carefully

- Pull it down until the top rim of the plunger lines up with the black 0.6 mL line.



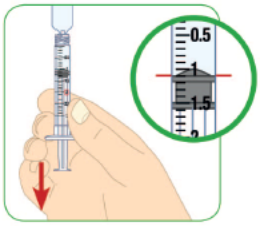
Please note that the instructions for using WFI in a plastic or glass ampoule are correct and do not carry this error, as shown in the second image below.

<u>CORRECT TEXT - Filling the 3 mL syringe with 1.1 mL water for injection from plastic or glass ampoule</u>

With the syringe still in the ampoule, pull the plunger down carefully,

- Pull down until the top rim of the plunger lines up with the black 1.1 mL line.
- You must check for air pockets or air bubbles in your 3 mL syringe. See steps 6-8 below on removal of air pockets and air bubbles from the syringe.
- Remove the syringe from the plastic ampoule.

Attach the needle to the syringe.



If you do use 0.6 mL WFI, you would be at risk of administering a dose of Myalepta with a concentration higher than 5 mg/mL. This may cause adverse effects such as reactions around the site of the injection. If the dose you have been prescribed to take from the vial is less than the full dose of 5 mg, a higher concentration could also mean that you may administer a dose higher than prescribed by your doctor, up to a maximum of 5mg.

[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