Date>

Myalepta (metreleptin) 5.8 mg vial: shortage and mitigation plan

Dear Healthcare Professional,

Amryt Pharmaceuticals DAC in agreement with the European Medicines Agency (insert: and the National Competent Authority) would like to inform you of the following:

Summary

- **Myalepta (metreleptin) 5.8mg vial is out of stock until 15th March 2023 which is related to a delay in batch release from the manufacturing site. The supply shortage is not related to a quality defect of the product or a safety issue.**

- **The shortage does not affect the 11.3mg vials, which should be used instead while the 5.8 mg vials are not available.**

- **It is important that treatment is not interrupted. Patients who normally receive 5.8mg vials (prescribed a dose of between 2.5mg to 5.0mg per day (which equates to 0.5mL to 1.0mL)) should now receive 11.3 mg vials with their usual Kits as normally supplied with the 5.8mg vial, that is:**

    - **One Kit 1 (which contains a 3ml syringe and a 21-gauge, 40mm needle for reconstituting Metreleptin), and**
    - **One Kit 4 (which contains a 1ml syringe and a 30-gauge 13mm needle for injecting Metreleptin).**

- **healthcare professionals should prescribe the patient's usual metreleptin dose in both milligrams (mgs) and the volume in millilitres (mls), and state the 11.3mg vial and Kits 1 and 4 are to be dispensed.**
  The Instructions for Use (IFU) for the 11.3mg vials have been revised, and translated into languages of member states affected, and will be attached as a supplementary IFU with the patient's Myalepta vials.

Background on the safety concern

Myalepta is indicated as an adjunct to diet as a replacement therapy to treat the complications of leptin deficiency in:

• in adults and children 2 years of age and above with confirmed congenital generalised lipdystrophy (LD) (*Berardinelli-Seip syndrome*) or acquired generalised LD (*Lawrence syndrome*)

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

The safety of patients using Metreleptin is at risk if they abruptly discontinue their Metreleptin dose as a result of worsening hypertriglyceridaemia and associated pancreatitis, particularly in patients with risk factors for pancreatitis (e.g. history of pancreatitis, severe hypertriglyceridaemia). In addition, the patient's LD disease is at risk of progressing if left untreated. With respect to the availability of therapeutic alternatives for patients with LD prescribed Myalepta, no alternative approved treatment option exists.

Taking into account the safety risks to the patient if they abruptly discontinue Myalepta and the fact that no alternative approved treatment exists, patients must use alternative vial sizes to achieve their daily dose. **Please ensure that you prescribe metreleptin in both mg AND ml and <u>state the 11.3mg vial and Kits 1 and 4 are to be dispensed.</u>**

The patient will be supplied with the same kits to reconstitute and administer the 11.3mg vial of Metreleptin which they previously received to reconstitute and administer the 5.8mg vial of Metreleptin:

- one Kit 1 which contains a 3ml syringe and a 21-gauge, 40mm needle for reconstituting Metreleptin and
- one Kit 4 which contains a 1ml syringe and a 30-gauge, 13mm needle for injecting Metreleptin).

The Instructions for Use (IFU) for the 11.3mg vials have been revised (See attached IFU – APPENDIX A):

- Patients will administer the **same dose in mg AND ml** using their usual 1ml syringe but the reconstitution steps for 11.3 mg vial are different than those for the 5.8 mg vial and these steps are described in the revised IFU.

Please note MYALEPTA is reconstituted with sterile water. The vials may still appear filled with product after withdrawal of the required dose. Remaining solution should be discarded after use.

<u>Further information on recommendations to healthcare professionals</u>

Please find enclosed a sample letter for you to provide to your patients (Appendix B). 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 (Appendix C).

<u>Call for reporting</u>
If your patient experiences any adverse reactions, please report as usual via the national reporting system. Please also report to Amryt Pharmaceuticals DAC by email: medinfo@amrytpharma.com or freephone: 00 800 4447 4447.

Please contact us by email if you have any questions: medinfo@amrytpharma.com or freephone: 00 800 4447 4447.

Kind regards,

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Communication plan for Direct Healthcare Professional Communication

DHPC COMMUNICATION PLAN	
Medicinal product(s)/active substance(s)	Myalepta (Metreleptin) 5.8mg powder for solution for injection
Marketing authorisation holder(s)	Amryt Pharmaceuticals DAC
Safety concern and purpose of the communication	Shortage of Myalepta (Metreleptin) 5.8mg vials, prescribing physicians to prescribe 11.3mg instead of 5.8mg vial. Revised IFU for 11.3mg to be provided to patients also.
DHPC recipients	Prescribing physicians, Pharmacists and Nurses who may be impacted by the shortage (to be agreed at member state level)
Member States where the DHPC will be distributed	Spain and Portugal

Timetable *Delete steps which are not applicable*	**Date**
DHPC and communication plan (in English) agreed by CHMP/CMDh	01/03/2023
Submission of translated DHPCs to the national competent authorities for review	01/03/2023
Agreement of translations by national competent authorities	03/03/2023
Dissemination of DHPC	03/03/2023