**Malta, 27th October 2010**
**Circular No. P16/2010**

Dear Healthcare Professional,

## Re: European Medicines Agency reviews treatment recommendations for Fabrazyme

The European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) has reviewed its previous recommendations on the use of Fabrazyme (agalsidase beta) during the ongoing supply shortage. This was triggered by an increase in reported adverse events in patients treated with the lower dose of Fabrazyme that has been introduced during the shortage. Fabrazyme is used to treat the rare, inherited enzyme-deficiency disorder, Fabry disease. Temporary treatment recommendations to manage patients relying on this medicine have been in place since the start of the supply shortage and have been regularly updated. Fabrazyme is centrally authorized and so can be marketed in all EU countries including Malta.

The CHMP is now recommending that physicians switch back to prescribing the full dose of Fabrazyme according to the authorised product information, depending on the availability of enzyme replacement therapy and the severity of the disease.

In making their recommendation, the Committee took the outcome of a consensus group of experts in Fabry disease into account. The group met twice in October 2010, and included physicians with experience in Fabry disease and patient representatives working together to prioritise patients with Fabry disease during the ongoing supply shortage. The Committee also looked at spontaneous reports of adverse events and data from the Fabry registry.

The CHMP noted that since the introduction of a lower dose of Fabrazyme in June 2009, there has been a steady increase in the number of reported adverse events, matching the increase in the number of patients on the lower dose. At first, most of the events were pain-related, soon followed by reports



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of events affecting the heart, the central nervous system and the kidneys. This pattern suggests a progression of Fabry disease. Recently, a decrease in number of reported adverse events has been observed, which reflects the fact that more patients have either been switched to Replagal or have started receiving a full dose of Fabrazyme again. Despite this, the Committee observed that a subgroup of patients seems to be doing well on the lower Fabrazyme dose.

The CHMP also noted that monitoring plasma or urine GL-3 levels does not appear to add value to the clinical management of the patients while on a lower dose.

The updated CHMP temporary treatment recommendations for Fabrazyme are as follows:

- Patients who require enzyme replacement therapy for Fabry disease should be prescribed the authorised dose of either Fabrazyme (1.0 mg/kg once every two weeks) or Replagal (0.2 mg/kg once every two weeks).
- Low doses of Fabrazyme should be limited to those patients who are stable and prefer to remain on a low dose.
- Patients and prescribers are advised that a deterioration of the condition has been observed in patients on lower dose. Pain, cardiac manifestations and deafness are the usual manifestations of Fabry disease progression.

These recommendations do not change the currently approved product information for Fabrazyme.

The CHMP remains concerned about the continued supply shortages of Genzyme's medicines and is closely monitoring the implementation of their improvement measures to prevent similar manufacturing and quality problems in the future.

1. The Medicines Authority has participated in the discussions held at the EMA and is in agreement with the full **press release** issued by the EMA, attached here for your perusal. A **question-and-answer** document with more information about the outcome of this assessment is also available.

***Healthcare professionals are encouraged to regularly check the Medicines Authority website for product safety updates as these are issued on an ongoing basis.***



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