20th December 2011

Circular No. P20/2011

Dear Healthcare Professional,

Re: European Medicines Agency confirms positive benefit-risk balance of somatropin-containing medicines

Somatropin is a human growth hormone authorised in Malta as Saizen click-easy, Humatrope, Norditropin simpleXx and Genotropin. It is used to treat a number of conditions associated with impaired growth and short stature, including children who fail to grow adequately due to a lack of growth hormone, Turner syndrome or chronic renal insufficiency and short children born small for gestational age. The European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) has finalised its review of somatropin-containing medicines and has confirmed that the benefit-risk balance of these medicines remains positive. However, prescribers are reminded to strictly follow the approved indications and doses and to carefully consider the warnings and precautions for somatropin-containing medicines.

The review of somatropin products had started in December 2010 based on initial results from a long-term epidemiological study* in patients treated with somatropin-containing medicines during childhood for idiopathic lack of growth hormone and idiopathic or gestational short stature. The study results had suggested a possibly increased risk of mortality with somatropin therapy compared with the general population. In particular, an increased risk of mortality due to bone tumours and subarachnoid or intracerebral haemorrhage was observed. In addition to the epidemiological study, the CHMP considered all available data on the safety of somatropin-containing medicines in its review, including data from clinical trials, registries, cohorts and from spontaneous reports of side effects, to assess the impact on the overall benefit-risk balance of these medicines.

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The CHMP concluded that the study had significant methodological limitations and that the other safety data examined did not corroborate a potentially higher risk of mortality associated with somatropin-containing medicines.

Taking into account all available data, the Committee considered that the benefit-risk balance of somatropin-containing medicines remains positive in the approved indications and doses. The CHMP took the opportunity of this review to harmonise the existing contra-indications, warnings and precautions for these medicines throughout the European Union. The harmonised wording emphasises that somatropin must not be used if there is any evidence of a tumour activity, and that the recommended maximum daily dose should not be exceeded. The Committee will review any new important data on the safety of somatropin-containing medicines that may emerge and will communicate the outcome as appropriate.

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. Healthcare professionals are encouraged to maintain vigilance on somatropin products. Suspected Adverse Drug Reactions may be reported using the Medicines Authority yellow card scheme or online at http://www.medicinesauthority.gov.mt/pub/adr.doc or to the marketing authorisation holder or their local representatives.

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*The French safety study, "Santé Adulte GH Enfant" (SAGhE), was initiated in October 2007 and aims at improving the knowledge on recombinant growth hormone and evaluating the health of young adults who have been treated during childhood with recombinant growth hormone. Using the national compulsory France-Hypophyse register, investigators of the SAGhE study identified more than 10,000 young adults who started a recombinant growth hormone treatment between 1985 and 1996. The available analysis covers approximately 7,000 of these patients. The study is funded by the European Commission and conducted by a European consortium of paediatric endocrinologist, epidemiologists and biostatisticians, involving eight EU countries. The study is still ongoing and further results, especially from the EU countries, are expected by the end of 2012.

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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