European Calcified Tissue Society
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Brussels, 30 September 2019

Dr Harald Enzmann
Chair of the Committee for Medicinal Products for Human Use (CHMP)
European Medicines Agency

CC : Mrs Zaïde Frais, Head of Human Medicines Evaluation
Mr Jordi Llinares Garcia, Scientific & Regulatory Management Department,
Mrs Heidi Maria Janssen, Endocrinology, Metabolism & Cardiovascular, heidi-

Re: Letter of concern on lack of access to new osteoporosis medications in Europe

Dear Dr Enzmann,

With this letter, the Board of the European Calcified Tissue Society (ECTS), wants to express its concern about the repeated failure in recent years to make new osteoporosis drugs, approved in many other countries, available to patients in Europe.

Most recently, on June 27 2019, The European Medicines Agency Human Medicines Committee (CHMP) recommended the refusal of the marketing authorisation for romososumab (Evenity®), a first-in-class antibody treatment for osteoporosis. This follows on a similar refusal of another new bone building treatment (abaloparatide (Eladynos ®) in 2018.

In the present case, the use of this antibody against sclerostin has been shown in randomized controlled trials to be superior to the current standard of care (alendronate) in reducing vertebral and non-vertebral fractures in postmenopausal women with severe osteoporosis. This recommendation came as a surprise to many, since romososumab has already been approved in several countries, including the US, Canada, Australia, South Korea and Japan.

The reason for the negative consensus by the Agency was its opinion that the benefits of romosozumab did not outweigh the risks. Specifically, while cardiovascular adverse events were at placebo level, results from the active comparator trial suggested that romosozumab was associated with an increased risk for side effects on the heart or circulatory system that were not clearly explained and that could not be easily attributed to certain groups at higher risk. In addition, on combined analyses of the data, there were more deaths in patients aged over 75 years given the drug. With respect to its beneficial effects, it was stated that the benefit was not so convincing in patients with less severe disease.

For the ECTS board, representing a major organisation in Europe for researchers and clinicians working in the musculoskeletal field, it is unclear why romosozumab was found not sufficiently safe to be introduced as an osteoporosis treatment in Europe. It is difficult to explain why the

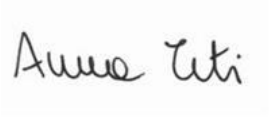
cardiovascular data are read differently in Europe than in other countries. We also wonder if the EMA may not have been made sufficiently aware that this is not a chronic treatment that patients will be taking for many years but a short course of 12 months of bone-stimulating treatment then followed by bisphosphonates to maintain the effects. There is also still the possibility that the imbalance in cardiovascular events was found because bisphosphonates like alendronate may have slight cardioprotective effects. We cannot explain to our patients that an effective osteoporosis drug is considered safe to Americans and Australians but not to Europeans. The argument that the benefit was not so convincing in patients with less severe disease holds for all osteoporosis drugs. Moreover, this does not seem a rational argument against market authorisation since romosozumab was not expected to be used as a first line drug for osteoporosis in most countries.

In the field of osteoporosis there is a great need for new drugs with anabolic properties for patients with severe osteoporosis and for those continuing to fracture under available therapy or who have had their once-in-a-lifetime allowed anabolic drug teriparatide. It is now the second time that the threshold for getting osteoporosis drugs available to our patients in Europe is different compared to the rest of the world.

In March 2018, along the same line abaloparatide (Eladynos ®) was refused market authorisation by EMA because it was judged that the benefits did not outweigh the risks, such as an increase in heart rate and palpitations. So again, an effective osteoporosis drug was not made available to European patients while it is available in many countries world-wide. Although we completely respect the Europe autonomy in these matters, we do not understand why the threshold for approval of osteoporosis drugs has become so very high in Europe when the clinical and scientific data presented is the same. We do not experience a similar discrepancy in drug access for cardiovascular diseases, diabetes or rheumatic diseases and wonder why there is such a disparity in osteoporosis treatment. Is osteoporosis less of a concern in Europe than other conditions with similar effects on survival and quality of life?

This places patients with severe osteoporosis in Europe at a disadvantage as they can only be treated with drugs that have a demonstrably lower efficacy than what would have been available to them in the rest of the world.

We express our hope that these arguments will be taken into consideration during the re-examination of the June 2019 opinion.



Prof Anna Teti
ECTS President

on behalf of ECTS Board of Directors