

MEDIA RELEASE • COMMUNIQUE AUX MEDIAS • MEDIENMITTEILUNG**Once-yearly Aclasta[®] approved in EU to treat osteoporosis caused by steroid treatment in men and postmenopausal women**

- *Steroids, widely used to treat inflammatory conditions, can cause bone loss and increase risk of fractures in up to 50% of patients on long-term therapy¹*
- *European approval based on data showing Aclasta better at increasing bone mass than oral risedronate, a current established therapy^{2,3}*
- *Clinical trial results also reaffirm efficacy and safety of Aclasta, used in more than 500,000 patients worldwide since launch in 2007^{4,5}*
- *Approval is fifth indication for once-yearly Aclasta, already approved worldwide to treat postmenopausal osteoporosis⁶*

Basel, June 26, 2009 – Once-yearly Aclasta[®] (zoledronic acid 5 mg)* has been approved in the European Union to treat men and postmenopausal women with osteoporosis caused by long-term use of glucocorticoids, commonly known as steroids⁶. Glucocorticoids are widely used to treat inflammatory conditions such as asthma and rheumatoid arthritis, but also cause bone loss and can increase the risk of fracture in up to 50% of patients on long-term glucocorticoid therapy¹.

The new indication for men and women with glucocorticoid-induced osteoporosis (GIO) is based on study data showing that Aclasta, given once a year as a 15-minute infusion, is more effective at treating bone loss than daily oral risedronate, a current established therapy^{2,3}.

The study results, recently published in *The Lancet*, show that Aclasta produced a significantly greater increase in bone mineral density (BMD) than risedronate at six months, indicating a faster onset of efficacy².

“Oral bisphosphonates have been used for many years for the treatment of GIO, but they are associated with poor compliance as patients frequently fail to take them as prescribed,” said Professor David M. Reid, Head of the Division of Applied Medicine at the University of Aberdeen, UK. “Available data show that patients who remember to take their medicines only half of the time receive little or no protection⁷.”

He added: “The approval of Aclasta is a significant step forward, as it is more effective and faster-acting than a current established therapy for the treatment of GIO and has the advantage of year-long compliance and sustained osteoprotection.”

This is the fifth indication for Aclasta, which is approved to treat osteoporosis in men and postmenopausal women, including those who have experienced a low-trauma hip fracture. Aclasta is the only bisphosphonate approved in the EU and US to reduce the

* The tradename is Reclast[®] in the US and Aclasta[®] in the rest of the world.

risk of fractures at all key osteoporotic fracture sites, like the hip, spine, and other bones in the treatment of postmenopausal osteoporosis⁸. It is also approved to treat Paget's disease of the bone.

In the US, the same medicine under the trade mark Reclast[®] has also been approved by the Food and Drug Administration (FDA) to treat and prevent GIO in men and women. In May it was approved in the US as the only therapy to prevent postmenopausal osteoporosis with less frequent dosing (i.e. a single dose every two years)⁹.

The GIO indication is important because it is estimated that between 700,000 and 1.3 million adults in Western Europe, and between 1.5 and 2.7 million adults in the US, are receiving prolonged courses of oral glucocorticoids^{10,11}. Up to 50% of patients receiving long-term glucocorticoid therapy are at increased risk of fracture, as their use is associated with side effects such as bone loss and consequently osteoporosis¹.

"This European approval marks another important achievement for Aclasta by adding to the broad spectrum of patients who can now be treated with this therapy," said Trevor Mundel, MD, Global Head of Development at Novartis Pharma AG. "Aclasta has a strong efficacy and safety profile established during eight years of clinical trials. Since its launch in 2007, Aclasta has been used in more than 500,000 patients, demonstrating that an annual infusion has become a valuable treatment option."

The latest approval was based on a study of 833 men and women which investigated both the prevention and treatment of GIO (288 and 545 patients respectively)². The study had several advantages over previous trials studying the effects of bisphosphonate drugs on GIO, including the large sample size, the inclusion of both prevention and treatment subgroups, and an excellent retention rate.

The study showed that over one year, a single intravenous infusion of Aclasta produced increases in BMD of the lumbar spine and femoral neck, trochanter and total hip that were significantly greater than those seen with once-daily oral risedronate (Actonel[®])².

The greater efficacy of Aclasta was evident at six months in both the treatment group (Aclasta 4.03%, risedronate 2.70%; P=0.0002) and prevention group (Aclasta 2.34%, risedronate 0.36%; P<0.0001)². Aclasta was better than risedronate at increasing lumbar spine BMD at 12 months in both the treatment group (Aclasta 4.1%, risedronate 2.7%; P=0.0001) and prevention group (Aclasta 2.6%, risedronate 0.6%; P<0.0001)².

Results from the study showed that Aclasta is generally safe and well tolerated², supporting previous clinical trial evidence from more than 14,000 patients⁴. The most common adverse events associated with Aclasta were transient post-dose symptoms such as fever and muscle pain. Most of these symptoms occurred in the first three days after Aclasta administration and resolved within the same period of time. Post-dose symptoms can be reduced by taking paracetamol or ibuprofen shortly after the Aclasta infusion^{2,6,8}.

In this trial there were no cases of osteonecrosis of the jaw or delayed fracture healing, and no evidence of an increased risk of atrial fibrillation².

Zoledronic acid, the active ingredient in Aclasta/Reclast, is also available under the trade name Zometa[®] for use in oncology indications.

Disclaimer

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management regarding future events, and involve known and unknown risks, uncertainties and other factors that may cause actual results with Aclasta to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that Aclasta will be approved for any additional indications or labeling in any market. Nor can there be any guarantee that Aclasta will achieve any particular levels of revenue in the future. In particular, management's expectations regarding Aclasta could be affected by, among other things, unexpected regulatory actions or delays or government regulation generally; unexpected clinical trial results, including unexpected new clinical data and unexpected additional analysis of existing clinical data; the company's ability to obtain or maintain patent or other proprietary intellectual property protection; competition in general; government, industry and general public pricing pressures; the impact that the foregoing factors could have on the values attributed to the Novartis Group's assets and liabilities as recorded in the Group's consolidated balance sheet, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and Exchange Commission. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those anticipated, believed, estimated or expected. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

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