AstraZeneca

news release

2003-12-23

EXANTAÔ (XIMELAGATRAN) RECEIVES FIRST APPROVAL

First indication for prevention of venous thromboembolic events in major orthopaedic surgery

AstraZeneca has received its first regulatory approval for Exanta™ (ximelagatran) in France for the prevention of venous thromboembolic events in major orthopaedic (hip or knee replacement) surgery. France is the Reference Member State for the European Union (EU) Mutual Recognition Procedure for Exanta. Subject to approval, launches of Exanta in this first 'proof of principle' indication are expected to take place later in 2004.

Exanta is the first oral treatment in a new World Health Organisation class of direct thrombin inhibitors (DTIs) and is the first new oral anticoagulant approved since the introduction of warfarin almost 60 years ago. Exanta benefits from administration as a fixed oral dose, has a rapid onset and offset of action and shows low potential for food and drug interactions. Importantly, coagulation monitoring is also not necessary in treatment with Exanta.

The approval of Exanta for this first indication in France is based on the METHRO study programme, involving an early postoperative start of Exanta treatment, with initial injectable dosing administered at least four hours after the completion of surgery, followed by oral Exanta 24mg twice daily for up to 11 days. This approval reflects clinical practice that is becoming increasingly common in Europe and allows use in conjunction with spinal anaesthesia with the oral dosing route enabling treatment to be easily continued following discharge from hospital. More than half of patients undergoing major orthopaedic surgery develop VTE in the absence of preventative anticoagulant treatment, and while effective treatments are available, no treatment regimen to date has successfully balanced efficacy and bleeding risk with oral dosing.

Regulatory submissions for prevention of stroke in atrial fibrillation and treatment of VTE, have already been filed in France as part of the EU Mutual Recognition Procedure. In the US, the Food and Drug Administration (FDA) submissions for use of Exanta in stroke prevention in patients with atrial fibrillation and long-term secondary prevention of VTE have also been filed alongside the orthopaedic surgery file for use of Exanta in prevention of VTE in total knee replacement.

"Exanta offers a fundamentally new approach to prevention of thrombosis, one of the largest causes of morbidity and mortality in the western world", commented Dr Hamish Cameron, Vice President, Head of Exanta, AstraZeneca. "We are very

AstraZeneca AB
SE-151 85 Södertälje
Sweden

Tel +46 8 553 260 00
Fax +46 8 553 290 00
www.astrazeneca.com
www.astrazeneca.se

Reg Office AstraZeneca AB (publ)
SE-151 85 Södertälje Sweden
Reg No 556011-7482
VAT No SE556011748201

pleased to announce this approval as the first step in introducing this innovative new anticoagulant to patients."

Thrombosis leads to the occlusion of blood vessels and prevents the circulation of blood to the heart (myocardial infarction) and brain (stroke). When blood clots break away, they can lead to thromboembolism in the lungs (pulmonary embolism), limbs (deep vein thrombosis) or within any blood vessels (venous thrombosis). Each year, nearly four million people experience thrombosis worldwide and those at greatest risk include people with atrial fibrillation, those who have experienced a previous cardiac event such as a myocardial infarction, and patients following orthopaedic surgery (OS: total hip or knee replacement surgery). Although existing treatments are effective, they have many limitations. Several require subcutaneous or intravenous administration, whilst current oral treatments are limited by risk of drug and food interactions, the need for regular coagulation monitoring and dose titration.

For further information, please see www.astrazenecapressoffice.com or contact:

NOTES TO EDITORS

- Exanta is a trademark of the AstraZeneca group of companies.
- * METHRO: **ME**lagatran for **THR**ombin inhibition in **O**rthopaedic surgery study that compared injectable low molecular weight heparinsinitiated the evening before surgery, with preoperative (METHRO II) or post-operative (METHRO III) initiation of melagatran (active form) followed by oral ximelagatran in 4,688 patients undergoing total hip or knee replacement.
- AstraZeneca is a major international healthcare business engaged in the research, development, manufacture and marketing of prescription pharmaceuticals and the supply of healthcare services. It is one of the top five pharmaceutical companies in the world with healthcare sales of over $17.8 billion and leading positions in sales of gastrointestinal, oncology, cardiovascular, neuroscience and respiratory products. AstraZeneca is listed in the Dow Jones Sustainability Index (Global and European) as well as the FTSE4Good Index.

Media Enquiries:
Staffan Ternby, 070-557 4300
Chris Major, +44 (0) 207 304 5028

Investor Relations:
Staffan Ternby, 070-557 4300
Mina Blair-Robinson, +44 207 304 5084