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Corlentor® receives approval for use in heart failure

Approval brings promise of better prognosis and improved quality of life for millions of chronic heart failure patients in Spain.

Madrid, Spain, 15 February 2012 – Laboratorios Farmacéuticos Rovi (ROVI) announced today that the company's heart rate lowering agent, **Corlentor**® (ivabradine), the first selective I_f channel inhibitor, has been approved by the European Commission for the treatment of patients with chronic heart failure.[1] Corlentor® (ivabradine) is a product that has been developed by *Les Laboratoires Servier* and is marketed by them as Procolaran®.

The European Commission's decision to authorise this new indication for ivabradine followed the review of data from the SHI_fT trial, the largest-ever morbi-mortality study of treatments for chronic heart failure involving more than 6000 patients. It demonstrated that the treatment significantly reduced the risk of death and hospitalisation from heart failure, and improved the quality of life of people living with the disease.[2,3] This reduction in mortality was highly significant in patients with a heart rate of 75 beats per minute (bpm), or above, for whom ivabradine is now indicated.[1]

Professor Michel Komajda, Co-Chairman of the SHIFT Executive Committee commented: "The decision to authorise this new indication for ivabradine is good news for doctors and patients, and is a significant step forward in the treatment of heart failure. While ACE inhibitors and beta-blockers remain the main stay in the treatment of heart failure, the results of the SHI_fT trial demonstrate that a reduction in heart rate when elevated with ivabradine improves clinical outcomes and symptoms, prevents disease progression, and has beneficial effect on daily activities and the quality of life of heart failure patients".

About chronic heart failure

Chronic heart failure affects 1.2 million patients in Spain (10% of the population over 60 years of age).[4] It is a disabling condition and, despite improvements in treatment and management, generally has a poor prognosis, with a survival of only 50% after five years from the diagnosis. In Spain, heart failure is the third cause of mortality, which means 15% of all the cardiovascular deaths, and it is the first cause of hospitalization. Heart failure impairs the heart's ability to pump effectively and to maintain sufficient circulation to meet the body's needs. It is most commonly caused by acute (myocardial infarction) or chronic (angina pectoris) ischaemia (coronary artery disease).[5, 6]

About Ivabradine

Ivabradine was launched in February 2007 in Spain for the treatment of stable angina. It is the only drug to selectively reduce heart rate by inhibiting one of the electrical signals that determine the heart rate, called pacemaker I_f current.[7] Ivabradine reduces heart-rate without significantly decreasing blood pressure or the ability of the heart muscle to pump blood.[7,8]

The additional indication extends its use to the treatment of chronic heart failure in patients with normal (sinus) rhythm and whose heart rate is 75 bpm or above, in combination with standard therapy including beta-blocker therapy or when beta-blocker therapy is contraindicated or not tolerated.[7]

Ivabradine is already indicated in the symptomatic treatment of chronic stable angina pectoris in coronary artery disease adults with normal sinus rhythm unable to tolerate or with a contra-indication to the use of beta-blockers or in combination with beta-blockers in patients inadequately controlled with an optimal beta-blocker dose and whose heart rate is > 60 bpm.

In Spain, Ivabradine is marketed as Procoralan® by *Les Laboratoires Servier* and as Corlentor® by Laboratorios Farmacéuticos Rovi.

About the SHI$_f$T study

SHI_fT (**S**ystolic **H**eart failure treatment with the I_f inhibitor ivabradine **T**rial) is a randomised, double-blind placebo controlled study involving 6,505 people in 37 countries. This study set out to evaluate whether the addition of the I_f inhibitor, ivabradine, to optimal guidelines-based treatment improves cardiovascular outcomes in patients with moderate to severe chronic heart failure, reduced left ventricular ejection fraction and heart rate of 70 bpm or above.[2]

SHI_fT showed that the I_f inhibitor ivabradine reduced the risk of death from heart failure by 26% (p=0.014), and the risk of hospitalisation by 26% (p<0.0001). The benefits were seen even though the study patients were already taking currently recommended heart failure treatments.[2] In the subgroup of patients with heart rate above 75 bpm at baseline, Ivabradine reduced the risk of cardiovascular death by 17% (p=0.0166) and all cause death by 17%(p=0.0109).

A sub-study of 1944 patients from the main study population, showed that the reduction in heart rate achieved through treatment with Ivabradine was associated with almost double the improvement in quality of life compared to the control group. This improvement was observed in both the disease related component and the social component of the scores.[3]

Quality of life assessments were conducted using the Kansas City Cardiomyopathy Questionnaire, a 23-item, self-administered questionnaire that quantifies physical function, symptoms (frequency, severity and recent change), social function, self-efficacy and knowledge, and quality of life.[3]

In an echocardiography sub-study, Ivabradine was shown to lead to a reduction in the heart's left ventricle end-systolic volume (the blood volume remaining in the left ventricle after contraction), which resulted in improved efficiency of the left ventricle and overall heart function.[9]

About ROVI

ROVI is a fully-integrated, profitable Spanish specialty pharmaceutical company engaged in the research, development, in-licensing, manufacturing and marketing of small molecule and specialty biologic drugs. The Company has a diversified portfolio of products that it markets in Spain through its specialized sales force, calling on specialist physicians, hospitals and pharmacies. ROVI's portfolio of 27 principal marketed products is currently anchored by the internally-developed, second generation low molecular weight heparin, Bemiparin. ROVI's research and development pipeline is focused primarily on addressing currently unmet medical needs by developing new LMWH-based products and expanding applications for its existing LMWH-based products. ROVI manufactures the active biological ingredient (Bemiparin) for its principal proprietary product and product candidates and the injectable pharmaceutical products developed by its in-house research team, and utilises its state-of-the-art filling and packaging capabilities to provide a broad array of toll manufacturing services to leading international pharmaceutical companies, primarily in the area of pre-filled syringes. For more information, visit http://www.rovi.es

About Servier

Servier is France's leading independent pharmaceutical company and the country's second largest drug company. Servier is present in 140 countries. R&D at Servier spans a range of therapeutic fields, with the main areas of focus being cardiovascular disease, neuroscience, cancer, metabolic disorders, and rheumatology. In the field of cardiovascular disease in particular, Servier is one of the principal research organizations dedicated to the development of new medicines. Servier has a long-standing interest in the field of cardiovascular disease, as attested by the fact that 63% of Servier's global turnover from medicines is made up of drugs targeting cardiovascular diseases. For more information, visit www.servier.com

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