



Corporate Press Release

6 December 2012

XIFAXAN[®] 550mg (rifaximin- α) registered for reduction of recurrence of episodes of overt Hepatic Encephalopathy in the EU*

Alfa Wassermann and Norgine are pleased to announce that they have received European Marketing Authorisation for XIFAXAN[®] 550mg (rifaximin- α) / REFERO[®] / TARGAXAN[®] / TIXTELLER[®] in the reduction of recurrence of episodes of overt hepatic encephalopathy (HE) in patients \geq 18 years of age, in a number of EU territories*. HE is a potentially life-threatening neuropsychiatric condition associated with liver cirrhosis¹.

First launches in Europe are expected in the first half of 2013.

Rifaximin- α , developed by Alfa Wassermann, is currently marketed in many countries worldwide, including the US in a number of indications.

A pivotal trial by Bass and colleagues (2010)² demonstrated the efficacy of twice-daily (bid) treatment with XIFAXAN[®] 550mg in patients with HE.

Hepatic encephalopathy results from increased serum toxic substances such as ammonia arising from gut bacteria, which is not efficiently removed by the damaged liver¹ and then enters the brain causing a spectrum of neuropsychiatric disorders ranging from mild intellectual impairment, changes in mental state, confusion, to personality changes, depressed level of consciousness and even coma³. Also, hepatic encephalopathy is associated with poorer employment and financial status, as well as increased burden on the caregiver.⁴

XIFAXAN[®] 550mg is a gut specific antibiotic which targets Gram +ve and Gram -ve ammonia producing aerobes and anaerobes to reduce the plasma ammonia load that is associated with the development of hepatic encephalopathy⁵.

In common with most countries around the world, Europe has a serious problem with the increasing incidence of liver cirrhosis⁶, hepatic encephalopathy and the associated cost of treatment. Hepatic encephalopathy was estimated to be responsible for 55,000 hospitalisations at a total cost of \$1.2 billion per year in the USA in 2007.^{7,8}

The European countries specified in the approval will be amongst some of the first markets via which Alfa Wassermann and Norgine enter the hepatic encephalopathy therapy area, with a medicine that has the potential to make a significant impact on treatment outcome² and improve the quality of life for sufferers and their caregivers.⁹

The EU licence follows the registration of XIFAXAN[®] 550mg in Australia in May 2012 for the prevention of the recurrence of hepatic encephalopathy where other treatments have failed or are contraindicated. XIFAXAN[®] 550mg received marketing approval in the U.S. in March 2010 for the reduction in risk of overt hepatic encephalopathy (HE) recurrence in patients 18 years of age or older.

**Approved status granted via DCP in the following countries: Austria, Belgium, Czech Republic, Denmark, Finland, Germany, Greece, Hungary, Ireland, Italy, Luxembourg, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Spain, Sweden, United Kingdom*

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About Alfa Wassermann

Alfa Wassermann is a private pharmaceutical group with Head Quarters in Bologna, Italy with its own Research, Development and Manufacturing facilities. In 2011, Alfa Wassermann net sales were above €330million and the company employs over 1400 people. It has a growing number of affiliate companies in both Europe as well as in emerging markets such as Russia, China and Mexico. Its main product rifaximin- α is a gut-selective antibiotic which has been prescribed for 24 years, under the Trade Names of NORMIX[®], XIFAXAN[®] and others, in 33 countries, including the USA where Salix Pharmaceuticals is the exclusive licensee. Alfa Wassermann has also developed other important products: Sulodexide (VESSEL[®]), a heparinoid for thromboembolic diseases, and Parnaparin (FLUXUM[®]), a low molecular weight heparin for the treatment and prophylaxis of deep-vein thrombosis. For more information, please visit ALFA WASSERMANN's web site at www.alfawassermann.it ALFA WASSERMANN[®], the ALFA WASSERMANN logo, NORMIX[®] and XIFAXAN[®] are registered trademarks of Alfa Wassermann group of companies

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About Norgine

Norgine is an independent, successful European specialty pharmaceutical company that has been established for over 100 years and has a presence in all major European markets. In 2011, Norgine's net product sales were €250 million and the company employs over 1000 people.

Norgine's focus is the development and marketing of pharmaceutical products that address significant unmet clinical needs in therapeutic areas such as gastroenterology, hepatology and supportive care.

The Company currently markets a range of products in various markets in its key therapeutic areas e.g. MOVICOL[®] for the treatment of constipation and faecal impaction, MOVIPREP[®] a bowel cleansing preparation, Klean-Prep[®] for large bowel preparation prior to colonoscopy or surgery, XIFAXAN[®] for the treatment of traveller's diarrhoea and hepatic encephalopathy and ORAMORPH[®] for the treatment of moderate to severe pain associated with cancer.

Norgine is active in research and development and currently has products in various stages of clinical development. Norgine manufactures most of its own products in Hengoed, UK and Dreux, France.

For more information: www.norgine.com

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References

1. Prakash, R. and K.D. Mullen, *Mechanisms, diagnosis and management of hepatic encephalopathy*. Nat Rev Gastroenterol Hepatol, 2010; **7**(9): 515-25.
2. Bass, N.M., et al., *Rifaximin treatment in hepatic encephalopathy*. N Engl J Med, 2010; **362**(12): 1071-81.
3. Bajaj, J.S., *Review article: the modern management of hepatic encephalopathy*. Aliment Pharmacol Ther, 2010; **31**(5): 537-47.
4. Bajaj, J.S., et al., *The multi-dimensional burden of cirrhosis and hepatic encephalopathy on patients and caregivers*. Am J Gastroenterol, 2011; **106**(9): 1646-53.
5. XIFAXAN Summary of Product Characteristics, 2012.
6. The Australian Liver Foundation. Facts on liver disease. Available at: http://www.liver.org.au/liver_diseases.htm Accessed March 2012.
7. Huang, E., E. Esrailian, and B.M. Spiegel, *The cost-effectiveness and budget impact of competing therapies in hepatic encephalopathy - a decision analysis*. Aliment Pharmacol Ther, 2007; **26**(8): 1147-61.
8. Leise, M.D. and W.R. Kim, *Rifaximin in hepatic encephalopathy: is an ounce of prevention worth a pretty penny?* Gastroenterology, 2010; **139**(4): 1416-8.
9. Sanyal, A., et al., *Randomised clinical trial: rifaximin improves health-related quality of life in cirrhotic patients with hepatic encephalopathy - a double-blind placebo-controlled study*. Aliment Pharmacol Ther, 2011; **34**(8): 853-61.

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