



Corporate Press Release: Monday 28th January 2013

NEW PRODUCT LAUNCH

TARGAXAN[®] 550 (Rifaximin-alpha 550 mg tablets) launched in the UK

Norgine Pharmaceuticals Limited and Alfa Wassermann are pleased to announce the launch of TARGAXAN[®] 550 in the UK - the only treatment available in the UK that is licensed for 'the reduction in recurrence of episodes of overt hepatic encephalopathy (HE) in patients \geq 18 years of age'¹, a potentially life-threatening neuropsychiatric condition associated with liver disease.

The pivotal clinical trial by Bass et al (2010)², in which patients in remission from recurrent episodes of hepatic encephalopathy due to cirrhosis who were treated with TARGAXAN 550 mg twice-daily (bd) with or without lactulose*, were compared with patients given placebo (bd) with or without lactulose* over 6 months, demonstrated:

- A 58% relative reduction in the risk of breakthrough episodes of overt hepatic encephalopathy over 6 months (Hazard ratio 0.42; $p < 0.001$). Thus the numbers needed to treat (NNT) = 4
- A 50% relative reduction in the risk of hospitalisations caused by HE over 6 months (Hazard ratio 0.50; $p = 0.01$). Thus the numbers needed to treat (NNT) = 9

*91% of patients in both groups were taking lactulose.

Hepatic encephalopathy encompasses a spectrum of neuropsychiatric abnormalities seen in patients with established liver disease and is commonly associated with liver cirrhosis.^{3,4} Patients with hepatic encephalopathy may experience symptoms ranging from subtle neurological abnormalities (e.g. mood alterations, changes in reaction times in daily activities such as driving), to severe neurological impairment (e.g. where a patient has difficulty moving and communicating) and in extreme cases patients may present with coma.⁵

Hepatic encephalopathy has been shown to have a significantly negative impact on patients' health-related quality of life (HRQoL).^{6,7,8,9,10} Indeed it has also been shown that a lower HRQoL may act as an indicator for further episodes of HE.¹¹

- Liver disease is on the increase. In the UK there has been a 25% increase in liver deaths between 2001 and 2009.¹²
- This is in contrast to other major causes of death which have been in decline. Over 70% of patients with liver disease die in hospital.¹²
- A regularly used benchmark of cost, length of hospital stay, is prolonged for individuals with chronic liver disease, with a reported average of 10.2 days.¹³
- 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 2007.¹⁴

TARGAXAN 550 is a gut specific antibiotic which targets Gram positive and Gram negative ammonia producing species. It is thought that it may inhibit the division of urea-deaminating bacteria, thereby reducing the production of ammonia and other compounds that are believed to be important in the development of hepatic encephalopathy¹.

TARGAXAN 550 (Rifaximin-alpha) is available at an NHS price of £259.23 for a month's supply of 56 tablets.

Andrew Langford, Chief Executive of the British Liver Trust, welcomes the increased use of TARGAXAN 550 for as many people with hepatic encephalopathy as is needed. Langford says "Liver disease in itself is a huge problem for people and their families to deal with but is a 'double whammy' when people go on to develop hepatic encephalopathy, which for many will seem like dementia and/or serious mental health illness. Current treatment requires patients to take very large doses of laxatives which makes a 'bad situation a lot worse' and can lead to a lack of dignity and dehumanisation of the person with the encephalopathy. A universally used treatment that alleviates the symptoms of encephalopathy and does not have the severe side effects that current treatment has is going to have huge benefit to the health and quality of life of both the patients and their families."

Andrew Burroughs, Consultant Physician and Professor of Hepatology at the Royal Free Hospital London says, "TARGAXAN 550 is an important drug that significantly improves quality of life for patients and their partners and families. It also reduces the repeated admissions to hospital that often these patients are subject to, and should result in cost savings to the NHS."

The UK is the first European market in which Norgine enters the hepatic encephalopathy therapy area, with a medicine that has the potential to make a significant impact on treatment outcomes² and improve the quality of life for sufferers and their caregivers.⁹

Bob Cuffe, UK General Manager for Norgine, said “It is wonderful for Norgine to be able to bring to the market this medicine, with all its proven benefits, in such a short space of time. We believe TARGAXAN 550 has the potential to change the way in which UK patients with this debilitating condition are managed and we hope marks the first of many novel therapeutic agents that Norgine will bring to aid the fight against Liver Disease and its various complications”.

For more information on liver disease and for patient support materials please refer to the British Liver Trust at: <http://www.britishlivertrust.org.uk/home.aspx>

Ends

Notes to editors:

The UK licence states 'Rifaximin-alpha is indicated for the reduction in recurrence of episodes of overt hepatic encephalopathy in patients \geq 18 years of age' (see the Summary of Product Characteristics - SmPC) for more details.”

About Norgine

Norgine is a successful, independent European specialty pharmaceutical company that has been established for over 100 years and has a presence in all major European markets. In 2012, Norgine’s net product sales were c€250 million and the company employs over 1,000 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[®] (XIFAXANTA[™]) for the treatment of travellers’ diarrhoea 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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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 1,400 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-alpha 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

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