



CORPORATE PRESS RELEASE

NICE CONSULTATION ON TARGAXAN[®] 550 (RIFAXIMIN- α) ANNOUNCED: A NEW TREATMENT FOR LIFE-THREATENING CONDITION LINKED TO LIVER DISEASE

London. 27 November 2013. Norgine confirms that it has received the National Institute for Health and Care Excellence's (NICE) Appraisal Consultation Document (ACD) on TARGAXAN[®] 550 (rifaximin- α 550mg).ⁱ Norgine markets this novel treatment which is licensed for the reduction in recurrence of episodes of overt hepatic encephalopathy in patients of 18 years of age and over.ⁱⁱ Hepatic encephalopathy is a serious and potentially life-threatening neuropsychiatric condition associated with liver disease that affects around 10,000 patients in the UK.^{iii,iv,v}

The Appraisal Committee has acknowledged both the clinical effectiveness of TARGAXAN[®] 550 and several cost-effectiveness arguments submitted by Norgine, in particular the health economic model, but has asked for further clarity on a few aspects of the company's submission. We welcome the Committee's request for additional analyses and a further opportunity to demonstrate the value which this innovative treatment can offer patients and their carers living with hepatic encephalopathy in England and Wales.

Norgine looks forward to responding to these requests by the end of the consultation period. The new consultation period will run from November 27th until December 18th 2013 to allow all concerned stakeholders the opportunity to express their views and provide additional evidence to NICE.

Norgine is expecting a final decision from NICE in 2014.

Peter Martin, Chief Operating Officer at Norgine said: "We have confidence in the clinical efficacy of TARGAXAN[®] 550 and its value to the NHS, patients and their carers. It is important to consider treatments that help prevent difficult-to-treat conditions that require long and costly stays in hospitals. Norgine has already obtained positive health technology assessments for TARGAXAN[®] 550 (also called XIFAXAN[®] 550) in Scotland and Australia.

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He added: “We will continue to engage with NICE to address its additional information requests with the ultimate aim of ensuring that all patients who could benefit can access TARGAXAN[®] 550. This treatment offers a significant advance as it can alleviate the substantial burden on patients, their families and healthcare systems and improve quality-of-life. It is particularly critical as there is currently no cure for hepatic encephalopathy apart from liver transplantation.”

Norgine currently holds marketing rights in Australia, Belgium, Denmark, Finland, France, Germany, Luxembourg, MENA, Netherlands, New Zealand, Norway, Republic of Ireland, Sweden, United Kingdom and Switzerland.

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Notes to editors

About XIFAXAN[®] 550/ TARGAXAN[®] 550

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About Hepatic Encephalopathy

Hepatic encephalopathy is the term used to describe a complex and variable neuropsychiatric condition of patients with acute or chronic liver disease, more commonly associated with cirrhosis. Patients with hepatic encephalopathy may experience symptoms ranging from subtle, clinically indiscernible neurological abnormalities, to severe neurological impairment.

Bass et al, 2010: XIFAXAN[®] 550 / TARGAXAN[®] 550 Pivotal Clinical Trial

The pivotal clinical trial by Bass et al (2010), in which patients in remission from recurrent episodes of hepatic encephalopathy due to cirrhosis who were treated with rifaximin-α 550mg 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.

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

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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 critical and supportive care.

Norgine owns a manufacturing and development site in Hengoed, UK and a manufacturing site in Dreux, France.

For more information, please visit www.norgine.com

About Alfa Wassermann

Alfa Wassermann is a private pharmaceutical group with headquarters in Bologna, Italy with its own Research, Development and Manufacturing facilities. In 2012, Alfa Wassermann net sales were above €360million and the company employs over 1,300 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 website at www.alfawassermann.it.

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References:

ⁱ NICE, Appraisal Consultation Document, 'Rifaximin- α for maintaining remission for episodes of hepatic encephalopathy', published 27th November 2013 and available online at www.nice.org.uk

ⁱⁱ TARGAXAN[®] 550[▼] Summary of Product Characteristics,

www.medicines.org.uk/emc/medicine/27427/SPC/TARGAXAN+550+mg+film-coated+tablets/

ⁱⁱⁱ Gitlin N, Lewis DC, Hinkley L. The diagnosis and prevalence of subclinical hepatic encephalopathy in apparently healthy, ambulant, non-shunted patients with cirrhosis. *J Hepatol.* 1986;3(1):75-82.

^{iv} Gilberstadt SJ, Gilberstadt H, Zieve L, Buegel B, Collier RO, Jr., McClain CJ. Psychomotor performance defects in cirrhotic patients without overt encephalopathy. *Arch Intern Med.* Apr 1980;140(4):519-521

^v Das A, Dhiman RK, Saraswat VA, Verma M, Naik SR. Prevalence and natural history of subclinical hepatic encephalopathy in cirrhosis. *J Gastroenterol Hepatol.* May 2001;16(5):531-535.