European Commission approves Esmya® 5 mg for intermittent treatment in the long term management of Uterine Fibroids (myomas)

Budapest, Hungary – 28 May 2015 – **Gedeon Richter Plc. ("Richter") announces that the European Commission (EC) has granted approval for the intermittent use of Esmya® 5 mg in the long term management of uterine fibroids.** This decision follows a positive opinion from the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) on 23 April 2015 and is applicable for all Member States in the European Economic Area.

The initial Marketing Authorization for Esmya® was granted for the pre-operative treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age. The present extension of indication adding the intermittent treatment courses of Esmya® provides an opportunity to women to benefit from long term medical management of uterine fibroids and potentially avoid surgery.

The approval is based on the assessment of two long-term Phase III studies, PEARL III extension and PEARL IV, involving 132 and 451 patients respectively, both designed to evaluate the efficacy and safety of ulipristal acetate as a long-term treatment of uterine fibroids:

- **PEARL III Study and its extension** assessed the efficacy and safety of ulipristal acetate 10 mg over a total of 4 intermittent 3-month treatment courses.[1]
- **PEARL IV Study** assessed the efficacy and safety of ulipristal acetate 5 and 10 mg over a total of 4 intermittent 3-month treatment courses.[2]

Both studies confirmed the efficacy and safety of intermittent use of ulipristal acetate. Efficacy was demonstrated by a reduction of bleeding, fibroid volume and pain and ultimately an improvement in the quality of life of women suffering from symptomatic uterine fibroids.

The results of the PEARL IV study demonstrated that 70% of the patients on the 5 mg dose were in amenorrhea after the fourth treatment course. In addition, fibroid volume reduction from baseline was on average 71.8% and uterine volume decreased significantly during the study. Furthermore, the use of ulipristal acetate showed an improvement in quality of life and control of pain in comparison to baseline, even during the off treatment intervals. These results confirmed already published data from the PEARL III and PEARL IV Part 1 studies.

"We are delighted with this significant step forward for Esmya®, as it means more choice for physicians and patients in need of highly effective and convenient medical therapy for women suffering from uterine fibroids", said Erik Bogsch, Managing Director of Gedeon Richter Plc. "We remain committed to the development of female healthcare products which improve quality of life for the female population in all age groups."

"The PEARL III and IV studies have confirmed the benefits of repeated intermittent use of Esmya® in long term management of uterine fibroids. We can now propose medical therapy to many women suffering from this condition and potentially avoid surgical interventions." added Dr Dace Matule, investigator in PEARL III and PEARL IV.

The full Esmya® 5 mg tablets product information containing the revised SmPC is publicly available both in the registers of the European Commission and of the National Institute of Pharmacy and Nutrition Register in Hungary together with their respective online sites: www.ema.europa.eu and www.ogyei.gov.hu.

About uterine fibroids

Uterine fibroids are the most common benign, solid tumours of the female genital tract, affecting between 20% and 40% of women of reproductive age. The condition is characterized by excessive uterine bleeding, anaemia, pain, frequent urination or incontinence, and infertility. Uterine fibroids are commonly treated surgically. Symptomatic uterine fibroids are the leading reason for hysterectomy. It is estimated that about 300,000 surgical procedures are performed annually in the EU for uterine fibroids, including approximately 230,000 hysterectomies. Available treatments were limited to short-term pre-operative use and comprise of either ulipristal acetate (Esmya) or gonadotropin releasing hormone (GnRH) agonists. Surgery may not be a suitable option for all patients, e.g. for medical or personal reasons or if the woman would rather wait that the symptoms of uterine fibroids decrease as result of menopause. Thus, there was a medical need for a long-term medical treatment of fibroids.

About Esmya®

Esmya® 5mg tablets containing ulipristal acetate is a first-in-class, orally active, selective progesterone receptor modulator characterised by a tissue specific mixed progesterone antagonist/agonist effect. It reversibly blocks the progesterone receptors in target tissues. As previously published in the New England Journal of Medicine [3,4,5] the short term treatment with Esmya® 5mg proved to be effective to stop uterine bleeding, correct anaemia and shrink fibroid volume. It improves quality of life and has no castration side effects unlike GnRH agonists. Recently published data[1,2] confirmed the efficacy and safety of repeated intermittent use of Esmya® 5mg in long term management of uterine fibroids allowing women to avoid surgical intervention.

About Richter

Gedeon Richter Plc. (www.richter.hu), headquartered in Budapest/Hungary, is a major pharmaceutical company in Central Eastern Europe, with an expanding direct presence in Western Europe. Richter's consolidated sales were approximately EUR 1.1 billion (US$ 1.5 billion), while its market capitalization amounted to EUR 2.1 billion (US$ 2.5 billion) in 2014. The product portfolio of Richter covers almost all important therapeutic areas, including gynaecology, central nervous system, and cardiovascular areas. Having the largest R&D unit in Central Eastern Europe, Richter's original research activity focuses on CNS disorders. With its widely acknowledged steroid chemistry expertise, Richter is a significant player in the female healthcare field worldwide. Richter is also active in biosimilar product development.

For further information

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[2] Donnez, J; Hudecek, R; Donnez, O. et al. Efficacy and Safety of repeated use of ulipristal acetate in uterine fibroids. Fertil Steril 2015; 103(2):519-27

[3] Donnez J, Tatarchuk TF, Bouchard P, et al. Ulipristal acetate versus placebo for fibroid treatment before surgery. N Engl J Med 2012;366(5):409-20.

[4] Donnez J, Tomaszewski J, Vazquez F. et al. Ulipristal acetate versus leuprolide acetate for uterine fibroids. N Engl J Med 2012;366(5):421-32.

[5] Stewart EA. Uterine fibroids and evidence-based medicine--not an oxymoron.N Engl J Med. 2012;366(5):471-73