Press Release

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AWMSG and SMC recommends/accepts FIRAZYR® (icatibant) as an option for the symptomatic treatment of acute attacks of Hereditary Angioedema (HAE) in adults (with C1-esterase inhibitor deficiency) in Wales and Scotland respectively.

Not for US Release

Basingstoke, UK – 12th March, 2012 –Shire Pharmaceuticals Ltd, a subsidiary of Shire plc (LSE: SHP, NASDAQ:SHPGY) the global specialty biopharmaceutical company, has announced that the All Wales Medicine Strategy Group (AWMSG) and the Scottish Medicines Consortium (SMC) have recommended/accepted FIRAZYR (icatibant) for use within Wales and Scotland respectively. Firazyr is the first and only subcutaneous treatment for acute Type I and Type II hereditary angioedema (HAE) attacks licensed for self-administration in Europe[1].

HAE patients experience recurrent attacks (swellings) in different parts of the body which, in some cases, can be life threatening[2,3]. Firazyr has already been available and used in England for several years but until now, availability in Scotland and Wales has been restricted to only some individually funded cases.

“There are around 140 people living with HAE in Scotland and Wales and the addition of Firazyr will provide these patients with access to a treatment approach that combines the convenience of being the first ready to use, self-administered subcutaneous injection with proven efficacy and tolerability that will facilitate earlier treatment of acute attacks”, commented Dr Stephen Jolles, Consultant Immunologist at the University Hospital Wales.

The comprehensive clinical development program for Firazyr, including the peer reviewed data from the FAST 1, 2 and 3 trials, was the basis for the efficacy and safety analysis presented[4,5]. The Evaluation of the Safety of Self-Administration with Icatibant (EASSI) clinical trial, which supported the variation in the label by the European Commission for self-administration of Firazyr, was also considered as part of the submission to AWMSG and SMC[6,7].

“We are very pleased about the availability of another therapy to help patients with HAE in both Wales and Scotland. Firazyr offers patients the option of a simple, self-administered, sub-cutaneous injection to help manage these debilitating angioedema swellings”, commented Ann Price, Patient Representative, HAE UK.

Janis Clayton, VP & General Manager Shire UK & Ireland said, “Shire HGT are very pleased with the recommendations of AWMSG and SMC with regard to Firazyr. We believe that this will provide another valuable therapy option for patients with HAE in

both Wales and Scotland and we are working with the key centres to make sure that appropriate patients can be offered Firazyr as a treatment option for their acute hereditary angioedema attacks."

About FIRAZYR (icatibant)
The active substance, icatibant, is a specific bradykinin B2 receptor antagonist. It represents a novel, targeted, subcutaneously-administered approach to the treatment of HAE attacks designed to block the effects of bradykinin, the key mediator of oedema formation. Icatibant is a synthetic decapeptide (a peptide containing ten amino acids)[1].

For patients who have never previously received icatibant, the first treatment should be given in a medical institution or under the guidance of a physician[1]. In cases of insufficient relief or recurrence of symptoms after treatment with icatibant, patients should seek medical advice, and subsequent doses should be given in a medical institution[1]. The decision to initiate self-administration should only be taken by a physician experienced in the diagnosis and treatment of HAE[1].

Patients with laryngeal attacks should always seek medical advice and be managed in an appropriate medical institution after self-administration of icatibant, until the physician considers discharge to be safe[1].

Icatibant has an orphan drug designation status in the EU for treatment of hereditary angioedema. Where commercially available, the drug is supplied in a pre-filled 3 ml syringe. Icatibant can be stored at up to 25 degrees Celsius without refrigeration[1].

Important Safety Information
Almost all subjects who were treated with icatibant in clinical trials developed reactions at the site of injection (characterized by skin irritation, swelling, pain, itchiness, erythema, and burning sensation)[4]. Caution should be observed when icatibant is administered to patients with acute ischaemic heart disease or unstable angina pectoris and in the weeks following a stroke[1].

About HAE
HAE is a rare genetic disease. Type I and type II HAE are caused by low levels or a dysfunction of C1 esterase inhibitor (C1-INH). Reduced C1-INH activity can lead to elevated plasma levels of bradykinin, the key mediator of HAE symptoms[4].

HAE is characterized by recurrent sudden attacks of oedema (swelling) of the skin (hands, arms, feet, legs, thighs, face, and genitals) or the mucous membranes (gastrointestinal tract, larynx or voice box)[8]. The swelling can be disfiguring and painful, especially in the case of abdominal attacks. Laryngeal attacks are potentially life-threatening due to the risk of suffocation. Unlike angioedemas caused by allergic reactions, signs and symptoms such as hives and itching do not occur in HAE[8]. Signs and symptoms of HAE do not respond to standard treatments for allergic angioedema.

To contact HAE UK, please see: www.haeuk.org

Recommendation from AWMSG
Icatibant (Firazyr) is recommended as an option for use within NHS Wales for the symptomatic treatment of acute attacks of hereditary angioedema (HAE) in adults (with C1 esterase inhibitor deficiency).

This recommendation applies only in circumstances where the approved Wales patient access scheme is utilised.

AWMSG is of the opinion that icatibant (Firazyr) is suitable for specialist only prescribing within NHS Wales for the above indication.

All Wales Medicines Strategy Group Final Appraisal Recommendation – 0512: Icatibant (Firazyr) February 2012

Recommendation from SMC
ADVICE: following a resubmission

icatibant acetate (Firazyr) is accepted for use within NHS Scotland. Indication under review: Symptomatic treatment of acute attacks of hereditary angioedema (HAE) in adults (with C1-esterase-inhibitor deficiency).

Icatibant treatment resulted in symptom relief in patients suffering acute abdominal, cutaneous and/or laryngeal attacks of hereditary angioedema.

This SMC advice takes account of the benefits of a Patient Access Scheme (PAS) that improves the cost-effectiveness of icatibant. This SMC advice is contingent upon the continuing availability of the Patient Access Scheme in NHS Scotland.

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Notes to editors

SHIRE PLC

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