PRESS RELEASE

Two rare disease therapies approved in Scotland to be made available for people living with Fabry disease and epidermolysis bullosa

- Elfabrio® ▼ (pegunigalsidase alfa), a novel enzyme replacement therapy (ERT), has been approved for restricted use in adult patients with symptomatic Fabry disease in Scotland.
- Filsuvez® (birch bark extract gel) – the first licenced treatment in Europe to treat junctional and dystrophic epidermolysis bullosa (EB) – has also been approved via the Scottish Medicines Consortium's ultra orphan medicines pathway for an initial 3-year period whilst further safety and efficacy data is collected.
- Rare diseases affect around 8% (436,000) of the Scottish population.[1] The availability of both treatments addresses significant unmet patient need while supporting the Scottish Government's action plan on rare diseases.

MANCHESTER, UK, 8th July 2024 – Chiesi, the international research-focused biopharmaceutical group, today announced that the Scottish Medicines Consortium (SMC) has published final advice on two rare disease therapies. Elfabrio® (pegunigalsidase alfa), a novel enzyme replacement therapy (ERT), has been approved as a treatment option for Fabry disease in adults, while birch bark extract gel has been approved as a treatment option for junctional and dystrophic epidermolysis bullosa (EB), subject to data collection under the SMC's ultra-orphan medicines framework.[2,3,4]

The decision on pegunigalsidase alfa marks an important step forward for the Fabry community, where there is a significant unmet patient need. The condition, which affects around 1 in 40,000 people,[5] is a debilitating genetic disease that can severely impact the quality of life of Fabry patients.[6] It can cause chronic pain and progressive damage to vital organs, such as the heart, kidneys and brain.[7] Research has shown that Fabry disease can reduce life expectancy in women by 15 years and in men by 20 years.[8]

The decision from the SMC offers an additional treatment option for those living with Fabry disease, bringing access for Scottish patients in line with England and Wales following approval by the National Institute for Health and Care Excellence (NICE) in 2023.[9] Pegunigalsidase alfa will be available for eligible adult patients in Scotland from 8th July.

The approval of birch bark extract gel subject to data collection provides further access for the rare disease community. EB, sometimes referred to as 'butterfly skin', is the name for a group of rare, genetic skin disorders that cause the skin to become very fragile, with even minor trauma or friction causing severe blisters and wounds deep within the skin, leading to pain, scarring and constant itching. Those living with the condition can have a high risk of developing squamous cell carcinoma, infections and premature death.[10] EB is usually diagnosed in babies or children.[11] Birch bark extract gel is the only licenced therapy for junctional and dystrophic EB, and will be made available to eligible patients in Scotland following agreement between Chiesi and the Scottish Government on the data collection requirements, expected by September.

"*People living with all types of EB desperately need treatments that can positively impact their symptoms and improve their overall quality of life, so it is hugely encouraging that the first treatment for patients with junctional and dystrophic EB was recommended by NICE in September last year and has now been recommended by the SMC, making the treatment available across the UK. On behalf of the EB community, I would like to thank Chiesi and the SMC for facilitating this approval, and all our members who supported the application. There is still much work to do to ensure approved treatments are available for all types of EB, but this*

is a promising first step. It provides hope today and will hopefully be a catalyst for future therapies", said Tony Byrne, Chief Executive Officer, DEBRA UK.

The approvals support the Scottish Government's action plan for rare diseases by improving access to specialist treatments, one of the four key priorities set out in the UK Rare Diseases Framework.[12] It also represents an important milestone towards driving equal access to innovative therapies for rare diseases across all UK nations.

"*The positive announcements for pegunigalsidase alfa and birch bark extract gel by the SMC are a result of close collaborative working between patient organisations, the NHS, the SMC and Chiesi. Today, we celebrate this outcome together and reinforce our deep commitment to supporting as many people living with a rare disease as possible, ensuring they can lead the lives they deserve,"* said David Garzón Lafuente, Head of Rare Diseases, Chiesi UK&I. *"At Chiesi, we're determined to deliver equal access to therapies for those eligible people who may benefit*."

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About Fabry disease

Rare diseases affect around 8% (436,000) of the Scottish population,[1] while an estimated 1 in 40,000 people live with Fabry disease,[5] a rare, progressive, X-linked inherited lysosomal storage disorder, caused by a genetic mutation, which leads to an inherited deficiency of enzyme α-galactosidase A. This is normally responsible for the breakdown of globotriaosylceramide (Gb3).[9,13] The abnormal storage of Gb3 increases with time and, accordingly, Gb3 accumulates, primarily in the blood vessel and tissues.[13] The ultimate consequences of Gb3 deposition range from episodes of pain and impaired peripheral sensation to end-organ failure.[9,13] Patients with Fabry disease may be treated by intravenous infusion with enzyme replacement therapy (ERT) to replace the function of the missing α-galactosidase A enzyme.[9,14] Alternatively, patients aged 12 and over with an amenable mutation may be treated with oral chaperone therapy.[15]

About Elfabrio® (pegunigalsidase alfa)

Elfabrio® (pegunigalsidase alfa) is a pegylated recombinant form of human α-galactosidase-A.[16] The amino acid sequence of the recombinant form is similar to the naturally occurring human enzyme.[16] Pegunigalsidase alfa supplements or replaces α-galactosidase A, the enzyme that catalyses the hydrolysis of the terminal α-galactosyl moieties of oligosaccharides and polysaccharides in the lysosome, reducing the amount of accumulation of Gb_3 and globotriaosylsphingosine (Lyso-Gb_3).[16]

The efficacy and safety profile of pegunigalsidase alfa was evaluated using data from a clinical trials programme, which consisted of 142 patients with Fabry disease (94 males and 48 females) of which 112 received pegunigalsidase alfa 1 mg/kg every other week.[16] These studies show that pegunigalsidase alfa is generally well tolerated, with the most common adverse reactions being infusion-related reactions (reported by 6.3% of patients), followed by hypersensitivity and asthenia (reported each by 5.6% of patients).[16,17]

Renal function: The renal function was evaluated through the estimated glomerular filtration rate (eGFR – CKD-EPI equation) and its annualised measurement slope was the primary endpoint for efficacy in two phase 3 studies in previously ERT-treated adult Fabry patients: BALANCE (main study), a randomised, double blinded, head-to-head comparison with agalsidase beta, after switch from agalsidase beta at month 12 (primary analysis) and month 24, and an open label single arm study, after switch from agalsidase alfa, both followed by a long-term extension study.[16] No final conclusion on non-inferiority over agalsidase beta as measured by the annualised eGFR can be retrieved from the main study given that the data

for the primary endpoint comparison at month 12 was not on its own sufficiently informative due to the design and size of the trial.[16] Nevertheless, the median eGFR slopes from baseline to month 24 of pegunigalsidase and the comparator agalsidase beta appeared close.[16] At month 12, the mean slopes for eGFR in the ITT population were -2.507 mL/min/1.73 m²/year for the pegunigalsidase alfa arm and - 1.748 for the agalsidase beta arm (difference -0.759 [-3.026, 1.507].[16] At month 24, the median slopes for eGFR in the ITT population were -2.514 [-3.788; -1.240] mL/min/1.73 m²/year for the pegunigalsidase alfa arm and -2.155 [-3.805; -0.505] for the agalsidase beta arm (difference -0.359 [-2.444; 1.726]).[16]

Pegunigalsidase alfa is approved in the European Union, Northern Ireland, and Great Britain for long-term ERT in adult patients with a confirmed diagnosis of Fabry disease (deficiency of alpha-galactosidase).[16] Pegunigalsidase alfa is also approved in the United States for the treatment of adults with confirmed Fabry disease.[18] The Great Britain Summary of Product Characteristics for pegunigalsidase alfa can be found at https://www.medicines.org.uk/emc/product/14960/smpc#gref.

About epidermolysis bullosa

Epidermolysis bullosa (EB) is a heterogenous group of rare inherited skin disorders caused by mutations in the genes that encode skin anchoring proteins of the dermo-epidermal junction. It is characterised by very fragile skin that is prone to blistering and erosions due to minor trauma or friction, with the resulting wounds usually extending through multiple layers of the skin surface. As well as the high wound burden, there is impaired wound healing and debilitating symptoms such as pain, pruritis, scarring, deformity, and immobility. There are also several systemic complications (for example anaemia, increased risk of infections, osteoporosis, and squamous cell carcinoma). These all can carry considerable morbidity and increased mortality risk.[19,20]

About Filsuvez® (birch bark extract gel)

Birch bark extract is a sterile gel for cutaneous application use for the treatment of partial thickness wounds associated with dystrophic and junctional EB in patients six months and older.

Birch bark extract gel is approved by the European Medicines Agency and available across Europe.

The Great Britain Summary of Product Characteristics for birch bark extract gel can be found at www.medicines.org.uk/emc/product/13971/smpc.

About Chiesi Group

Chiesi is a research-oriented international biopharmaceutical group that develops and markets innovative therapeutic solutions in respiratory health, rare diseases, and specialty care. The company's mission is to improve people's quality of life and act responsibly towards both the community and the environment.

By changing its legal status to a Benefit Corporation in Italy, the US, and France, Chiesi's commitment to create shared value for society as a whole is legally binding and central to company-wide decision-making. As a certified B Corp since 2019, we're part of a global community of businesses that meet high standards of social and environmental impact. The company aims to reach Net-Zero greenhouse gases (GHG) emissions by 2035.

With over 85 years of experience, Chiesi is headquartered in Parma (Italy), with 31 affiliates worldwide, and counts more than 7,000 employees. The Group's research and development centre in Parma works alongside 6 other important R&D hubs in France, the US, Canada, China, the UK, and Sweden.

For further information please visit www.chiesi.uk.com.

About Chiesi Global Rare Diseases

Chiesi Global Rare Diseases is a business unit of the Chiesi Group established to deliver innovative therapies and solutions for people affected by rare diseases. As a family business, Chiesi Group strives to create a world where it is common to have a therapy for all diseases and acts as a force for good, for society and the planet. The goal of the Global Rare Diseases unit is to ensure equal access so as many people as possible can experience their most fulfilling life. The unit collaborates with the rare disease community around the globe to bring voice to underserved people in the health care system.

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