PRESS RELEASE

NICE highly specialised technologies guidance released for Filsuvez® gel (birch bark extract) in the treatment of epidermolysis bullosa

- *The National Institute for Health and Care Excellence (NICE) has recommended birch bark extract gel for the treatment of partial thickness wounds associated with dystrophic and junctional epidermolysis bullosa (EB) in patients six months and older.*
- *The NICE recommendation means up to 175 patients in England could be eligible for treatment at a time.*
- Birch bark extract gel is the first licenced treatment in Europe to treat junctional and dystrophic epidermolysis bullosa.

MANCHESTER, UK, 28 September 2023 – Chiesi, the international research-focused biopharmaceutical and healthcare group, today announced that the National Institute for Health and Care Excellence (NICE) has released its highly specialised technologies appraisal guidance for the use of Filsuvez® gel (birch bark extract) under the terms of a confidential commercial arrangement.[1] Following the guidance, up to 175 patients could now gain access to the treatment at a time.[2]

NICE recommended birch bark extract gel in its final draft guidance last month for routine NHS use in patients with partial thickness wounds associated with dystrophic and junctional epidermolysis bullosa (EB) in people aged six months and over.[3]

Birch bark extract is a topical gel formulation containing multiple birch triterpenes (betulin, betulinic acid, oleanolic acid, lupeol and erythrodiol). It modulates inflammatory mediators and is associated with the activation of intracellular pathways known to be involved in keratinocyte differentiation and migration, wound healing and closure.[4]

"Having spent the last eight years developing this treatment for the rare, devastating, and life-changing disease, EB, we are pleased to bring the first NICE recommended product for routine NHS use," said Stephen Joyce, General Manager of Amryt DAC (a Chiesi company). *We are immensely grateful to the healthcare professionals, patient organisations and NICE who have made this day possible, and are now actively working to make the treatment available to prescribe in line with NHS systems and processes."*

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 have a high risk of developing squamous cell carcinoma, infections and premature death.[5] EB is usually diagnosed in babies or children, however some milder forms can be diagnosed in adults.[6]

The NICE recommendation is based on data from EASE, which is the largest ever global phase 3 trial in EB, that enrolled dystrophic EB (DEB) and junctional EB (JEB) patients across 49 sites in 26 countries. 223 patients were enrolled, including 156 paediatric patients. The study consisted of two phases, a 90-day double-blind phase (DBP), and a 24-month open-label phase (OLP) with the primary endpoint being the proportion of

patients with first complete target wound closure within 45 days. The target wound had to be a partial thickness wound of at least 21 days old and less than 9 months in age and between 10 cm^2 and < 50 cm^2 in size. Patients were randomised to be treated with birch bark extract gel or vehicle control gel at least every 4 days, to all wounds, either directly or to the dressing, so that the gel was in direct contact with the wound. EASE met its primary endpoint; complete wound closure was achieved in 41.3% of wounds treated with birch bark extract gel versus 28.9% with control gel (p=0.013; relative risk [RR] 1.44, 95% confidence interval [CI] 1.01–2.056).[5] Mean body surface area percentage (BSAP) for patients treated with birch bark extract gel in the DBP showed a numerical reduction from 12.1% at study entry to 6.1% on completion of the EASE study at 27 months.[7]

Birch bark extract gel was well tolerated with a similar incidence of patients with adverse events (AEs) in both groups (81.7% and 80.7% for birch bark extract gel and vehicle control gel, respectively). The majority of these AEs were mild or moderate in severity.[5] In the summary of the safety profile, the most frequently observed adverse reactions were wound complication (in 11.6% of EB patients and 2.9% of patients with other partial thickness wounds (PTW)), application site reaction (in 5.8% of EB patients), wound infections (in 4.0% of EB patients), pruritus (in 3.1% of EB patients and 1.3% of patients with other PTW), pain of skin (in 2.5% of patients with other PTW) and hypersensitivity reactions (in 1.3% of EB patients). There were no clinically relevant differences in the reactions reported in EB patients compared to patients with other PTW.[4] Data from the OLP support a reassuring long-term safety profile of birch bark extract gel.[7]

"*Following the Chiesi acquisition of Amryt earlier this year, we are delighted to be able to bring this important treatment to people living with EB. This debilitating condition has a profound daily impact, and treatments that can improve wound healing are essential,"* said Tom Delahoyde, Managing Director of Chiesi in the UK and Ireland, Chiesi Limited.

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About 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 Amryt

Amryt is a global commercial-stage biopharmaceutical company focused on developing and commercialising innovative treatments to help improve the lives of patients with rare and orphan diseases. In 2023, Chiesi acquired Amryt in a move to expand its rare disease medicine portfolio.

About Chiesi Group

Chiesi is an international, research-focused biopharmaceuticals 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), operates in 31 countries, and counts more than 6,500 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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