

FDA Issues a Complete Response Letter (CRL) Regarding the NDA for Idebenone for Leber Hereditary Optic Neuropathy (LHON) in the United States

Idebenone remains marketed in multiple countries outside the US as a treatment for LHON

BOSTON – March 5, 2026 – Chiesi Global Rare Diseases, a business unit of the Chiesi Group established to deliver innovative therapies and solutions for people living with rare diseases, today announced that the U.S. Food and Drug Administration (FDA) issued a Complete Response Letter (CRL) for idebenone for the treatment of adolescents and adults with Leber Hereditary Optic Neuropathy (LHON).

In the letter, the FDA stated that it is unable to approve the application in its current form. The Agency requested additional clinical data from adequate and well-controlled studies to further demonstrate the safety and effectiveness of idebenone in LHON, as well as clarification and updates to certain chemistry, manufacturing, and nonclinical information. The FDA also indicated that issues related to a referenced Drug Master File must be addressed before approval can be considered. No new clinical safety concerns were identified in the CRL.

“Although this outcome is not what we hoped for, we’re deeply grateful to the patients, families, and investigators whose dedication has enabled critical advancements in LHON research,” said **Giacomo Chiesi, Executive Vice President, Chiesi Global Rare Diseases**. “Their contributions have generated important insights that will continue to inform future scientific efforts. We remain committed to championing the needs of the LHON community and to supporting ongoing research efforts that may one day lead to new treatment options and improved care pathways.”

“Today’s decision does not diminish the strength and perseverance of the LHON community. Patients, families, clinicians, and industry partners have worked tirelessly to advance their understanding of LHON. These continued efforts remain essential as we push for ongoing progress. We will keep advocating for the resources, research, and support needed to bring future treatment options to those who urgently need them,” said **Malinda Marsh, Chris Marsh, and Lissa Poincenot, Parents of children affected by LHON and Co-Founders of LHON Collective**.

The application was supported by data from a pivotal randomized, double-blind, placebo-controlled study (RHODOS) and a Phase 4 open-label interventional study (LEROS), which evaluated the safety and efficacy of idebenone in adolescent and adult participants with LHON across primary mitochondrial DNA mutations.^{1,2}

About LHON

Leber Hereditary Optic Neuropathy (LHON) is an inherited mitochondrial disorder that leads to progressive, rapid, and severe vision loss. It is caused by genetic mutations that impair the ability of retinal ganglion cells — the nerve cells in the eye responsible for transmitting visual information — to produce the energy they need to function properly and remain healthy. Retinal ganglion cells located in the macular region of the retina (the area responsible for sharp, detailed central vision and color perception) are especially sensitive to this dysfunction, which explains why LHON initially and primarily affects central vision. Central vision is critical for detailed tasks such as reading, driving, and recognizing faces.

LHON often begins as a sudden, painless, clouding or blurring accompanied by loss of sharpness and color vision.³ In 75% of cases, the onset of vision loss occurs in one eye first,

followed by the other eye within a few weeks or months.⁴ Beyond vision impairment, the condition often has a profound and lifelong impact on independence, education, employment, and quality of life.

LHON can affect about 1 in 15,000 to 50,000 people worldwide and predominantly affects young people between the ages of 15 and 35, with men being 3-5 times more likely to develop the disease.⁵

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, France and Colombia, Chiesi's commitment to creating shared value for society as a whole is legally binding and central to company-wide decision-making. As a certified B Corp since 2019, Chiesi is 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 90 years of experience, Chiesi is headquartered in Parma (Italy), with 31 affiliates worldwide, and counts more than 7,500 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 more information visit www.chiesi.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 living with 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.

For more information visit: www.chiesirarediseases.com