UCB News

European Commission approves KYGEVVI®▼ (doxecitine and doxribtimine) as first and only treatment for Thymidine Kinase 2 Deficiency (TK2d)

- **European Commission approval**: KYGEVVI® (doxecitine and doxribtimine) 2g/2g powder for oral solution is the first and only treatment option in the European Union indicated for the treatment of paediatric and adult patients with genetically confirmed thymidine kinase 2 deficiency (TK2d) with an age of symptom onset on or before 12 years.[1]
- **Burden of disease**: TK2d is an ultra-rare, life-threatening, genetic mitochondrial disease characterized by progressive and severe muscle weakness (myopathy).[2]
- **Supporting data**: Use of KYGEVVI® led to improvements in motor function, as well as a reduction in use of ventilatory and feeding support.[1]

Brussels (Belgium) 31 March 2026, 07:00 (CEST) – UCB (Euronext Brussels: UCB), a global biopharmaceutical company, today announced that the European Commission (EC) has granted marketing authorization under exceptional circumstances for KYGEVVI (doxecitine and doxribtimine) for the treatment of paediatric and adult patients with genetically confirmed thymidine kinase 2 deficiency (TK2d) with an age of symptom onset on or before 12 years.[1] It is the first and only approved treatment for TK2d.

"The European Commission's approval of KYGEVVI marks a historic milestone for the TK2d community. For the first time, people across Europe living with this ultra-rare, life-threatening mitochondrial disease have access to an approved treatment beyond supportive care," said Donatello Crocetta, Chief Medical Officer at UCB. "KYGEVVI is designed to support mitochondrial DNA maintenance in skeletal muscle, addressing a key biological driver of TK2d. We are deeply grateful to the patients, families, advocates, investigators, and clinical trial teams whose partnership, trust, and resilience made this achievement possible."

"TK2d has a profound impact on people living with the condition and their families and, until now, they have faced a heavy burden of unmet treatment need with incredible resilience," said Caterina Garone, Associate Professor of Medical Genetics, University of Bologna, Italy. "The TK2d community has waited a long time for this moment which brings them new hope and marks an important step forward in how clinicians can manage this devastating disease."

Clinical efficacy

Supporting data for EC approval came from pooled data from two studies* of treatment with KYGEVVI (doxecitine and doxribtimine) in patients with genetically confirmed TK2d with age of symptom onset ≤12 years. These studies investigated the impact of treatment on functional outcomes (i.e. motor milestones, ventilatory support, feeding support) as well as survival.[1,4,9,10,11,12,13] In the studies, KYGEVVI was well tolerated with the most commonly reported adverse reactions of diarrhea (86%), vomiting (28%), abdominal pain (including abdominal pain upper) (26%).[1]

- **Developmental motor milestone ability**: A decrease in the loss of motor milestones was observed following treatment initiation with KYGEVVI; 26/31 (84%) patients regained one or more motor milestones (e.g. sitting upright unassisted, holding head upright unassisted).[1]
- **Ventilatory support**: Prior to treatment start, 18/39 (46%) participants initiated ventilatory support and no participants discontinued ventilatory support. After initiation of treatment, 5/21 (24%) participants started ventilatory support while 5/23 (22%) discontinued ventilatory support.[1]

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- **Feeding support**: Prior to treatment start, 12/39 (31%) participants had a feeding tube. After initiation of treatment, 4/28 (14%) participants started feeding support, with 2 of these participants subsequently discontinuing feeding support after initiation of treatment[1]

About TK2d
TK2d is an ultra-rare, life-threatening, genetic mitochondrial disease characterized by progressive (worsening over time) and severe muscle weakness (myopathy).[2,3,4,5] TK2d can impact all parts of a person's daily life and wellbeing and can become worse over time and impact the ability to walk, eat and breathe independently, often necessitating around-the-clock caregiver support.[3,4,6] It is often fatal, with those experiencing initial symptoms on or before the age of 12 years facing a high risk of premature death (often occurring within 3 years after symptom onset).[7] It is estimated that the worldwide prevalence of TK2d is 1.64 [0.5, 3.1] cases per 1,000,000 people.[8]

About KYGEVVI®
The primary mechanism of action of KYGEVVI (doxecitine and doxribtimine) is the incorporation of pyrimidine nucleosides deoxycytidine (dC) and deoxythymidine (dT) into skeletal muscle mitochondrial deoxyribonucleic acid (DNA) to restore mitochondrial DNA copy number and improve skeletal muscle function in patients with TK2d. Doxecitine and doxribtimine likely utilize residual TK2 activity as well as cytosolic phosphorylation pathways such as thymidine kinase 1 and deoxycytidine kinase to increase mitochondrial DNA precursors deoxycytidine triphosphate and deoxythymidine triphosphate in the mitochondria.[1]

KYGEVVI was supported through EMA's PRIority MEdicines (PRIME) scheme, which provides early and enhanced scientific and regulatory support to medicines that have a potential to address patients' unmet medical needs. Marketing authorization under exceptional circumstances may be granted to medicines where the applicant is unable to provide comprehensive data on efficacy and safety under normal conditions of use, because the condition to be treated is rare or because collection of full information is not possible or is unethical.[14]

The EC approval follows the recent approval of KYGEVVI by the U.S. Food and Drug Administration (FDA) for the treatment of adults and pediatric patients living with thymidine kinase 2 deficiency (TK2d), with an age of symptom onset on or before 12 years.[15]

**These two studies comprise 39 participants with an age of TK2d symptom onset ≤12 years - the median age of TK2d symptom onset was 1.89 years (Q1, Q3 = 1.2, 2.7) and the median duration of treatment was 91.4 months (Q1, Q3 = 80.2, 117.8; all treated > 5 years). Survival was compared to an external control group, after matching on Age of Symptom Onset Category. Information on functional outcomes in the treated patients (motor milestones, ventilatory support, and feeding support) was collected during the pre- and post-treatment period and analyzed.[1]*

For more information about the trials visit: https://clinicaltrials.gov/study/NCT03845712 (TK0102/NCT03845712) and https://clinicaltrials.gov/study/NCT03701568 (MT-1621-101/NCT03701568).

KYGEVVI® ▼ (doxecitine and doxribtimine) EU/EEA** Important Safety Information[1]

Increase in Liver Transaminases
Elevated liver enzymes and liver dysfunction/failure have been observed as a clinical manifestation of TK2d. In clinical studies elevations in alanine aminotransferase [ALT] and/or aspartate aminotransferase [AST] have occurred in patients with TK2d following treatment with KYGEVVI. Transaminase levels should be checked prior

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to initiation of treatment, and changes in liver function monitored periodically during treatment with KYGEVVI and according to routine patient management.

Gastrointestinal disturbances
Gastrointestinal disturbances such as diarrhoea, vomiting, and abdominal pain (including abdominal pain upper) are very commonly reported adverse reactions with doxecitine and doxribtimine treatment. In the pooled safety population 37 out of 50 participants (74%) experienced diarrhoea early after treatment initiation (<3 months). The majority of events of diarrhoea were mild to moderate in severity and were generally self-limiting or improved with temporary dose reduction. Of 133 events of diarrhoea, 12% (16/133) required dose reduction with a median duration of 80 days (Q1, Q3=33.0, 201.5). None of the 50 participants discontinued due to gastrointestinal disturbances, including diarrhoea.

Please consult the summary of product characteristics in relation to other side effects, full safety and prescribing information.

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***EU/EEA means European Union/European Economic Area*

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

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About UCB

UCB, Brussels, Belgium (www.ucb.com) is a global biopharmaceutical company focused on the discovery and development of innovative medicines and solutions to transform the lives of people living with severe diseases of the immune system or of the central nervous system. With more than 9 000 people in approximately 40 countries, the company generated revenue of €7.7 billion in 2025. UCB is listed on Euronext Brussels (symbol: UCB). Follow us on X: @UCB_news

Forward-looking statements

This document contains forward-looking statements, including, without limitation, statements containing the words "potential", "believes", "anticipates", "expects", "intends", "plans", "seeks", "estimates", "may", "will", "continue" and similar expressions. These forward-looking statements are based on current plans, estimates and beliefs of management. All statements, other than statements of historical facts, are statements that could be deemed forward-looking statements, including estimates of revenues, operating margins, capital expenditures, cash, other financial information, expected legal, arbitration, political, regulatory or clinical results or practices and other such estimates and results. By their nature, such forward-looking statements are not guaranteeing future performance and are subject to known and unknown risks, uncertainties, and assumptions which might cause the actual results, financial condition, performance or achievements of UCB, or industry results, to be materially different from any future results, performance, or achievements expressed or implied by such forward-looking statements contained in this document.

Important factors that could result in such differences include but are not limited to: global spread and impacts of wars, pandemics and terrorism, the general geopolitical environment, climate change, changes in general economic, business and competitive conditions, the inability to obtain necessary regulatory approvals or to obtain them on acceptable terms or within expected timing, costs associated with research and development, changes in the prospects for products in the pipeline or under development by UCB, effects of future judicial decisions or governmental investigations, safety, quality, data integrity or manufacturing issues, supply chain disruption and business continuity risks; potential or actual data security and data privacy breaches, or disruptions of our information technology systems, product liability claims, challenges to patent protection for products or product candidates, competition from other products including biosimilars or disruptive technologies/business models, changes in laws or regulations, exchange rate fluctuations, changes or uncertainties in tax laws or the administration of such laws, and hiring, retention and compliance of its employees. There is no guarantee that new product candidates will be discovered or identified in the pipeline, or that new indications for existing products will be developed and approved. Movement from concept to commercial product is uncertain; preclinical results do not guarantee safety and efficacy of product candidates in humans. So far, the complexity of the human body cannot be reproduced in computer models, cell culture systems or animal models. The length of the timing to complete clinical trials and to get regulatory approval for product marketing has varied in the past and UCB expects similar unpredictability going forward. Products or potential products which are the subject of partnerships, joint ventures or licensing collaborations may be subject to disputes between the partners or may prove to be not as safe, effective or commercially successful as UCB may have believed at the start of such partnership. UCB's efforts to acquire other products or companies and to integrate the operations of such acquired companies may not be as successful as UCB may have believed at the moment of acquisition. Also, UCB or others could discover safety, side effects or manufacturing problems with its products and/or devices after they are marketed. The discovery of significant problems with a product similar to one of UCB's products that implicate an entire class of products may have a material adverse effect on sales of the entire class of affected products. Moreover, sales may be impacted by international and domestic trends toward managed care and health care cost containment, including pricing pressure, political and public scrutiny, customer and prescriber patterns or practices, and the reimbursement policies imposed by third-party payers as

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well as legislation affecting biopharmaceutical pricing and reimbursement activities and outcomes. Finally, a breakdown, cyberattack or information security breach could compromise the confidentiality, integrity and availability of UCB's data and systems.

Given these uncertainties, the public is cautioned not to place any undue reliance on such forward-looking statements. These forward-looking statements are made only as of the date of this document, and do not reflect any potential impacts from the evolving event or risk as mentioned above as well as any other adversity, unless indicated otherwise. The company continues to follow the development diligently to assess the financial significance of these events, as the case may be, to UCB.

UCB expressly disclaims any obligation to update any forward-looking statements in this document, either to confirm the actual results or to report or reflect any change in its forward-looking statements with regard thereto or any change in events, conditions or circumstances on which any such statement is based, unless such statement is required pursuant to applicable laws and regulations.

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