FOR IMMEDIATE RELEASE

Vueway® (Gadopiclenol) Receives Positive CHMP Opinion

The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) recommended approval of the macrocyclic, high-relaxivity Vueway® (Gadopiclenol) in adults and pediatric patients older than 2 years of age.

MILAN, Italy October 12, 2023 – Bracco Imaging S.p.A., an innovative world leader delivering end-to-end products and solutions through a comprehensive portfolio inclusive of precision diagnostic imaging modalities, today received notification that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted a positive opinion recommending approval of Vueway® (Gadopiclenol) solution for injection for magnetic resonance imaging (MRI) for use in adult and pediatric patients aged 2 years and older with magnetic resonance imaging (MRI) of the CNS (brain, spine, and surrounding tissues) and several body organs (liver, kidney, pancreas, breast, lung, prostate, and musculoskeletal system). The European Commission is expected to issue its decision by the end of 2023.

Vueway® (Gadopiclenol), is a new macrocyclic gadolinium-based contrast agent (GBCA), very stable and with the highest relaxivity among all the other GBCAs on the market today [1] , so that its approved dose is exactly half of that approved for other macrocyclic GBCAs for similar indications[2]. It was approved by the United States Food and Drug Administration (US FDA) in September 2022.

"The high relaxivity of Vueway® has shown to allow an improvement of its risk-benefit profile by reducing exposure without compromising imaging performance" said **Alberto Spinazzi**, MD, Chief Medical and Regulatory Officer at Bracco Imaging" Vueway® will provide healthcare professionals with an important new option for their patients, as well as for the environment. We eagerly anticipate its arrival to the European market."

The CHMP opinion is based on the results from two prospective, large-scale, randomized, double-blind, crossover clinical studies, PICTURE and PROMISE, conducted in more than 500 adult patients undergoing contrast-enhanced MRI and aimed at comparing the safety and efficacy of 0.05 mmol/kg Gadopiclenol compared with 0.1 mmol/kg Gadobutrol.[3,4] The PICTURE trial demonstrated comparable diagnostic efficacy at half dose in MRI of the central nervous system,[5] the PROMISE trial in MRI of the head and neck, chest, breast, liver, pancreas, pelvis organs, and the musculoskeletal system.[6]

Gadopiclenol offers a two-to-three-fold higher relaxivity than available GBCAs [1] for use with any MRI scanner, regardless of field strength. The contrast agent's macrocyclic structure also confers high stability.[7]The end result is adequate diagnostic efficacy at a Vueway® dose which lower than those approved for other macrocyclic GBCAs in

clinical use [2], while minimizing the risk of gadolinium retention in brain and body tissues, and possibly reducing release of gadolinium in the environment. [7]

About gadolinium-based contrast agents

Gadolinium-based contrast agents (GBCAs) are used in magnetic resonance imaging (MRI) procedures to help enhance the visibility of certain tissues. Gadolinium is a rare earth metal that has unique magnetic properties that make it useful for MRI imaging.

About gadopiclenol

Gadopiclenol, initially invented by Guerbet with subsequent contribution of Bracco IP, is a new macrocyclic gadolinium-based contrast agent (GBCA) with high relaxivity. The efficacy and safety of gadopiclenol have been evaluated in MRI of the Central Nervous System, head and neck, thorax, abdomen, pelvis, and musculoskeletal system (For US reference, refer to the approved USPI).

Details on Phase III clinical trials are available on www.ClinicalTrials.gov:

- Efficacy and Safety of Gadopiclenol for Central Nervous System (CNS) Magnetic Resonance Imaging (MRI) Full Text View - ClinicalTrials.gov
- Efficacy and Safety of Gadopiclenol for Body Magnetic Resonance Imaging (MRI) Full Text View –gov

About the PICTURE trial[1]

The PICTURE trial included 256 patients with known or highly suspected CNS lesion(s). All primary and secondary endpoints of the study were achieved. All blinded readers' evaluations indicated the superiority of the combined unenhanced/contrast-enhanced MRI with 0.05 mmol/kg gadopiclenol over unenhanced MRI alone for all lesion visualisation criteria ($p<0.0001$). For all three blinded readers, non-inferiority of 0.05 mmol/kg gadopiclenol to 0.1 mmol/kg gadobutrol (Gadavist) was demonstrated for all lesion visualisation criteria ($p<0.0001$). Results also indicated superior percent of contrast enhancement for all readers ($p<0.0001$), superior contrast-to-noise ratio for two out of three readers ($p<0.01$), and superior lesion-to-background contrast ratio with gadopiclenol for all readers ($p<0.0001$). In correlation with the greater contrast enhancement, the diagnostic quality of the images obtained with 0.05 mmol/kg gadopiclenol were in majority preferred over that provided by 0.1 mmol/kg gadobutrol by all three blinded readers ($p<0.001$).

About the PROMISE trial[2]

The PROMISE trial included 273 adult patients suspected of having an enhancing abnormality in one of three different body regions (head/neck, breast/thorax/abdomen/pelvis, or musculoskeletal). Off-site blinded readers with expertise in the respective body regions rated border delineation, internal morphology, and visual contrast enhancement. All primary and

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secondary endpoints of the study were achieved. For all blinded readers, 0.05 mmol/kg gadopiclenol was non-inferior to 0.1 mmol/kg gadobutrol for all visualisation parameters and all readers (P<.001), and superior to unenhanced images (P<.001). Two of three readers yielded higher percentage enhancement for gadopiclenol (P<.001). Lesion-to-background ratio did not differ. For most participants (75%–83%), readers reported no preference between 0.05 mmol/kg gadopiclenol and 0.1 mmol/kg gadobutrol images.

About Bracco Imaging

Bracco Imaging S.p.A. ("Bracco Imaging"), part of the Bracco Group, is an innovative world leader delivering end-to-end products and solutions through its comprehensive portfolio across diagnostic imaging modalities. Headquartered in Milan, Italy, Bracco Imaging's purpose is to improve people's lives by shaping the future of prevention and precision diagnostic imaging. The Bracco Imaging portfolio includes products and solutions for all key diagnostic imaging modalities: X-ray imaging, magnetic resonance imaging (MRI), Contrast Enhanced Ultrasound (CEUS), and Nuclear Medicine through radioactive tracers and novel PET imaging agents. Bracco Imaging has approximately 3,700 employees and operates in more than 100 markets globally. Bracco Imaging has a well-skilled and innovative Research and Development (R&D) organization with an efficient process-oriented approach and track record in the diagnostic imaging industry. R&D activities are located in four centers based in Italy, Switzerland, the United Kingdom and the United States. Bracco Group global revenues were 1.7 billion Euros in 2020. To learn more about Bracco Imaging, visit www.bracco.com.

THE BRACCO IMAGING AND GUERBET COLLABORATION

Bracco Imaging and Guerbet in December 2021 entered a worldwide collaboration on Gadopiclenol manufacturing and research and development activities. Gadopiclenol will be commercialized independently under separate brands. Both Guerbet and Bracco Imaging each own valuable intellectual property on Gadopiclenol. Furthermore, after an agreed transition period when Guerbet manufactures Gadopiclenol for both Guerbet and Bracco, both companies will manufacture the Gadopiclenol active ingredient and finished product.
The strategic collaboration is expected to accelerate access to Gadopiclenol and deliver innovation, as well as better care to patients and caregivers alike.

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[1] Robic C, Port M, Rousseaux O, et al. Physicochemical and Pharmacokinetic Profiles of Gadopiclenol: A New Macrocyclic Gadolinium ChelateWith High T1 Relaxivity. Invest Radiol 2019; 54: 475-484.

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[2] https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA0686-003002_15052023150215.pdf
https://www.medicines.org.uk/emc/product/14787/smpc
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https://www.medicines.org.uk/emc/product/349/smpc#gref

[3] https://clinicaltrials.gov/study/NCT03986138?intr=gadopiclenol&rank=8

[4] https://clinicaltrials.gov/study/NCT03996447?intr=gadopiclenol&rank=9

[5] Loevner LA, Kolumban B, Hutóczki G, et al. Efficacy and Safety of Gadopiclenol for Contrast-Enhanced MRI of the Central Nervous System: The PICTURE Randomized Clinical Trial. Invest Radiol. 2023; 58:307-313

[6] Kuhl C, Csőszi T, Piskorski W, Miszalski T, Lee JM, Otto PM. Efficacy and Safety of Half-Dose Gadopiclenol versus Full-Dose Gadobutrol for Contrast-enhanced Body MRI. Radiology 2023; 308: e222612

[7] Runge VM and Heverhagen, JT. Advocating the Development of Next-Generation High-Relaxivity Gadolinium Chelates for Clinical Magnetic Resonance. Invest Radiol. 2018 Jul;53(7):381-389