FOR IMMEDIATE RELEASE

Data Reinforcing Efficacy and Safety of Gadopiclenol in Contrast-Enhanced MRI of Certain Body Regions Published in Radiology

The results of the multicenter, international PROMISE clinical trial demonstrate that gadopiclenol provides similar lesion visualization and contrast enhancement at a gadolinium dose of 0.05 mmol/kg versus a full dose of gadobutrol (0.1 mmol/kg).[i]

Bracco has launched gadopiclenol as VUEWAY® (gadopiclenol) solution for injection and VUEWAY® (gadopiclenol) Pharmacy Bulk Package, following the 2022 approval of gadopiclenol by the United States Food and Drug Administration (U.S. FDA).[ii]

Gadopiclenol is highly stable and shows the highest relaxivity among the gadolinium-based contrast agents available for clinical use.[ii,iii,iv,v,vi,vii,viii]

Monroe Township, NJ, July 19, 2023 – Bracco Imaging, an innovative world leader delivering end-to-end products and solutions through a comprehensive portfolio inclusive of precision diagnostic imaging modalities, announced today the publication of the PROMISE trial in *Radiology*.[i]

The PROMISE study was a prospective, multinational, crossover (within-patient), double-blind comparison of the safety and efficacy of 0.05 mmol/kg gadopiclenol (VUEWAY) with 0.1 mmol/kg gadobutrol (Gadavist®) in adult patients referred for contrast-enhanced magnetic resonance imaging (MRI) of head and neck, thorax (including breast), abdomen (including liver, pancreas, and kidneys), pelvis (including ovaries, uterus, and prostate), and musculoskeletal (including extremities). Despite being administered at half the dose of gadobutrol, gadopiclenol provided a comparable degree of contrast enhancement and quality of morphologic assessment of lesions. The type and severity of adverse events (AEs) were similar with the two gadolinium-based contrast agents, with VUEWAY (4.2%) having a slightly lower rate to that of Gadavist (5.5%).[i]

The publication of the results of the PROMISE Study comes on the heels of those of the PICTURE clinical trial, which were published in *Investigative Radiology* and showed non-inferior quality of morphologic assessment of lesions of the brain and spine with 0.05 mmol/kg VUEWAY compared with 0.1 mmol/kg gadobutrol (Gadavist).[ix] The combined results of the PROMISE and PICTURE trials, and additional clinical evidence, supported the regulatory application for gadopiclenol submitted to the U.S. FDA, resulting in Priority Review and subsequent approval in 2022. Bracco has launched gadopiclenol in the U.S.

market as VUEWAY (gadopiclenol) injection and VUEWAY (gadopiclenol) Pharmacy Bulk Package, with a series of hospitals leading first clinical usage.

"Before gadopiclenol, most of the GBCAs available for clinical use were indicated for the brain, spine, or central nervous system with narrow indications for the body, such as the breast, liver, and heart,[i]" said Fulvio Renoldi Bracco, Vice-Chairman and CEO of Bracco Imaging. "The publication of this data reinforces VUEWAY injection as a boundary-pushing and novel MRI contrast agent across the central nervous system (the brain, spine, and surrounding tissues) and body (the head and neck, thorax, abdomen, pelvis, and musculoskeletal system).[ii]"

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 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 visualization 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.[i]

"The results of the PROMISE Study led to the approval of the use of gadopiclenol with MRI of the head and neck, thorax, abdomen, pelvis, and the musculoskeletal system,[ii]" said Alberto Spinazzi, MD, Chief Medical and Regulatory Officer at Bracco. "Of note, gadopiclenol was approved for both MRI of the central nervous system and of the body at the dose of 0.05 mmol/kg, which showed to provide similar contrast enhancement efficacy compared with a dose of 0.1 mmol/kg of Gadavist. This is thanks to the high relaxivity of gadopiclenol, the highest among all the available GBCAs.[ii,iii,IV,V,VI,VII,VIII]"

VUEWAY injection is a Group II agent within the American College of Radiology's classification of gadolinium-based agents relative to the risk of nephrogenic systemic fibrosis (NSF), indicating association with few if any, unconfounded cases.[x] It is approved 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 the body (head and neck, thorax, abdomen, pelvis, and musculoskeletal system).[ii]

VUEWAY injection is now available to order from Bracco Diagnostics Inc. Visit VUEWAY.com for more information, including its full Prescribing Information.

VUEWAY® (gadopiclenol) solution for injection

Indications

VUEWAY injection is indicated in adults and children aged 2 years and older for use with magnetic resonance imaging (MRI) to detect and visualize lesions with abnormal vascularity in:

- the central nervous system (brain, spine and surrounding tissues),
- the body (head and neck, thorax, abdomen, pelvis, and musculoskeletal system).

IMPORTANT SAFETY INFORMATION

WARNING: NEPHROGENIC SYSTEMIC FIBROSIS (NSF)

Gadolinium-based contrast agents (GBCAs) increase the risk for NSF among patients with impaired elimination of the drugs. Avoid use of GBCAs in these patients unless the diagnostic information is essential and not available with non-contrasted MRI or other modalities. NSF may result in fatal or debilitating fibrosis affecting the skin, muscle and internal organs.

- **The risk for NSF appears highest among patients with:**
  - **Chronic, severe kidney disease (GFR < 30 mL/min/1.73 m^2), or**
  - **Acute kidney injury.**
- **Screen patients for acute kidney injury and other conditions that may reduce renal function. For patients at risk for chronically reduced renal function (e.g. age > 60 years, hypertension, diabetes), estimate the glomerular filtration rate (GFR) through laboratory testing.**
- **For patients at highest risk for NSF, do not exceed the recommended VUEWAY dose and allow a sufficient period of time for elimination of the drug from the body prior to any re-administration.**

Contraindications

VUEWAY injection is contraindicated in patients with history of hypersensitivity reactions to VUEWAY.

Warnings

Risk of **nephrogenic systemic fibrosis** is increased in patients using GBCA agents that have impaired elimination of the drugs, with the highest risk in patients with chronic, severe kidney disease as well as patients with acute kidney injury. Avoid use of GBCAs among these patients unless the diagnostic information is essential and not available with non-contrast MRI or other modalities.

Hypersensitivity reactions, including serious hypersensitivity reactions, could occur during use or shortly following VUEWAY administration. Assess all patients for any history of a reaction to contrast media, bronchial asthma and/or allergic disorders, administer VUEWAY only in situations where trained personnel and therapies are promptly available for the treatment of hypersensitivity reactions, and observe patients for signs and symptoms of hypersensitivity reactions after administration.

Gadolinium retention can be for months or years in several organs after administration. The highest concentrations (nanomoles per gram of tissue) have been identified in the bone, followed by other organs (brain, skin, kidney, liver and spleen). Minimize repetitive GBCA imaging studies, particularly closely spaced studies, when possible.

Acute kidney injury requiring dialysis has occurred with the use of GBCAs in patients with chronically reduced renal function. The risk of acute kidney injury may increase with increasing dose of the contrast agent.

Ensure catheter and venous patency before injecting as **extravasation** may occur, and cause tissue irritation.

VUEWAY may **impair the visualization of lesions** seen on non-contrast MRI. Therefore, caution should be exercised when VUEWAY MRI scans are interpreted without a companion non-contrast MRI scan.

The most common adverse reactions (incidence ≥ 0.5%) are injection site pain (0.7%), and headache (0.7%).

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Please click here for full Prescribing Information for VUEWAY, including BOXED WARNING on Nephrogenic Systemic Fibrosis.

Manufactured for Bracco Diagnostics Inc. by Liebel-Flarsheim Company LLC - Raleigh, NC, USA 27616.

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 3,600 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 1.4 billion Euros in 2020. To learn more about Bracco Imaging, visit www.bracco.com.

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[i] Kuhl C, Csőszi T, Piskorski W et al. Efficacy and Safety of Half-Dose Gadopiclenol versus Full-Dose Gadobutrol for Contrast-enhanced Body MRI *Radiology*: Volume 308: Number 1—July 2023

[ii] Vueway® (gadopiclenol) solution for injection, 485.1 mg/mL/ Full Prescribing Information and Patient Medication Guide. Monroe Twp., NJ: Bracco Diagnostics Inc.; September 2022.

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

[iv] GADAVIST® (gadobutrol) Injection. Full Prescribing Information and Patient Medication Guide. Bayer HealthCare Pharmaceuticals Inc. Whippany, NJ; April 2022.

[v] DOTAREM® (gadoterate meglumine) Injection. Full Prescribing Information. Guerbet LLC. Princeton, NJ. April 2022.

[vi] CLARISCAN™ (gadoterate meglumine) injection for intravenous use. Full Prescribing Information and Patient Medication Guide. GE Healthcare. Chicago, IL; February 2020.

[vii] ProHance® (Gadoteridol) Injection, 279.3 mg/mL. Full Prescribing Information and Patient Medication Guide. Monroe Twp., NJ: Bracco Diagnostics Inc.; June 2022.

[viii] MultiHance® (gadobenate dimeglumine) injection, 529 mg/mL. Full Prescribing Information and Patient Medication Guide. Monroe Twp., NJ: Bracco Diagnostics Inc.; August 2018.

[ix] Loevner L, Kolumban B, Hutoczki G, et al. Efficacy and Safety of Gadopiclenol for Contrast-Enhanced MRI of the Central Nervous System. The PICTURE Randomized Clinical Trial. *Invest Radiol.* 2022 Dec.

[x] American College of Radiology. ACR Manual on Contrast Media. 2023.