



FOR IMMEDIATE RELEASE

Bracco Announces FDA Approval of Gadopiclenol Injection, a New Macrocyclic High-Relaxivity Gadolinium-Based Contrast Agent which will be commercialized as VUEWAY™ (gadopiclenol) injection and VUEWAY™ (gadopiclenol) Pharmacy Bulk Package by Bracco

VUEWAY injection is highly stable and shows the highest relaxivity among gadolinium-based contrast agents available for clinical useⁱ

VUEWAY injection is approved for use in adult and pediatric patients aged 2 years and older with magnetic resonance imaging (MRI) of the central nervous system (brain, spine, and surrounding tissues) and the body (head and neck, thorax, abdomen, pelvis and musculoskeletal system)ⁱⁱ

Monroe Township, NJ, September 21, 2022 – Bracco Diagnostics Inc., the United States (U.S.) subsidiary of Bracco Imaging S.p.A., an innovative world leader in diagnostic imaging, announced today that the U.S. Food and Drug Administration (FDA) has approved Gadopiclenol Injection, a new, highly stable macrocyclic gadolinium-based contrast agent (GBCA), which shows the highest relaxivity compared to all the other GBCAs available today in the United States.^{i,ii} Gadopiclenol Injection will be commercialized by Bracco as VUEWAY (gadopiclenol) injection and VUEWAY (gadopiclenol) Pharmacy Bulk Package. VUEWAY injection is approved for use with MRI in adults and pediatric patients aged 2 years and older to detect and visualize lesions in the central nervous system (brain, spine and associated tissues) and the body (head and neck, thorax, abdomen, pelvis and musculoskeletal system).ⁱⁱ The approved dose is 0.05 mmol/kg, which was shown to improve the detection and visualization of lesions over unenhanced MRI alone, and to provide similar diagnostic efficacy compared with 0.1 mmol/kg of the lower-relaxivity Gadobutrol injection in the approved indications.^{iii,iv} Please see Indications and Important Safety Information below, including Boxed Warning.

“The approval of Gadopiclenol Injection follows Priority Review, which is granted by the FDA for products that are considered significant improvements in safety or effectiveness when compared to standard options^v,” said Alberto Spinazzi, MD, Chief Medical and Regulatory Officer at Bracco. “This is because Gadopiclenol Injection, to be marketed by Bracco as VUEWAY injection, is a first-of-its-kind MRI agent that delivers the highest relaxivity and highest kinetic stability of all GBCAs on the market today.ⁱ Highly stable, clinical studies showed that VUEWAY injection provides effective contrast enhancement and diagnostic efficacy at half the approved dose of Gadobutrol injection and Gadobenate



dimeglumine injection, another high-relaxivity agent.^{iii,iv,vi} The positive benefit-risk profile of VUEWAY injection has been demonstrated across a large number of indications, including some for which GBCAs had not previously been approved in the United States.”

The pivotal Phase III studies supporting approval of VUEWAY injection were designed as crossover studies, within-patient comparisons of MRI of the CNS or MRI of the body with 0.05 mmol/kg VUEWAY injection or unenhanced MRI alone, and 0.05 mmol/kg Gadopichlenol with 0.1 mmol/kg Gadobutrol in adult patients.^{iii,iv} Even at half dose, MRI with Gadopichlenol was shown to be non-inferior to MRI with the full dose of Gadobutrol. In MRI of the CNS, the quality of visualization obtained with a half-dose of Gadopichlenol was preferred to that of Gadobutrol by all the blinded readers.

No major safety signals were reported during the development of VUEWAY in either adult or pediatric patients, and the adverse events reported during the two Phase III studies were similar for both of the products administered.ⁱⁱ

“During a year where we will celebrate our 95th anniversary, we are excited to deliver this unique MRI agent to the healthcare community and the patients they serve, a testament to our legacy of innovation,” said Fulvio Renoldi Bracco, Vice-Chairman & CEO of Bracco Imaging. “The approval of VUEWAY injection is representative of the commitment of our workforce comprised of more than 300 scientists and engineers who continuously strive to improve the diagnostic performance of medical imaging and patient outcomes.”

The introduction of VUEWAY injection is the result of a strategic, global collaboration between Bracco and Guerbet in both research, development, and manufacturing of the product signed in December 2021.

“This strategic collaboration will expand access to this important new contrast agent which has the potential to help improve diagnoses and ultimately improve patient care,” said Cosimo De Pinto, Senior Vice President of Sales and Marketing at Bracco Diagnostics Inc. “By exploring a flexible application of our intellectual property rights, we’ve seen that joining forces has led to meaningful innovation at a faster pace. One of the greatest barriers to health equity and access is overly strict adherence to traditional approaches to knowledge and information sharing. The more we collaborate, the more we unencumber healthcare delivery at moments when it matters most.”

Through this global collaboration, Guerbet and Bracco will commercialize the product independently under different brand names. A Centralized Application for Marketing Authorization to the European Medicines Agency (EMA) for Gadopichlenol Injection was submitted earlier this year.



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Visit VUEWAY.com for more information, including full Prescribing Information.

Gadopiclénol, initially invented by Guerbet with subsequent contribution of Bracco IP, is a new macrocyclic gadolinium-based contrast agent (GBCA) with high relaxivity.ⁱ The efficacy and safety of Gadopiclénol have been evaluated in MRI of the Central Nervous System, head and neck, thorax, abdomen, pelvis, and musculoskeletal system (refer to the approved USPI for full information).ⁱⁱ Details on Phase III clinical trials are available on www.ClinicalTrials.gov:

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

The Bracco Imaging and Guerbet Collaboration / The Guerbet and Bracco Imaging Collaboration

Bracco Imaging and Guerbet in December 2021 entered a worldwide collaboration on Gadopiclénol manufacturing and research and development activities. Gadopiclénol will be commercialized independently under separate brands. Both Guerbet and Bracco Imaging each own valuable intellectual property on Gadopiclénol. Furthermore, after an agreed transition period when Guerbet manufactures Gadopiclénol for both Guerbet and Bracco, both companies will manufacture the Gadopiclénol active ingredient and finished product.

The strategic collaboration is expected to accelerate access to Gadopiclénol and deliver innovation, as well as better care to patients and caregivers alike.

VUEWAY™ (gadopiclénol) injection Important Safety Information



WARNING: NEPHROGENIC SYSTEMIC FIBROSIS (NSF)

See full prescribing information for complete boxed warning

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-contrast MRI or other modalities.

- The risk for NSF appears highest among patients with:
 - Chronic, severe kidney disease (GFR <30 mL/min/1.73 m²), 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 (for example, age >60 years, hypertension or diabetes), estimate the glomerular filtration rate (GFR) through laboratory testing.

Indications and Usage

VUEWAY (gadopiclenol) injection is indicated in adult and pediatric patients 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 associated tissues), and the body (head and neck, thorax, abdomen, pelvis, and musculoskeletal system).

Contraindications

History of hypersensitivity reactions to VUEWAY.

Warnings and Precautions

- **Nephrogenic Systemic Fibrosis:** Gadolinium-based contrast agents (GBCAs) increase the risk for nephrogenic systemic fibrosis (NSF) among patients with impaired elimination of the drugs. Avoid use of GBCAs among these patients unless the diagnostic information is essential and not available with non-contrast MRI or other modalities. The GBCA-associated NSF risk appears highest for patients with chronic, severe kidney disease (GFR <30 mL/min/1.73 m²) as well as patients with acute kidney injury. The risk appears lower for patients with chronic, moderate kidney disease (GFR 30-59 mL/min/1.73 m²) and little, if any, for patients with chronic, mild kidney disease (GFR 60-89 mL/min/1.73 m²). NSF may result in fatal or debilitating fibrosis affecting the skin, muscle, and internal organs. Report any diagnosis of NSF following VUEWAY administration to Bracco Diagnostics, Inc. (1-800-257-5181) or FDA (1-800-FDA-1088 or www.fda.gov/medwatch). Screen patients for acute kidney injury and other conditions that may reduce renal function. Features of acute kidney injury consist of rapid (over hours to days) and usually reversible decrease in kidney function, commonly in the setting of surgery, severe infection, injury or drug-induced kidney toxicity. Serum creatinine levels and estimated GFR may not reliably assess renal function in the setting of acute kidney injury. For patients at risk for chronically reduced renal function (e.g.,



age >60 years, diabetes mellitus or chronic hypertension), estimate the GFR through laboratory testing. Among the factors that may increase the risk for NSF are repeated or higher than recommended doses of a GBCA and the degree of renal impairment at the time of exposure. Record the specific GBCA and the dose administered to a patient. 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 prior to re-administration. For patients receiving hemodialysis, physicians may consider the prompt initiation of hemodialysis following the administration of a GBCA in order to enhance the contrast agent's elimination. The usefulness of hemodialysis in the prevention of NSF is unknown.

- **Hypersensitivity Reactions:** With GBCAs, serious hypersensitivity reactions have occurred. In most cases, initial symptoms occurred within minutes of GBCA administration and resolved with prompt emergency treatment. Before VUEWAY administration, assess all patients for any history of a reaction to contrast media, bronchial asthma and/or allergic disorders. These patients may have an increased risk for a hypersensitivity reaction to VUEWAY.
- **Gadolinium Retention:** Gadolinium is retained for months or years in several organs. Linear GBCAs cause more retention than macrocyclic GBCAs. Consequences of gadolinium retention in the brain have not been established. Pathologic and clinical consequences of GBCA administration and retention in skin and other organs have been established in patients with impaired renal function. While clinical consequences of gadolinium retention have not been established in patients with normal renal function, certain patients might be at higher risk. These include patients requiring multiple lifetime doses, pregnant and pediatric patients, and patients with inflammatory conditions. Consider the retention characteristics of the agent when choosing a GBCA for these patients. Minimize repetitive GBCA imaging studies, particularly closely spaced studies when possible.
- **Acute Kidney Injury:** In patients with chronically reduced renal function, acute kidney injury requiring dialysis has occurred with the use of GBCAs. The risk of acute kidney injury may increase with increasing dose of the contrast agent. Do not exceed the recommended dose.
- **Extravasation and Injection Site Reactions:** Injection site reactions such as injection site pain have been reported in the clinical studies with VUEWAY. Extravasation during VUEWAY administration may result in tissue irritation. Ensure catheter and venous patency before the injection of VUEWAY.
- **Interference with Visualization of Lesions Visible with Non-Contrast MRI:** As with any GBCA, VUEWAY may impair the visualization of lesions seen on non-contrast MRI. Therefore, caution should be exercised when Gadopiclenol MRI scans are interpreted without a companion non-contrast MRI scan.



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Adverse Reactions:

In clinical trials, the most frequent adverse reactions that occurred in > 0.2% of patients who received VUEWAY included: injection site pain, headache, nausea, injection site warmth and coldness, dizziness, and localized swelling.

Adverse reactions that occurred with a frequency \leq 0.2% in patients who received 0.05 mmol/kg BW VUEWAY included: maculopapular rash, vomiting, worsened renal impairment, feeling hot, pyrexia, oral paresthesia, dysgeusia, diarrhea, pruritus, allergic dermatitis, erythema, injection site paresthesia, Cystatin C increase, and blood creatinine increase.

Use in Specific Populations

- **Pregnancy:** GBCAs cross the human placenta and result in fetal exposure and gadolinium retention. There are no available data on VUEWAY use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage or other adverse maternal or fetal outcomes.
- **Lactation:** There are no data on the presence of VUEWAY in human milk, the effects on the breastfed infant, or the effects on milk production. However, published lactation data on other GBCAs indicate that 0.01 to 0.04% of the maternal gadolinium dose is present in breast milk.
- **Pediatric Use:** The safety and effectiveness of VUEWAY have not been established in pediatric patients younger than 2 years of age.
- **Geriatric Use:** This drug is known to be substantially excreted by the kidney, and the risk of adverse reactions to this drug may be greater in patients with impaired renal function.
- **Renal Impairment:** In patients with renal impairment, the exposure of gadopichlenol is increased compared to patients with normal renal function. This may increase the risk of adverse reactions such as nephrogenic systemic fibrosis (NSF). Avoid use of GBCAs among these patients unless the diagnostic information is essential and not available with non-contrast MRI or other modalities. No dose adjustment of VUEWAY is recommended for patients with renal impairment. VUEWAY can be removed from the body by hemodialysis

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.



VUEWAY is a trademark of Bracco Imaging S.p.A.

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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.braccoimaging.com.

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- ⁱ 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.
 - ⁱⁱ Vueway™ (gadopiclenol) injection Full Prescribing Information. Monroe Twp., NJ: Bracco Diagnostics Inc.; September 2022.
 - ⁱⁱⁱ Clinical Study Report of Study GDX-44-011. Data on file.
 - ^{iv} Clinical Study Report of Study GDX-44-010. Data on file.
 - ^v US FDA. Priority Review. Available at: <https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/priority-review>. Accessed August 22, 2022.
 - ^{vi} Bendszus M, Roberts D, Kolumban B, et al. Dose Finding Study of Gadopiclenol, a New Macrocyclic Contrast Agent, in MRI of Central Nervous System. *Invest Radiol*. 2020 Mar;55(3):129-137.