New study of ultrasound enhancing agents in echocardiography reaffirms safety profile of LUMASON® (sulfur hexafluoride lipid-type A microspheres) for injectable suspension, for intravenous use or intravesical use

Data show only one non-serious adverse event reported with LUMASON ultrasound enhancing agent in 2,137 administrations

Monroe Township, NJ, July 15, 2019 – Bracco Diagnostics Inc., the U.S. subsidiary of Bracco Imaging S.p.A., one of the world’s leading companies in the diagnostic imaging business, shares the results of a new prospective clinical study of the use of ultrasound enhancing agents (UEAs) in transthoracic echocardiography reaffirming the proven safety profile of its LUMASON ultrasound enhancing agent. The overall incidence of adverse events (AEs) in the study was extremely low and the observed AEs were non-serious. The authors reported the rate of AEs following administration of LUMASON agent to be significantly lower than that after administration of the UEA Definity®. The study is published in the journal Echocardiography.¹

UEAs are used in echocardiography to improve image quality and provide real-time assessment of intracardiac blood flow in patients whose conditions, such as large body habitus, lung artifact, increased anterior–posterior diameter, and excessive cardiac motion, may impair image resolution and quality.²

“The positive impact of ultrasound enhancing agents is indisputable as they have significantly improved the quality and cost-effectiveness of cardiac clinical care, but these agents are underutilized by the clinical community due to concerns about potential allergic reactions,” said study investigator Stephen B. Heitner, MD, Clinical Echocardiography Laboratory, OHSU Hypertrophic Cardiomyopathy Center, Oregon Health & Science University. “Our study shows an extremely low overall incidence of adverse effects events with routine clinical use of ultrasound enhancing agents and confirms that they should be used with all appropriate patients, including those with known intra-cardiac shunts.”

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Study Design and Results
This was a prospective observational study conducted at Oregon Health & Science University to determine the rate and severity of AEs following UEA administration, assess whether microbubbles are safe when administered to patients with intracardiac shunts, and assess whether the rate and type of AEs differ significantly among LUMASON, Definity and Optison™, the three UEAs approved by the U.S. Food and Drug Administration.

Over a 15-month period, 5,476 echocardiographic studies with UEAs were performed in 5,013 patients. A total of 5,521 UEA administrations were completed: 2,137 with LUMASON, 3,306 with Definity and 78 with Optison. Due to the low number of procedures with Optison, no meaningful comparison between this agent and the other two UEAs could be made.

Overall incidence of AEs was low (14 AEs, 0.25%). All AEs were non-serious, and there were no AEs among the 33 patients known to have intra-cardiac shunts. AE rate was significantly higher with Definity (13 AEs, 0.39%) than with LUMASON (1 AE, 0.05%). Flank pain was the most commonly reported adverse effect event in patients administered with Definity (N=9). One patient who developed flank pain with Definity had tolerated the use of LUMASON on prior transthoracic echocardiography without incident. Intervention was required only for one patient who developed rash and dyspnea shortly after administration of Definity.

“In the United States and Europe, there has been an increased interest in using prospective observational studies to obtain more and reliable information on the safety of medicines in real-world clinical settings to inform health policy decisions,” stated Alberto Spinazzi, MD, Head, Global Medical and Regulatory Affairs, Bracco Group. “Post-approval studies like this one continue to demonstrate the low level of risk of UEA use in diagnostic imaging.”

About LUMASON ultrasound enhancing agent
LUMASON ultrasound enhancing agent, which has been marketed globally as SonoVue® since 2001, was initially approved in October 2014 by the FDA for use in adults with suboptimal echocardiograms to opacify the left ventricular chamber and to improve the delineation of the left ventricular endocardial border. LUMASON ultrasound enhancing agent then gained FDA approval in March 2016 for use in ultrasonography of the liver for characterization of focal liver lesions in adult and pediatric patients, and in December 2016, for use for the evaluation of suspected or known vesicoureteral reflux in pediatric patients.

An ultrasound contrast agent with a proven safety profile, LUMASON is made up of gas-filled microspheres that reflect the sound waves to enhance the echogenicity of the blood or urine, which results in an improvement in the diagnostic quality of the ultrasound images. The agent is packaged in a convenient three-part portable kit that does not require refrigeration or mechanical agitation. Each kit contains a LUMASON vial containing 25 mg of lipid-type A lyophilized powder and 60.7 mg sulfur hexafluoride headspace, a prefilled syringe containing 5 mL of Sodium Chloride 0.9% Injection, USP (Diluent), and a Mini-Spike.³
In late 2015, the Centers for Medicare and Medicaid Services (CMS) granted “pass-through” status for LUMASON reimbursement, under the Hospital Outpatient Prospective Payment System (HOPPS). Contrast material is not separately paid by Medicare for outpatient hospitals under HOPPS unless the product has “pass-through” status. This additional payment is unique to LUMASON ultrasound enhancing agent due to its new technology status. Effective October 1, 2016, CMS approved the request for coverage and coding for liver and/or abdominal ultrasound with contrast under the HOPPS indicating that Healthcare Common Procedure Coding System (HCPCS) code C9744 can be assigned for these procedures when performed in the hospital outpatient setting.

Please see Important Safety Information below.

INDICATIONS AND USAGE
LUMASON® is an ultrasound contrast agent indicated for use:

• in echocardiography to opacify the left ventricular chamber and to improve the delineation of the left ventricular endocardial border in adult patients with suboptimal echocardiograms
• in ultrasonography of the liver for characterization of focal liver lesions in adult and pediatric patients
• in ultrasonography of the urinary tract for the evaluation of suspected or known vesicoureteral reflux in pediatric patients

CONTRAINDICATIONS
LUMASON® is contraindicated in patients with:

• history of hypersensitivity reactions to sulfur hexafluoride lipid microsphere components or to any of the inactive ingredients in LUMASON

IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS CARDIOPULMONARY REACTIONS
Serious cardiopulmonary reactions, including fatalities, have occurred uncommonly during or following the injection of ultrasound contrast agents, including sulfur hexafluoride lipid microspheres [see Warnings and Precautions (5.1)]. Most serious reactions occur within 30 minutes of administration [see Warnings and Precautions (5.1)].

- Assess all patients for the presence of any condition that precludes administration [see Contraindications (4)].
- Always have resuscitation equipment and trained personnel readily available [see Warnings and Precautions (5.1)].

The risk for serious cardiopulmonary reactions may be increased among patients with unstable cardiopulmonary conditions (acute myocardial infarction, acute coronary artery syndromes, worsening or unstable congestive heart failure, or serious ventricular arrhythmias) [see Warnings and Precautions (5.1)].
Please see full Prescribing Information for LUMASON ultrasound contrast agent including boxed WARNING at https://www.braccoimaging.com/us-en/products/contrast-enhanced-ultrasound/lumason

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit https://www.fda.gov/Safety/MedWatch/default.htm or call 1-800-FDA-1088.

LUMASON is manufactured for Bracco Diagnostics Inc., Monroe Township, NJ 08831 by Bracco Suisse S.A., Plan-les-Ouates Geneve, Switzerland (LUMASON lyophilized powder vial-25 mg lipid-type A/60.7 sulfur hexafluoride gas); Vetter Pharma-Fertigung GmbH & Co. KG, 88212 Ravensburg, Germany (Sodium Chloride 0.9% Injection, USP); B. Braun Melsungen AG, 34212 Melsungen, Germany (Mini-Spike).

LUMASON and SONOVUE are registered trademarks of Bracco Diagnostics Inc. and its affiliated entities.

All other trademarks and registered trademarks are the property of their respective owners.

About Bracco Imaging
Bracco Imaging S.p.A., part of the Bracco Group, is one of the world’s leading companies in the diagnostic imaging business. Headquartered in Milan, Italy, Bracco Imaging develops, manufactures and markets diagnostic imaging agents and solutions that meet medical needs.

Bracco Imaging offers a product and solution portfolio for all key diagnostic imaging modalities: X-ray Imaging (including Computed Tomography-CT, Interventional Radiology, and Cardiac Catheterization), Magnetic Resonance Imaging (MRI), Contrast Enhanced Ultrasound (CEUS), and Nuclear Medicine through radioactive tracers. The diagnostic imaging portfolio is completed by a range of medical devices and advanced administration systems for contrast imaging products.

The company operates in over 100 markets worldwide, either directly or indirectly, through subsidiaries, joint ventures, licenses and distribution partnership agreements. With on-going research covering all key modalities, Bracco Imaging has a strong presence in key geographies: North America, Europe and Japan operating through the Joint Venture Bracco-Eisai Co. Ltd. The Company also operates in Brazil, South Korea, and China through the Joint Venture Bracco Sine Pharmaceutical Corp. Ltd.

Operational investments have been made in order to achieve top quality, compliant and sustainable eco-friendly production. Manufacturing activities are located in Italy, Switzerland, Japan, China, and Germany.

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Bracco Imaging is an innovative Research and Development (R&D) structure with an efficient process-oriented approach and a track record of innovation in the diagnostic imaging industry. R&D activities are managed in the three Research Centers located in Italy, Switzerland, and the USA.

To learn more about Bracco Imaging, visit www.braccoimaging.com.


3. LUMASON (sulfur hexafluoride lipid-type A microspheres) for injectable suspension, for intravenous use or intravesical use full Prescribing Information. Monroe Township, NJ: Bracco Diagnostics Inc., December 2016.

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