LIFE FROM INSIDE

Important Safety Information on SonoVue® (8 microlitres/ml powder and solvent for dispersion for injection) Use in Critically Ill Patients

SonoVue® (8 microlitres/ml powder and solvent for dispersion for injection) is an ultrasound contrast agent consisting of a suspension of tiny microbubbles (most microbubbles between 2 and 9 microns) with a unique structure made of an inert gas, sulphur hexafluoride, and a phospholipid shell that provides stability and prevents microbubble coalescence. When injected intravenously, Sonovue® strongly enhances the echogenicity of blood, which results in an improved signal-to-noise ratio.

Important New Safety Information

Following an evaluation of the benefits and risks of SonoVue® use in critically ill patients made to by the Committee on Human Medicinal Products (CHMP) of the European Medicines Agency (EMA), the decision was made to:

- **delete the contraindications for SonoVue® use in patients with recent acute coronary syndrome or clinically unstable ischaemic cardiac disease**, including: evolving or ongoing myocardial infarction, typical angina at rest within last 7 days, significant worsening of cardiac symptoms within last 7 days, recent coronary artery intervention or other factors suggesting clinical instability (for example, recent deterioration of ECG, laboratory or clinical findings), acute cardiac failure, Class III/IV cardiac failure, or severe rhythm disorders;
- **to insert SonoVue® use information on these patient populations into the Special Warnings and Precautions for Use section of the Product Information**.

Since its launch in 2001, four (4) cases of severe cardiac arrhythmia occurred following concomitant administration of SonoVue® and the direct-acting, inotropic agent dobutamine. Of note, these 4 cases occurred in patients with either ongoing myocardial infarction, or other factors suggesting clinical instability, acute cardiac failure, or severe rhythm disorders, where the use of dobutamine is specifically contraindicated. One case, occurred in a patient with dilated cardiomyopathy and severe heart failure. This patient experienced ventricular fibrillation and cardiac arrest during the stress-echo procedure; the adverse events were considered related to the administration of dobutamine by the reporter. In the further clinical course, the patient had multiple cardiac arrests and developed subsequent cardiac and multi-organ-failure. She died 19 days after the reported events.

In view of these rare events and the frequent use of dobutamine for stress echocardiographic procedures, the CHMP also decided to make sure SonoVue® is not used in combination with dobutamine in those patients for which the use of this pharmacologic stressor is contraindicated.

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Therefore, the CHMP decided to add the following contraindication to the Product Information of SonoVue®: **"SonoVue® should not be used in combination with dobutamine in patients with conditions suggesting cardiovascular instability where dobutamine is contraindicated".**

In summary:

- SonoVue® is no longer contraindicated in patients with recent acute coronary syndrome or clinically unstable ischaemic cardiac disease.
- Prescribers may use SonoVue® in this patient population using extreme caution, after a careful risk/benefit assessment and with close monitoring of vital signs during and after administration.
- SonoVue® should not be used in combination with dobutamine in patients with conditions suggesting cardiovascular instability where dobutamine is contraindicated.

To provide SonoVue® users and prescribers with this new important safety information, Bracco has agreed upon with EMA and sent out a "Dear Healthcare Professional Communication" (DHPC). This letter is intended to minimise any potential risk for the use of SonoVue® in critically ill patients, which may particularly benefit from more accurate diagnostic information obtained after administration of SonoVue®.

The original DHCP letter is attached.

Further Information

Sonovue® is approved for use in:

- Echocardiography
  SonoVue® is a transpulmonary echocardiographic contrast agent for use in patients with suspected or established cardiovascular disease to provide opacification of cardiac chambers and enhance left ventricular endocardial border delineation.
- Doppler of macrovasculature
  SonoVue® increases the accuracy in detection or exclusion of abnormalities in cerebral arteries and extracranial carotid or peripheral arteries by improving the Doppler signal to noise ratio.
  SonoVue® increases the quality of the Doppler flow image and the duration of clinically useful signal enhancement in portal vein assessment.
- Doppler of microvasculature
  SonoVue® improves display of the vascularity of liver and breast lesions during Doppler sonography, leading to more specific lesion characterisation.

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Call for reporting

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via their national reporting system.

Company Contact Points

Suspected adverse reactions should also be reported to Bracco International BV: *braccodsu@bracco.com*
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For further inquiries concerning the information contained in this communication please contact Professional Services: *Services.ProfessionalEurope@bracco.com*