SONOVUE®
(Sulfur hexafluoride suspension for injection)

CI008B04

Package Insert for Reconstitution, Administration and Dosage

See Product Monograph for complete product information

INDICATIONS AND CLINICAL USE

SonoVue (sulfur hexafluoride) is indicated for use with ultrasound imaging to enhance the echogenicity of the blood, which results in an improved signal-to-noise ratio. SonoVue should only be used in patients where examination without contrast enhancement is inconclusive.

- **Endocardial Border Delineation:** SonoVue can be used in echocardiography in patients with suspected or established cardiovascular diseases to improve visualization of cardiac chambers and endocardial border delineation, which assists in the assessment of left ventricular wall motion.
- **Diagnostic Assessment of Vessels:** SonoVue increases the accuracy in detection or exclusion of abnormalities in cerebral and extracranial carotid and peripheral arteries by facilitating the Doppler evaluation of blood flow. SonoVue increases the quality of Doppler image and the duration of clinically useful signal enhancement in abdominal and renal arteries and in portal vein assessment.
- **Assessment of Vesicoureteral Reflux:** Sonovue is indicated for use in ultrasonography of the urinary tract in pediatric patients for the evaluation of suspected or known vesicoureteral reflux.

Geriatrics (>65 years of age): Evidence from clinical studies and experience suggests that use in the geriatric population is not associated with differences in safety or effectiveness (See WARNINGS AND PRECAUTIONS – Special Populations).

Pediatrics (<18 years of age): Safety and efficacy in pediatric patients have not been established for use in echocardiography, nor in diagnostic assessment of vessels.

The product should be administered under the supervision of a qualified health professional who is experienced in the use of the diagnostic ultrasound contrast agents and in the management of hypersensitivity reactions, including severe allergic reactions. Appropriate management of therapy and complications is only possible when adequate diagnostic and treatment facilities are readily available.

CONTRAINDICATIONS

SonoVue® is contraindicated in:

- Patients who are hypersensitive to this drug or to any ingredient in the formulation or component of the container. For a complete listing, see the DOSAGE FORMS, COMPOSITION AND PACKAGING section of the product monograph.
- Patients with known right-to-left cardiac shunts. In these patients, microbubbles can bypass filtering by the lung and directly enter the arterial circulation.
- Patients with severe pulmonary hypertension (pulmonary artery pressure >90 mmHg), uncontrolled systemic hypertension, and adult respiratory distress syndrome.

SonoVue should not be used in combination with dobutamine in patients with conditions suggesting cardiovascular instability where dobutamine is contraindicated.

DOSAGE AND ADMINISTRATION

Endocardial Border Delineation: The recommended dose of SonoVue for visualization of cardiac chambers and endocardial borders delineation is 2 mL administered as an intravenous bolus injection during echocardiography performed at rest or stress. The recommended rate of administration of the injection is 2 mL over a period of 1 second. During a single examination, a second injection of 2 mL may be administered when deemed necessary by the physician.

Diagnostic Assessment of Vessels: The recommended dose of SonoVue for diagnostic assessment of vessels is 1.2 mL administered as an intravenous bolus injection during Doppler ultrasound. The recommended rate of administration of the injection is 1.2 mL over a period of 1 second; however, for transcranial Doppler a slower injection rate of 1.2 mL over 2-3 seconds is recommended to reduce blooming artifacts. During a single examination, a second injection of 1.2 mL may be administered when deemed necessary by the physician. Each injection described above should be followed immediately by an intravenous bolus injection flush of 5 mL of sodium chloride injection (0.9%) w/v, which is intended to enhance the imaging process. As the SonoVue kit does not provide a second syringe of sodium chloride injection 0.9% for this flush, the user must have this immediately available from another source.

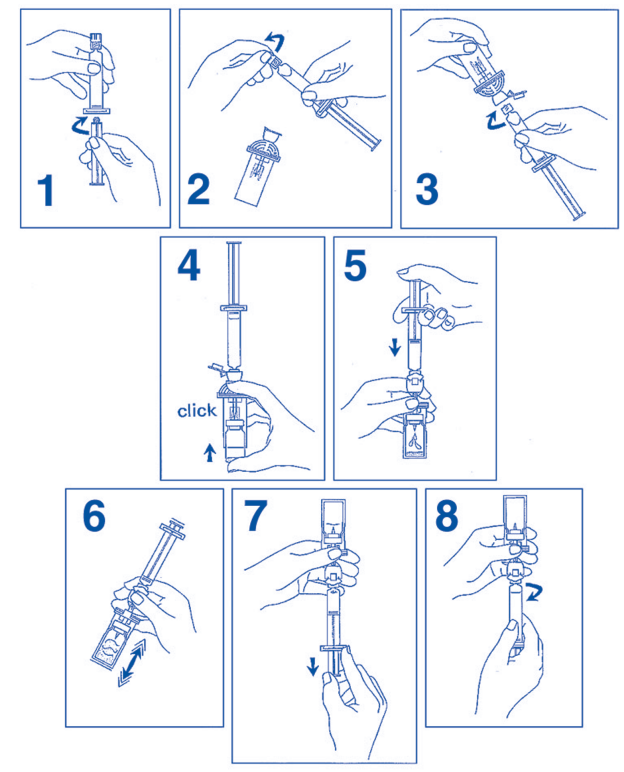
Ultrasonography of the Excretory Urinary Tract: The recommended dose of SonoVue for ultrasonography of the excretory urinary tract is 1 mL of reconstituted solution by intravesical Administration. Introduce a sterile 6F-8F urinary catheter into the bladder under sterile conditions. Empty the bladder of urine, and then fill the bladder with saline (normal sterile 0.9% sodium chloride solution) to approximately one third or half of its predicted total volume [(age in years + 2) x 30] mL. Inject the SonoVue dose and then continue filling the bladder with saline until the patient has the urge to micturate or there is the first slight sign of back pressure to the infusion. Immediately following the first voiding, the bladder may be refilled with normal saline for a second cycle of voiding and imaging, without the need of a second SonoVue administration.

Administration

Reconstitution

Prior to administration, SonoVue for Injection should be reconstituted with 5 mL of sterile sodium chloride injection (0.9%) to give a final concentration of 8 µL/mL of sulfur hexafluoride microbubbles. After adding the sodium chloride solution, the vial should be shaken vigorously for twenty seconds after which the desired volume of the product is withdrawn into a syringe for administration to the patient. As the SonoVue kit does not provide a second syringe of sodium chloride injection 0.9%, intended for the intravenous flush following injection of SonoVue, the user must have this immediately available from another source.

The method of reconstitution of the lyophilized product is as follows:



1) Connect the plunger rod by screwing it clockwise into the syringe.
2) Open Mini-Spike Plus 6/8R blister and remove syringe tip cap.
3) Open transfer system cap and connect the syringe to the transfer system by screwing it in clockwise.
4) Remove Flip cap plastic protective disk from the vial. Slide the vial into the transparent sleeve of the transfer system and press firmly to lock the vial in place.
5) Empty the contents of the syringe into the vial by pushing on the plunger rod.
6) Shake vigorously for 20 seconds to mix all the contents in the vial (white milky liquid).
7) For preparation of doses greater than or equal to 1 mL, invert the system and carefully withdraw SonoVue into the syringe. For preparation of doses less than 1 mL, withdraw 2 mL of the reconstituted suspension into the 5 mL syringe and measure the volume of SonoVue to inject by using the 0.2 mL graduations between the 1 mL and 2 mL marks.
8) Unscrew the syringe from the transfer system.

Single dose product. As with all parenteral drug products, syringes should be inspected visually for clarity, particulate matter, precipitate, discoloration and leakage prior to administration whenever solution and container permit. Solutions showing haziness, particulate matter, precipitate, discoloration or leakage should not be used. Following reconstitution of the lyophilisate and prior to injecting the product, it is mandatory to inspect the suspension to make sure that a homogeneous white milky liquid has been obtained. Discard the product if the suspension is not white, not milky, not homogeneous and/or if solid parts of the lyophilisate are seen in the suspension. Reconstituted product should be used within 6 hours. Discard unused portion.

OVERDOSAGE

No clinical signs or symptoms of overdosage with SonoVue have been reported to date. Repeated bolus doses of up to 52 mL of SonoVue (3 successive injections over 60 minutes) were administered to healthy volunteers in a safety study without any serious adverse events. For the 1776 subjects who received SonoVue 5 mg/mL, the mean cumulative dose was 7.16 mL (range: 0.2 to 70.5 mL). Eighty-five percent of subjects received cumulative doses ranging from >1 to 10 mL.

In the event of overdosage, treatment is directed toward the support of all vital functions, and prompt institution of symptomatic therapy.

STORAGE AND STABILITY

Store the kit before and after reconstitution at 15-25°C. Once reconstituted, the suspension should be used within 6 hours.

DOSAGE FORMS, COMPOSITION AND PACKAGING

SonoVue for Injection is supplied in a kit consisting of a clear glass vial containing 25 mg of lyophilized powder sealed under sulfur hexafluoride gas and capped with Flipcap closure, a Mini-Spike Plus 6/8R transfer system and a 5-mL prefilled syringe containing sterile 0.9% sodium chloride solution for reconstitution. Five kits are packaged per carton.

The headspace of the vial is filled with sulfur hexafluoride (SF6), approximately 58 mg. When reconstituted with 5 mL sodium chloride solution 0.9% (w/v), the resulting suspension contains approximately 48 µg/mL sulfur hexafluoride

Dosage form nonmedicinal ingredients:

Each vial of reconstituted lyophilized powder contains:
dipalmitoylphosphatidylglycerol (DPPG.Na) - 0.19 mg
distearoylphosphatidylcholine (DSPC) - 0.19 mg
palmitic acid - 0.04 mg
polyethylene glycol - 24.56 mg
sodium chloride (0.9% solution for reconstitution) – 5 mL

This leaflet was prepared by Bracco Imaging Canada, Montreal, Quebec, Canada H1J 2Z4.

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