

ERRATA
to the
FDA Briefing Document
Cardiovascular and Renal Drugs and
Drug Safety and Risk Management
Advisory Committee Meeting
May 2, 2011
Definity, Optison, and SonoVue

1. On page 53, Section 4.3.1.2 currently reads:

4.3.1.2 Nonfatal Serious Adverse Events

Bracco reports 30 serious adverse events in 6723 patients in all of their ongoing and completed sponsored clinical trials. Five of these were reported as being possibly caused by SonoVue. In two of these five cases, anaphylactic symptoms occurred within minutes of SonoVue administration. In another case, anaphylactic symptoms occurred within minutes of SonoVue and dipyridamole administration, making causative assessment more difficult (Table 19).

Table 1: SonoVue - Example Clinical Trial Serious Adverse Events

Causality (reported assessment)	Example Serious Adverse Events
Definite	“About 1 to 2 minutes after the intravenous injection of 2mL of SonoVue during a rest examination, the patient experienced anaphylactic shock , which consisted of heat sensation, asystole , loss of consciousness , and hypotension .”
Probable	“The patient was reported to have increased heart rate followed by extrasystole , bradycardia , and short term asystole (duration of 30 seconds).”
Probable	“The patient had a severe rash approximately 1 minute after the first administration of SonoVue...about 10 minutes after contrast medium, the patient developed a severe vagal reaction with nausea, syncope , and complete atrioventricular (AV) block ...”

Change to:

4.3.1.2 Serious Adverse Events

Bracco reports 30 serious adverse events, including deaths, in 6723 patients in all of their ongoing and completed sponsored clinical trials. Five of these were reported as being possibly caused by SonoVue. In two of these five cases, hypersensitivity symptoms occurred within minutes of SonoVue administration, anaphylaxis in one and a severe rash in the second. In another case, anaphylactic symptoms occurred within minutes of SonoVue and dipyridamole administration, making causative assessment more difficult (Table 19).

Table 2: SonoVue - Example Clinical Trial Serious Adverse Events

Causality (reported assessment)	Example Serious Adverse Events
Definite	“About 1 to 2 minutes after the intravenous injection of 2mL of SonoVue during a rest examination, the patient experienced anaphylactic shock , which consisted of heat sensation, asystole , loss of consciousness , and hypotension .”
Probable	“50 mg of dipyridamole...immediately followed by 3 mL of SonoVue [was administered]. The patient was reported to have increased heart rate followed by extrasystole , bradycardia , and short term asystole (duration of 30 seconds).”
Probable*	“The patient had a severe rash approximately 1 minute after the first administration of SonoVue... Immediately after the administration of methylprednisolone IV (and about 10 minutes after contrast medium), the patient developed a severe vagal reaction with nausea, syncope , and complete atrioventricular (AV) block ...”

* The vasovagal portion of this event was later reported as not directly related to SonoVue administration.