

Ultrasound contrast agent hypersensitivity in patients allergic to polyethylene glycol: position statement by the European Association of Cardiovascular Imaging

Roxy Senior ^{1*}, Jonathan R. Lindner², Thor Edvardsen^{3,4}, and Bernard Cosyns ⁵

¹Department of Cardiology, Royal Brompton Hospital, Imperial College London, London, UK; ²Knight Cardiovascular Institute, Oregon Health & Science University, Portland, OR, USA; ³Department of Cardiology, Oslo University Hospital, Postboks 4950 Nydalen, 0424 Oslo, Norway; ⁴Faculty of Medicine, University of Oslo, Postboks 1171, Blindern, 0318 Oslo, Norway; and ⁵Department of Cardiology, Centrum voor Hart en Vaatziekte (CHVZ), Universitair Ziekenhuis Brussel, Free University of Brussels, 101 Laarbeeklaan, 1090 Brussels, Belgium

Received 13 May 2021; editorial decision 25 May 2021; accepted 31 May 2021; online publish-ahead-of-print 24 June 2021

The Food and Drug Administration alert enhances our understanding of the mechanism of severe reactions to ultrasound-enhancing agents (UEAs). The known incidence of these reactions remains low and unchanged (1 in 10 000 administrations). Because the risk-to-benefit ratio for ultrasound contrast agents (UCAs) remains extremely low, we do not advise any changes to laboratory policy regarding indications for their use. The use of these agents should continue in situations where they have been shown to be impactful. Lipid-based UCAs (SonoVue and Luminity) are contraindicated in patients who have a history of prior hypersensitivity to these UEAs, to polyethylene glycol (PEG) (macrogol), or to PEG-containing products, such as certain bowel preps for colonoscopy or laxatives.

Keywords

ultrasound contrast agent • hypersensitivity • position statement • EACVI

This statement is in response to a recent alert by MedWatch, a product safety reporting body of the US Food and Drug Administration (FDA) regarding possible Type I immediate hypersensitivity to polyethylene glycol (PEG) present in lipid-based ultrasound contrast agents (UCAs) also known as ultrasound-enhancing agents (UEAs). These UCAs are approved by the FDA and European Medicine Agency (EMA) for clinical use. PEG is a part of lipid-based UCA as a constituent of the shell of Luminity, Lantheus Medical Imaging (known as Definity in the USA) and it is also present as an excipient (vehicle) in SonoVue, Bracco Diagnostics (known as Lumason in the USA). PEG stabilizes these lipid-based microbubbles either to facilitate the production of stable microbubbles or to allow longer persistence in the circulation.¹ PEG is not present in the protein-based UCA, Optison, and GE healthcare. PEG is an adjuvant in many topical enteral and parenteral drugs, including cardiovascular medicines, mRNA-based COVID-19 vaccines, and skin creams, cosmetics, and household products.

Although very rare, PEG allergy is known to occur.² The rarity of serious allergic reactions maybe be gauged by the very rare

occurrence of anaphylaxis after mRNA vaccine administration, which contains high concentrations of PEG, in 2–5 cases in a million. The very low event of hypersensitivity reactions with UCA in <1 in 10 000 also suggests a very low prevalence of any type of hypersensitivity, including serious allergies with PEG. Allergies with UCA are mostly ascribed to complement activation-related pseudoallergy (CARPA).³ However, PEG allergy is thought to be IgE-mediated. Both CARPA and IgE-mediated anaphylaxis are treated similarly with epinephrine, steroids, and antihistamines.⁴

UCAs are approved both by FDA and EMA for clinical use and endorsed by both European and American guidelines as Class 1 agents for the diagnosis of various cardiac conditions.^{5,6} UCA's provide crucial information that translates into improved patient outcomes based on its ability to detect or exclude life-threatening conditions and to direct physicians to administer life-saving therapies.^{4,5} In most cases, where UCA are indicated the benefits of UCA far outweigh the very low serious adverse events <1 in 10 000 administration observed with UCA. The new information on PEG allergy derived from historical data collected over

* Corresponding author. Tel: 447899990306. E-mail: roxyseini@cardiac-research.org

Published on behalf of the European Society of Cardiology. All rights reserved. © The Author(s) 2021. For permissions, please email: journals.permissions@oup.com.

