

PUBLICATION



# Dotarem<sup>®</sup>

Gadoteric acid

## Safety profile update:

the evidence of Symptoms Associated with Gadolinium Exposure (SAGE), from an analysis of EMA and FDA pharmacovigilance databases

In December 2021, members of the American College of Radiology Committee (ACR) on Drugs and Contrast Media proposed symptoms associated with gadolinium exposure (SAGE) to replace gadolinium deposition disease (GDD) and other GDD-equivalent terminologies.<sup>1</sup>

In early 2022, Shahid et al. published results of safety profiles of gadolinium based contrast media (GBCAs), regarding adverse events (AEs) representing SAGE, in FDA and EMA pharmacovigilance databases.<sup>2</sup>



*Shahid et al. (2022):*  
Use of Real-Life Safety Data From International  
Pharmacovigilance Databases to Assess the  
Importance of Symptoms Associated With  
Gadolinium Exposure (SAGE).

## OBJECTIVE

To appreciate the importance of these clinical manifestations in the overall population by assessing the weight of SAGE among the bulk of safety experiences reported to major health authorities.

## METHODS

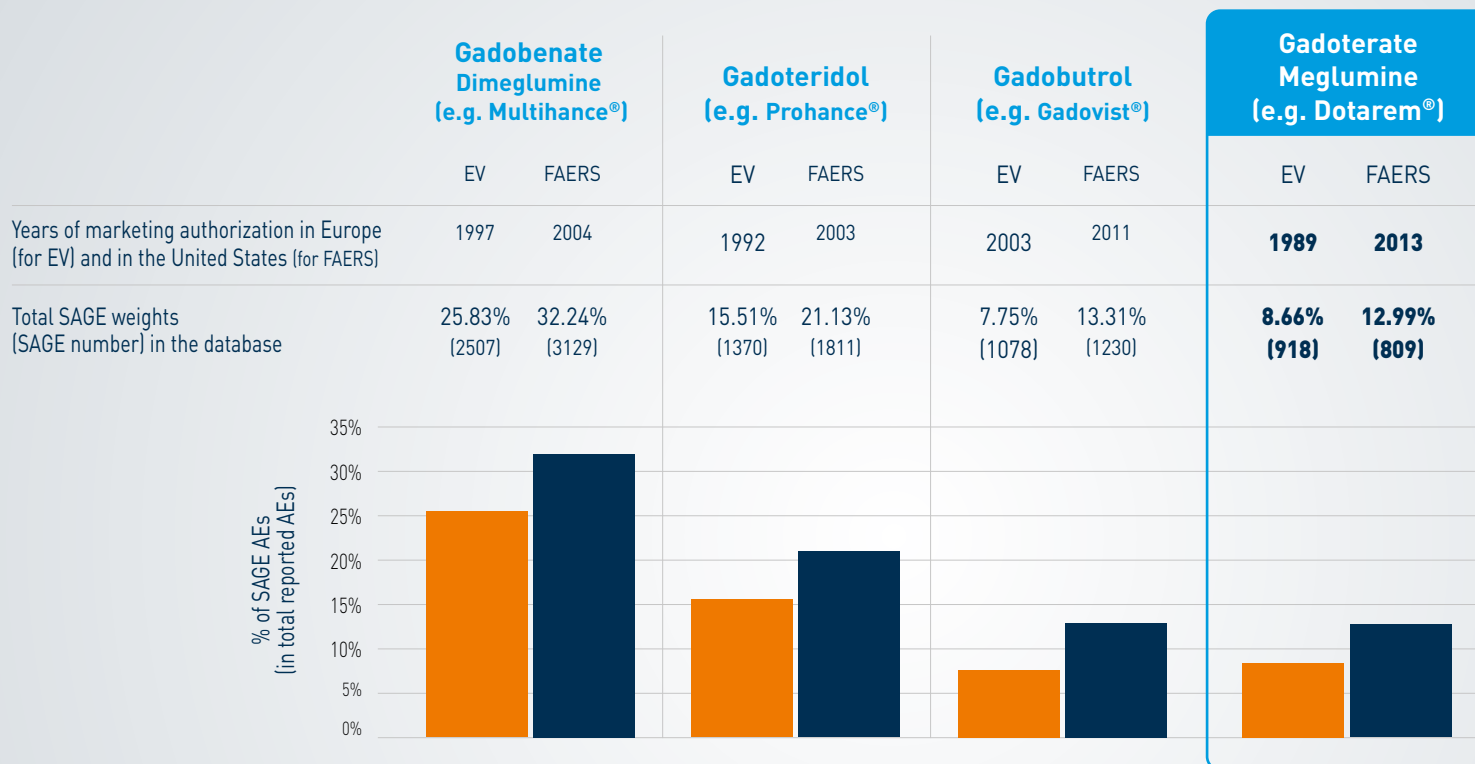
Assessed spontaneous reports of AEs in the publicly available databases:

- EMA EudraVigilance (EV) - up to Dec. 25, 2021
- FDA Adverse Event Reporting System (FAERS) - up to Sept. 30, 2021



## RESULTS AND DISCUSSIONS

**Figure 1: Total SAGE weights of different GBCAs in the databases.**



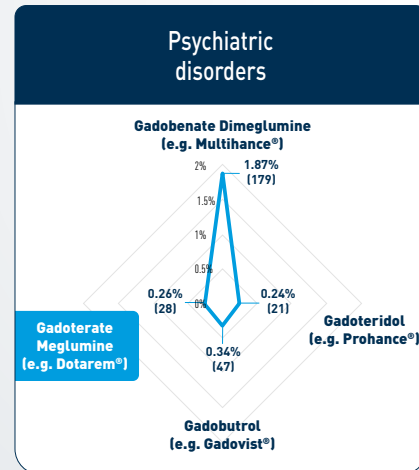
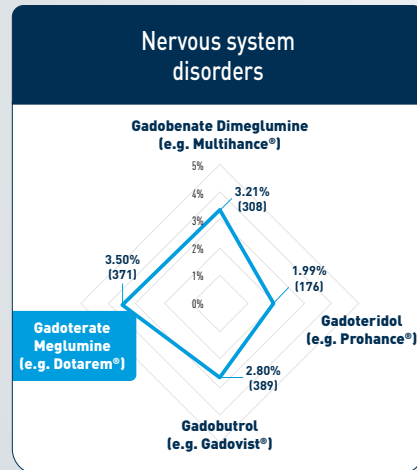
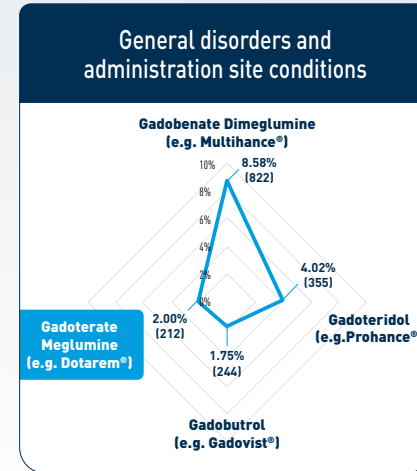
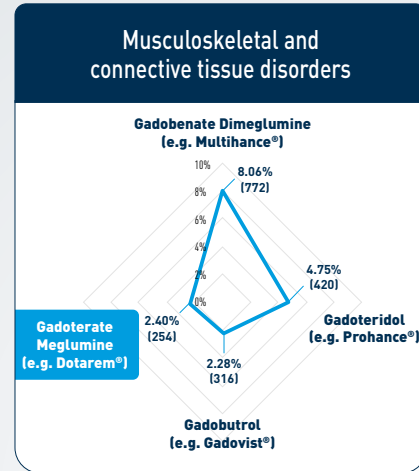
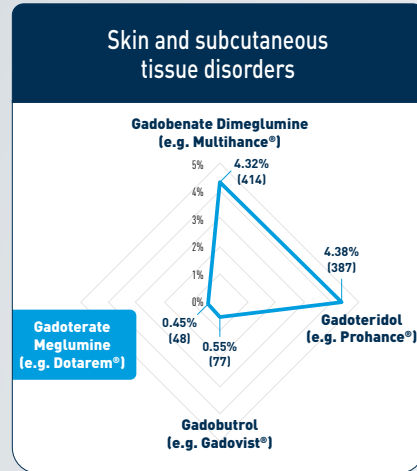
**Compared with other GBCAs, Gadoterate Meglumine (e.g. Dotarem®) demonstrated low SAGE percentages in the EMA (Eudravigilance) and the FDA real-world pharmacovigilance (FAERS) databases.**

\* **SAGE:** Symptoms Associated to Gadolinium Exposure; **EV:** Eudravigilance (EMA); **FAERS:** FDA Adverse Event Reporting System; **GBCA:** gadolinium-based contrast agent; **AE:** adverse event; **INN:** international nonproprietary name

- Gadoterate Meglumine is also known as gadoteric acid.
- INNs and corresponding brand names: Gadobenate Dimeglumine (Multihance®), Gadoteridol (Prohance®), Gadobutrol (Gadovist®), Gadoterate Meglumine (Dotarem®....).
- Data indicates brands with the same INN, including generics.

## RESULTS AND DISCUSSIONS (continued)

Figure 2: SAGE weights in different system organ classes (SOCs).



**Gadoterate Meglumine (e.g. Dotarem®) and Gadobutrol (e.g. Gadovist®) showed the lowest scores, in the most represented SOC.**

Gadobenate Dimeglumine (e.g. Multihance®) reached the highest SAGE scores in the most represented SOC, systematically. Gadoteridol (e.g. Prohance®) showed either high or intermediate positions.

The SAGE weights in the SOC “nervous system disorders” may have selection bias, as headaches, which are well-known acute physiologic reactions induced by GBCAs, were not segregated from SAGE in EV and FAERS.

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## CONCLUSION

This study showed that SAGE represents a significant percentage of the bulk of AEs reported to the health authorities for each GBCA.

This study provided real-life arguments suggesting that SAGE may be more prevalent with linear than macrocyclic GBCAs.



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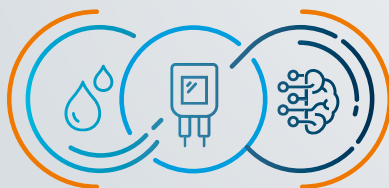
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References:

1. Robert J. McDonald, Jeffrey C. Weinreb, Matthew S. Davenport. Radiology. 2022 Feb;302(2):270-273.Symptoms Associated with Gadolinium Exposure (SAGE): A Suggested Term - PubMed (nih.gov)
2. Shahid I, Joseph A, Lancelot E. Use of Real-Life Safety Data From International Pharmacovigilance Databases to Assess the Importance of Symptoms Associated With Gadolinium Exposure. Invest Radiol. 2022 Apr 26. Dotarem® (Gadoteric Acid) is not registered in all countries. Be aware that indications posology and presentations may differ from country to country. For complete information please refer to country's local SmPC.

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