A Statement from NorthStar on Givinostat

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We have recently become aware of 3 cases of sudden death in children/young adults with DMD treated with givinostat.

The three cases have been reported by Italfarmaco to regulatory authorities, including the MHRA in the UK in line with regulatory requirements.

On the 20th October 2025, Italfarmaco, the company producing givinostat, released the following message for patient advisory groups (PAGs) with regard to the recently reported cases of death in patients with DMD treated with givinostat:

"The safety profile of givinostat is based on a double-blind, placebo-controlled, 18-month study in a total of 179 ambulant DMD patients aged 6 years or older on concomitant steroid treatment (EPIDYS Study)[1]. There were no fatalities reported during the EPIDYS trial in either the givinostat arm or the placebo arm.[2]

Globally, more than 1700 patients have been exposed to givinostat in clinical studies, during Expanded Access Programs, and in the commercial setting.[3]

As part of ongoing surveillance of the benefit to risk profile of givinostat in real world use and clinical trials, we are aware of 2 cases of sudden death in the open-label extension (OLE) study, 1 in the Netherlands (Sept 2025) and 1 in the USA (Oct 2024). We are also aware of 1 case of sudden death in the givinostat Expanded Access Programme in Germany (June 2025). The fatalities have been reported to competent authorities in accordance with local guidelines, including the MHRA.

To date, Italfarmaco has assessed that no reported deaths are related to givinostat. Therefore, based on currently available data, the benefit to risk profile of givinostat remains unchanged.

If the benefit to risk profile changes, we will alert physicians, the community, and liaise with the regulatory authorities appropriately.

We are not able to provide continuous updates unless the benefit risk profile does change. Due to patient privacy, we cannot share details in writing on these specific cases."

We, as clinicians, have only been provided with a summary of the circumstances of these cases which means that it is difficult for us to complete a full risk assessment. It is the role of the regulatory authorities (MHRA) to assess the risk benefit of any drug prescribed in the UK, through clinical trial, EAP or in routine NHS care. On the 22nd October, we have received confirmation from the MHRA that they have received the information related to the 3 cases and reassured us that they are assessing these at speed.

Based on the information available up to 22nd October 2025, there is no clear evidence that these deaths are directly related to givinostat or to one of the known side effects of givinostat. Other factors including co-morbidities and concomitant medications might have played a role in these cases. In response to these events, and while waiting for further information from the MHRA, we continue to closely monitor and evaluate any patient due to start treatment and /or

already receiving treatment to ensure an individualised assessment of risks and benefits of givinostat treatment. We will share any further information as and when it becomes available.

If you have any concerns please contact your neuromuscular team.

References

1. Duvyzat (givinostat) Summary of Product Characteristics (SmPC) Available online at: www.medicines.org.uk
2. Mercuri et al. Safety and efficacy of givinostat in Duchenne muscular dystrophy: a randomised, double-blind, placebo-controlled, multicentre, Phase 3 study. Lancet Neurology, April 2024, 23:4, P393-403
3. Data on file

22nd October 2025, *Prof Michela Guglieri, Dr Anne-Marie Childs, Dr Adnan Manzur, Prof Tracey Willis and Prof Francesco Muntoni on behalf of the NS Network*