# SFDA SAFETY SIGNAL

*"A signal is defined by the SFDA as reported information on a possible causal relationship between an adverse event and a drug, the relationship being unknown or incompletely documented previously. Usually m ore than a single report is required to generate a signal, depending upon the seriousness of the event and the quality of the information. A signal is a hypothesis together with data and arguments and it is important to note that a signal is not only uncertain but also preliminary in nature"*

**08-10-2025**

## Saudi Food and Drug Authority (SFDA) – Safety Signal of Onasemnogene abeparvovec and the Risk of Hypercalcaemia

*The Saudi Food and Drug Authority (SFDA) recommends all health care professionals to be aware of the safety signal of **Hypercalcaemia** associated with the use of **Onasemnogene abeparvovec**. The signal has been originated as a result of routine pharmacovigilance monitoring activities.*

**Introduction**

Onasemnogene abeparvovec injection is used to treat spinal muscular atrophy (SMA) with bi-allelic mutations in the survival motor neuron 1 (SMN1) gene. The treatment is an adeno-associated virus vector-based gene that works by copying the gene needed for the human SMN protein. [1] Hypercalcaemia can result when excessively calcium enters the extracellular fluid or when there is insufficient calcium excretion from the kidneys. Approximately 90% of cases of Hypercalcaemia are caused by hyperparathyroidism or malignancy. [2] The aim of this review is to evaluate the risk of Hypercalcaemia associated with the use of Onasemnogene abeparvovec and to suggest regulatory recommendations if required.

**Methodology**

Signal Detection team at SFDA performed a signal review using National Pharmacovigilance Center (NPC) database, and World Health Organization (WHO) database, VigiBase, with literature screening to retrieve all related information to assess the causality between Hypercalcaemia and Onasemnogene abeparvovec use. The search conducted on September 2025.

**Results**

**Cases Review:** Signal detection team at SFDA have searched Saudi national database and WHO database to find individual case safety reports (ICSRs) for the preferred terms (Hypercalcaemia , Blood calcium increased). The WHO database resulted in 10 global case-reports while no local cases found. The authors used signal detection tool (Vigilyze) to retrieve all global cases. [3] Authors also applied WHO-UMC causality assessment criteria on the extracted ICSRs. [4] Among them, three cases were possibly related to onasemnogene abeparvovec, six cases could not be assessed due to insufficient data, and the remaining case assessed as unlikely.

**Datamining:** The disproportionality of the observed and the expected reporting rate for drug/adverse drug reaction pair is estimated using information component (IC), a tool developed by WHO-UMC to measure the reporting ratio. Positive IC reflects higher statistical association while negative values indicates less statistical association. The IC result is (2.7) for this drug/ADRs combination which reflects positive statistical association. [4]

**Additional evidence:** Hypercalcaemia is listed in other country drug monograph as a less commonly reported clinical trial adverse reactions. [5]

**Conclusion**

The weighted cumulative evidence identified from assessed cases and disproportionality analysis are suggestive for causal association between Onasemnogene abeparvovec and Hypercalcaemia. Health care professionals and health regulators must be aware of the potential risk in drug recipients.

**Report Adverse Drug Events (ADRs) to the SFDA**

The SFDA urges both healthcare professionals and patients to continue reporting adverse drug reactions (ADRs) resulted from using any medications to the SFDA either online, by regular mail or by fax, using the following contact information:

National Pharmacovigilance Center (NPC)
Saudi Food and Drug Authority-Drug sector
4904 northern ring branch rd
Hittin District
Riyadh 13513 – 7148
Kingdom of Saudi Arabia
Toll free number: 19999
Email: NPC.Drug@sfda.gov.sa

**References:**


1- Mayoclinic- Onasemnogene abeparvovec-xioi (intravenous route) - Side effects & uses - Mayo Clinic: https://www.mayoclinic.org/drugs-supplements/onasemnogene-abeparvovec-xioi-intravenous-route/description/drg-20465053

2- Agraharkar, M., Dellinger, O., Gangakhedkar, A., & Batuman, V. (2023, April 26). *Hypercalcemia: Practice Essentials, pathophysiology, etiology*. Medscape. https://emedicine.medscape.com/article/240681-overview

3- Vigilyze.who-umc.org. 2025. [online] Available at: https://vigilyze.who-umc.org/

4- World Health Organization WHO (2013). WHO-UMC system for standardised case causality assessment. Available at https://www.who.int/publications/m/item/WHO-causality-assessment

5- ZOLGENSMA® (Onasemnogene abeparvovec Product Monograph) (MArch-2025). Available At: https://pdf.hres.ca/dpd_pm/00078817.PDF