Hydroxycarbamide may falsely elevate sensor glucose results from continuous glucose monitoring (CGM) systems

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Information on hydroxycarbamide and continuous glucose monitoring (CGM) systems

- Hydroxycarbamide (sometimes known as hydroxyurea) is an antineoplastic agent and immunomodulatory agent (ATC code: L01XX05) indicated for the treatment of patients with myeloproliferative conditions and sickle cell disease.
- The specific mechanism of action of hydroxycarbamide is not entirely known, however it is believed that the drug causes an immediate inhibition of the DNA synthesis by acting as a ribonucleotide reductase inhibitor, without interfering with the synthesis of the RNA or the protein. Another mechanism, by which hydroxycarbamide acts, is the elevation of foetal haemoglobin (HbF) concentration in sickle cell patients. HbF interferes with the polymerization of sickle haemoglobin (HbS) and thus impedes the sickling of red blood cells.
- Continuous glucose measurement (CGM)-devices are wearable sensors measuring glucose in the interstitial fluid based on selective oxidation at the sensor-electrode. These devices are used by diabetic patients to manage their diabetes.

Hydroxycarbamide is authorised in Malta as follows:

Active Ingredients	Product Name	Pharmaceutical Form	Classif-cation	Authorisation Number	MAH/license holder
Hydroxycarbamide	Hydroxycarbamide Medac	Hard capsules	POM	AA565/51501	Central Procurement and Supplies Unit

Information from the EMA about the safety concern

- This safety concern was identified during the review of the 8th periodic safety update single assessment (PSUSA) for hydroxycarbamide which began on 14 March 2024 and concluded on 11 July 2024.
- The Pharmacovigilance Risk Assessment Committee (PRAC) considered a causal relationship between hydroxycarbamide and falsely high CGM sensor glucose readings leading to hypoglycaemia is at least a reasonable possibility, when considering the available data on interference of hydroxycarbamide with CGM systems, from the literature, including in some cases a close temporal relationship, and in view of a plausible mechanism of action.
- The key message is that the interference of hydroxycarbamide with certain CGM systems may result in falsely elevated glucose readings which can lead to hypoglycaemia if sensor glucose results are relied upon to dose insulin.

- The signal of 'Drug-device interaction' potentially leading to hypoglycaemia by falsely elevated glucose levels measured by continuous glucose measurement (CGM)-devices caused by hydroxycarbamide was identified from literature provided by the US FDA on 18 Apr 2023.
- During the EU procedure three publications, of which two case reports and one study, presented evidence for this signal.
- Two publications were case reports, one in 69-year-old women and other in 62-year old man both with type 1 diabetes mellitus taking hydroxycarbamide for essential thrombocytopenia and polycythemia vera, respectively. Both patients had high glucose readings on their CGM-devices following hydroxycarbamide administration.
- The third publication was a study about inaccurate glucose sensor readings after hydroxycarbamide intake in hospitalised patients after total pancreatectomy with islet auto transplantation. Dexcom CGM-device data was matched with Point of Care (POC) glucose measurements for 28 patients, aged 15-25 of which 57% experienced impaired data.
- The mechanism by which hydroxycarbamide interferes with these CGM devices is not proven, but possibly it is directly oxidised at the electrode falsely elevating the test results.

The PRAC concluded that the product information of products containing hydroxycarbamide should be amended accordingly to reflect information on interference with sensor glucose results in section 4.4 of the SmPC and section 2 of patient information leaflet.

More about the procedure

This safety issue was described in the context of periodic safety update report single assessment (PSUSA) for hydroxycarbamide. The PRAC recommendation has been forwarded to the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh).

On 25 July 2024, the CMDh has endorsed the PRAC's position and the product information of hydroxycarbamide containing products will be amended accordingly through a submission of a variation by the Marketing Authorisation Holder concerned.

Information for Healthcare Professionals

- Hydroxycarbamide may falsely elevate sensor glucose results from certain continuous glucose monitoring (CGM) systems which may lead to hypoglycaemia if sensor glucose results are relied upon to dose insulin.
- If CGM systems are to be used concurrently with hydroxycarbamide treatment, the CGM prescriber should be consulted with about the need to consider alternative glucose monitoring methods.

Information to patients

- If you have diabetes and are using a continuous glucose monitor (CGM) to test your blood glucose, you need to be aware that hydroxycarbamide (also known as hydroxyurea) may

cause falsely high sensor glucose readings from certain sensors. This could result in using more insulin than needed, leading to low blood sugar (hypoglycaemia).

- Talk to the physician that prescribed your CGM about whether it is safe to use while you are taking hydroxycarbamide.

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance with hydroxycarbamide containing medicines. Suspected Adverse Drug Reactions (side effects) may be reported using the Medicines Authority Form and sending it to: Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000 **or** online to http://www.medicinesauthority.gov.mt/adrportal or to the marketing authorisation holder or their local representatives.

Post-Licensing Directorate

Medicines Authority

Healthcare professionals and patients are encouraged to regularly check the Medicines Authority website for product safety updates as these are issued on an ongoing basis.

Feedback Form

The Malta Medicines Authority thanks you for the time taken to read this safety circular. The dissemination of safety circulars is an important process whereby Regulatory Authorities can communicate important issues with respect to the safety of medicines, in order to protect and enhance public health.

The Malta Medicines Authority kindly invites your anonymous feedback about the regulatory action being communicated. This may be returned by folding this form (address side up), stapling the ends and then posting (no stamp required).

Feedback:

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