

From the Chief Medical Officer
Professor Sir Michael McBride



HSS(MD) 35/2023

FOR ACTION

Chief Executives, Public Health Agency/HSC Trusts/NIAS
Deputy Secretary SPPG
GP Medical Advisers, SPPG
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OOHs Medical Managers (for onward distribution to staff)

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PLEASE SEE ATTACHED FULL CIRCULATION LIST

Dear Colleague

**MHRA DRUG SAFETY UPDATE AND NATIONAL PATIENT SAFETY ALERT-
CALCIUM CHLORIDE, CALCIUM GLUCONATE: POTENTIAL RISK OF
UNDERDOSING WITH CALCIUM GLUCONATE IN SEVERE HYPERKALAEMIA**

Calcium salts (either calcium chloride or calcium gluconate) are used to stabilise the myocardium and prevent cardiac arrest in patients experiencing severe hyperkalaemia. However, the two salts are not equivalent in terms of calcium dose. Ensure the correct dose is administered to avoid underdosing of calcium. If treated sub-optimally, hyperkalaemia can be fatal.

Advice for healthcare professionals:

- calcium salts (either calcium chloride or calcium gluconate) are used to stabilise the myocardium and prevent cardiac arrest – **these two products are not dose-equivalent**
- be alert to the risk of inadvertent underdosing if calcium gluconate is used instead of calcium chloride and verify the calcium salt details before administration: 30ml of calcium gluconate 10% provides 6.8mmol of calcium (equivalent to 10ml of calcium chloride 10%)
- administration must be by slow intravenous injection of the whole dose over 10 minutes (see advice on dosing below)
- repeat doses may be required as the effect of calcium is temporary, lasting 30 to 60 minutes
- The Medicines and Healthcare products Regulatory Agency (MHRA) have issued a [National Patient Safety Alert](#) to ask providers to review local guidance, including electronic mobile applications, quick reference guides and supporting materials for clinicians *report suspected adverse reactions associated with calcium gluconate on a [Yellow Card](#)
- report medication errors or near misses via local risk management systems and medication errors resulting in patient harm on a [Yellow Card](#)

Calcium salts and treatment of severe hyperkalaemia

Treatment of severe hyperkalaemia (plasma concentration ≥ 6.5 mmol/l) is a medical emergency and treatment must not be delayed. Calcium gluconate is used to stabilise the myocardium and prevent arrhythmias and cardiac arrest.

Calcium salts have previously been used off-label for the treatment of myocardial excitability in severe hyperkalaemia, but the MHRA recently authorised the use of calcium gluconate in acute severe hyperkalaemia and in cardiac resuscitation due to severe hyperkalaemia. Calcium gluconate therapy should be started only in cases of documented severe hyperkalaemia. It should not be routinely administered during cardiac arrest.

Updated [Clinical Practice Guidelines in the Treatment of Acute Hyperkalaemia in Adults](#) were published in 2020.¹ Calcium salts do not reduce the serum potassium but are given to protect the heart. The guideline recommends use of either calcium chloride or calcium gluconate. However, the salts are not equivalent in terms of calcium dose. To achieve the recommended calcium dose of 6.8 mmol, 30ml of calcium gluconate 10% or 10ml calcium chloride 10% must be used. Both calcium gluconate and calcium chloride preparations are available in 10ml vials at 10% (w/v) concentration, therefore 3 vials of calcium gluconate are required to reach the appropriate dose but only 1 vial of calcium chloride. The method of administration should be by slow intravenous injection, which may need to be repeated.

ECG changes may provide evidence of potassium toxicity but are not always present initially. ECG monitoring is advised for potassium levels above 6.0 mmol/L. Calcium gluconate should show an effect on ECG abnormalities within 3 minutes of administration and its action is expected to last for 30 to 60 minutes. A 30ml bolus dose of calcium gluconate 10% should be given by intravenous injection over 10 minutes. The effect of calcium salts is temporary so consider a repeat dose if ECG abnormalities remain within 5 to 10 minutes after the initial dose is complete.

Calcium salts do not lower potassium levels. The risk of arrhythmias and cardiac arrest increases in proportion to severity of hyperkalaemia. Measures to lower potassium levels and to address underlying causes of hyperkalaemia must be taken immediately.

Review of underdosing of calcium gluconate

The MHRA has reviewed available UK data related to inappropriate use of calcium gluconate and identified isolated cases where medication errors have occurred, including one death, where 10ml of calcium gluconate was used during cardiopulmonary resuscitation (Yellow Card [literature report](#)²). Reports from the National Reporting Learning System received since the guideline was updated³ indicate that 6 incidents showed incorrect calcium gluconate administration and monitoring in the

¹ Alfonzo and others. [Clinical practice guidelines. Treatment of acute hyperkalaemia in adults, June 2020. The Renal Association](#), pages 73-76 (viewed on 01 November 2022)

² Vallis-Booth E, Moore S. [Fatal overdose of Taxus baccata plant matter treated in a rural district general hospital](#). BMJ Case Rep 2022;15: e243896.

³ Data from 01 August 2020 to 31 August 2022

context of severe hyperkalaemia and cardiac arrest (5 fatal, 1 unknown outcome). The safety concerns in these incidents related to calcium gluconate underdosing; lack of repeat dosing where indicated; lack of potassium-lowering treatment and lack of or inappropriate ECG monitoring.

Following a review by the MHRA and advice from the [Commission on Human Medicines](#), the product information for these medicines will be updated to more clearly define the safe and effective administration of calcium gluconate for severe hyperkalaemia and to warn of the potential for underdosing.

The MHRA recently authorised use of calcium gluconate for the treatment of myocardial excitability in severe hyperkalaemia, which was previously off-label. Healthcare professionals are reminded that calcium gluconate is not usually recommended for the treatment of cardiac arrest except for where there is concomitant severe hyperkalaemia.⁴ Bolus injection is recommended in these circumstances.

The MHRA have also issued a [National Patient Safety Alert](#) following consultation with NHS England and bodies in Scotland, Wales, and Northern Ireland, as well as the UK Kidney Association.

Report suspected reactions on a Yellow Card

Please continue to report suspected adverse drug reactions to the [Yellow Card scheme](#). Healthcare professionals, patients, and caregivers are asked to submit reports using the Yellow Card scheme electronically using:

- the [Yellow Card website](#)
- the Yellow Card app; download from the [Apple App Store](#) or [Google Play Store](#)
- some clinical IT systems for healthcare professionals (EMIS, SystemOne, Vision, MiDatabank, and Ulysses)
-

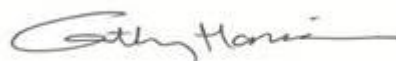
When reporting please provide as much information as possible, including information about batch numbers, medical history, any concomitant medication, onset timing, treatment dates, and product brand name.

The complete MHRA Drug Safety update is available at the following link [MHRA Drug Safety Update-Calcium chloride, calcium gluconate: potential risk of underdosing with calcium gluconate in severe hyperkalaemia](#).

Yours sincerely



Prof Sir Michael McBride
Chief Medical Officer



Professor Cathy Harrison
Chief Pharmaceutical Officer

⁴ Deakin C and others. [Resuscitation Council UK. 2021 Resuscitation Guidelines. Special Circumstances Guidelines. Treatment of hyperkalaemia](#) (viewed on 01 November 2022).

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This letter is available on the Department of Health website at <https://www.health-ni.gov.uk/topics/professional-medical-and-environmental-health-advice/hssmd-letters-and-urgent-communications>