

South African National Essential Medicine List
Adult Hospital Medication Review Process
Component: Poisonings

MEDICINE REVIEW:

1. Executive Summary

Date: October 2018
Medicine (INN): Glucagon
Medicine (ATC): H04AA01
Indication (ICD10 code): Beta-blocker and calcium channel blocker overdose [R00.1/I95.9 + (T46.1/X44.99/X64.99/Y14.99)]
Patient population: Adults
Prevalence of condition: Unclear
Level of Care: Hospital /secondary level
Prescriber Level: Medical officer
Current standard of Care: n/a
Efficacy estimates: (preferably NNT) n/a
Motivator/reviewer name(s): Dr H Dawood
PTC affiliation: Greys hospitals PTC

2. Name of author(s)/motivator(s): Dr H Dawood

3. Author affiliation and conflict of interest details

Affiliation: Greys hospital and Caprisa, UKZN; Chair of the Adult Hospital Level Committee (2017-2020)

Conflict of interests: Pfizer- SA Pneumococcal summit attendance; MSD: SAASP - Attendance of meetings; MSD: ECMID - Conference attendance; ACTA study- DSMB member; Adcock Ingram & Novartis - Speaker fees; IDSSA – President elect; HpCA – Ethics Committee member.

4. Introduction/ Background

Glucagon is used as part of the standard treatment in the management of beta-blocker and calcium channel blocker overdoseⁱ. However, a review of the evidence is required to evaluate the evidence for glucagon in beta-blocker and calcium channel blocker overdoses

5. Purpose/Objective i.e. PICO:

-P: adults

-I: glucagon

-C: none

-O: treatment of beta-blocker and calcium channel blocker overdose.

6. Methods:

a. **Data sources:** Cochrane Database of Systematic Reviews, MedLine, PubMed searches.

b. **Search strategy:** Studies evaluating glucagon as part of the standard treatment in the management of beta-blocker and calcium channel blocker overdose were identified.

c. **Evidence synthesis and quality:**

Beta blocker overdose: There were no studies in humans but animal studies were found. Glucagon appeared to have no effect on survival rate in animals.

The evidence supporting the use of glucagon in the management of patients with beta-blocker overdoses is limited to animal studies.

Calcium channel blocker overdose: There are animal studies and three case reports describing the use of glucagon in the management of calcium channel blocker overdose. In the case reports, glucagon appears to be safe and effective in the management of hemodynamic instability associated with calcium channel blocker poisonings.

The evidence supporting the use of glucagon in the management of patients with beta-blocker overdoses and calcium channel blocker overdose is limited to animal studies and case reports respectively (See Appendix I ^{ii, iii, iv, v, vi}).

More research is needed to determine the appropriate role for glucagon in treating patients with beta blocker and calcium channel blocker poisoning.

7. Alternative agents: n/a

EVIDENCE TO DECISION FRAMEWORK

	JUDGEMENT	SUPPORTING EVIDENCE & ADDITIONAL CONSIDERATIONS
QUALITY OF EVIDENCE	<p>What is the overall confidence in the evidence of effectiveness?</p> <p>Confident Not confident Uncertain</p> <p><input type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/></p>	Lack of randomised controlled trials, available evidence includes animal data and case reports.
BENEFITS & HARMS	<p>Do the desirable effects outweigh the undesirable effects?</p> <p>Benefits outweigh harms Harms outweigh benefits Benefits = harms or Uncertain</p> <p><input type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/></p>	
THERAPEUTIC INTERCHANGE	<p>Therapeutic alternatives available:</p> <p>Yes No</p> <p><input type="checkbox"/> <input checked="" type="checkbox"/></p> <p>List the members of the group: n/a</p> <p>List specific exclusion from the group: n/a</p>	<p>Rationale for therapeutic alternatives included: n/a</p> <p>References: n/a</p> <p>Rationale for exclusion from the group: n/a</p> <p>References: n/a</p>
VALUES & PREFERENCES / ACCEPTABILITY	<p>Is there important uncertainty or variability about how much people value the options?</p> <p>Minor Major Uncertain</p> <p><input type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/></p> <p>Is the option acceptable to key stakeholders?</p> <p>Yes No Uncertain</p> <p><input type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/></p>	

RESOURCE USE	How large are the resource requirements?	More intensive <input type="checkbox"/> Less intensive <input type="checkbox"/> Uncertain <input checked="" type="checkbox"/>	Cost of medicines <table border="1"> <thead> <tr> <th>Medicine</th> <th>Cost (ZAR)</th> </tr> </thead> <tbody> <tr> <td>Glucagon 1 mg/ml, injection</td> <td>301.79</td> </tr> </tbody> </table>		Medicine	Cost (ZAR)	Glucagon 1 mg/ml, injection	301.79
	Medicine	Cost (ZAR)						
Glucagon 1 mg/ml, injection	301.79							
		* Contract circular RT297-2019 Additional resources: n/a						
EQUITY	Would there be an impact on health inequity?	Yes <input type="checkbox"/> No <input type="checkbox"/> Uncertain <input checked="" type="checkbox"/>						
FEASIBILITY	Is the implementation of this recommendation feasible?	Yes <input type="checkbox"/> No <input type="checkbox"/> Uncertain <input checked="" type="checkbox"/>						

Type of recommendation	We recommend against the option <input checked="" type="checkbox"/>	We suggest not to use the option or to use the alternative <input type="checkbox"/>	We suggest using either the option or the alternative <input type="checkbox"/>	We suggest using the option <input type="checkbox"/>	We recommend the option <input type="checkbox"/>
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Recommendation: Based on this review, the Adult Hospital Level Committee does not recommend glucagon for the treatment of beta-blocker or calcium channel blocker overdose.

Rationale: The evidence is insufficient (available data includes animal data and case series) for the Adult Hospital Level Committee to make a recommendation for the use of protamine for the treatment of beta-blocker or calcium channel blocker overdose.

Level of Evidence: III Expert opinion

Review indicator:

Evidence of efficacy	Evidence of harm	Price reduction
<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>

VEN status:

Vital	Essential	Necessary
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

NEMLC MEETING OF 6 DECEMBER 2018:

NEMLC ratified the medicine review for glucagon and accepted the recommendations proposed by the Adult Hospital Level Committee.

Monitoring and evaluation considerations: adverse events, use: n/a

Research priorities: n/a

References:

NDoH_EDP_Glucagon_Poisonings_19Oct2018_v3.0

ⁱ Resuscitation Council of South Africa. Bradycardia management algorithm. Available at:

<http://www.resus.co.za/index.php/bradycardia-management>

ⁱⁱ Bailey B. Glucagon in beta-blocker and calcium channel blocker overdoses: a systematic review. *J Toxicol Clin Toxicol.* 2003;41(5):595-602.

ⁱⁱⁱ Boyd R, Ghosh A. Towards evidence based emergency medicine: best BETs from the Manchester Royal Infirmary. Glucagon for the treatment of symptomatic beta blocker overdose. *Emerg Med J.* 2003 May;20(3):266-7.

^{iv} Doyon S, Roberts JR. The use of glucagon in a case of calcium channel blocker overdose. *Ann Emerg Med.* 1993 Jul;22(7):1229-33.

^v Walter FG, Frye G, Mullen JT, Ekins BR, Khasigian PA. Amelioration of nifedipine poisoning associated with glucagon therapy. *Ann Emerg Med.* 1993 Jul;22(7):1234-7.

^{vi} Mahr NC, Valdes A, Lamas G. Use of glucagon for acute intravenous diltiazem toxicity. *Am J Cardiol.* 1997 Jun 1;79(11):1570-1.