National Essential Medicine List
Primary Healthcare Medication Review Process
Component: Palliative care

MEDICINE MOTIVATION:

1. Executive Summary

Date: 29 July 2017
Medicine (INN): Betamethasone/ dexamethasone
Medicine (ATC): H02AB01/H02AB02
Indication (ICD10 code): Anorexia, where there is a profound impact on quality of life, and when treating the underlying cause is not possible or effective. (Z51.5)
Patient population: Adult palliative care patients
Prevalence of condition: unknown
Level of Care: Primary health care or hospital level
Prescriber Level: Trained palliative care doctor /palliative care teams
Current standard of Care: Nil on EML – new STG
Efficacy estimates: (preferably NNT) n/a
Motivator/reviewer name(s): Motivator: Dr S.R. Krause. Reviewer: Renee de Waal
PTC affiliation: n/a

2. Name of author(s)/motivator(s)

Renee de Waal

3. Author affiliation and conflict of interest details

University of Cape Town
No conflicts of interest

4. Introduction/ Background

Anorexia (the loss of appetite for food) is part of the disease process in many life limiting conditions. Despite limited evidence, corticosteroids (dexamethasone in particular) are sometimes used in palliative care patients to treat anorexia, only if it has a significant impact on quality of life. The EML PHC ERC received a motivation for betamethasone for this indication from the Palliative Care TWG. The rationale for betamethasone rather than dexamethasone is that oral dexamethasone is available only through section 21 motivation. In contrast, betamethasone, which is considered equivalent to dexamethasone for this indication by palliative care clinicians, is easier to access.

5. Purpose/Objective i.e. PICO question [comparison to current standard of care for a specific indication]:

-P *(patient/population):* Adult palliative care patients
-I *(intervention):* Betamethasone (or dexamethasone)
-C *(comparator):* Placebo, no treatment
-O *(outcome):* 1. Efficacy (improvement in appetite) 2. Adverse effects

(P) Amongst adult palliative care patients with anorexia, in whom treatment of the underlying cause is not effective or possible, is **(I)** betamethasone compared to **(C)** placebo/no treatment **(O)** effective in terms of improvement in appetite, with minimal/acceptable side effects?

6. Methods:

a. Data sources

Pubmed - searches conducted on 29 July 2017

b. Search strategy

Study inclusion criteria:
Type of studies: RCTs and systematic reviews

Search terms:
("palliative care"[MeSH Terms] OR ("palliative"[All Fields] AND "care"[All Fields]) OR "palliative care"[All Fields]) AND ("anorexia"[MeSH Terms] OR "anorexia"[All Fields]) AND ("adrenal cortex hormones"[Pharmacological Action] OR "adrenal cortex hormones"[MeSH Terms] OR ("adrenal"[All Fields] AND "cortex"[All Fields] AND "hormones"[All Fields]) OR "adrenal cortex hormones"[All Fields] OR "corticosteroids"[All Fields])

Search retrieved 40 articles.

Substituting the term 'betamethasone' for 'corticosteroids' retrieved 2 articles – neither relevant to this review. Substituting the term 'dexamethasone' for 'corticosteroids' retrieved 11 articles – all were already found in the first search. Substituting the terms 'life threatening illness' or 'life limiting illness' for 'palliative care' retrieved 2 and 3 articles respectively: only 1 (narrative review) was not found in the first search.

The search found:

- 1 systematic review (that included 6 RCTs);
- 3 uncontrolled prospective or retrospective cohort studies; and
- 3 narrative reviews.

The systematic review described 6 randomised controlled trials, with various outcome measures. None involved betamethasone; 3 involved dexamethasone - 2 of those compared with placebo. Improvement in appetite was not the primary outcome of either trial.

c. Evidence synthesis

Author, date	*Type of study*	*n*	*Population*	*Intervention*	*Comparators*	*Primary outcome*	*Effect sizes*	*Comments*
Miller et al, 2014	Systematic review, no meta-analysis							Relevant included studies described below.
Moertel et al, 1974	Randomised controlled trial	116	Patients with unresectable adenocarcinoma, who were unsuitable for chemotherapy	Dexamethasone 0.75 mg 4 times daily; dexamethasone 1.5 mg 4 times daily	Placebo	Survival; symptoms: proportions of patients who reported that appetite improved	Two weeks from baseline: 57% of dexamethasone patients, and 44% of placebo patients reported improved appetite (not statistically significant); 4 weeks from baseline: 55% and 26% reported improvements respectively ($p<0.05$).	Authors didn't state why the dexamethasone groups were combined in the results section. Adverse effects (oedema) similar between groups.
Bruera et al, 2004	Randomised controlled trial	51	Patients with advanced cancer, and chronic nausea despite metoclopramide treatment	Dexamethasone 10 mg twice daily. (Plus both groups received metoclopramide 10 mg 4 hourly.)	Placebo	Quality of life and overall well-being after 7 days' treatment. Appetite (and several other symptoms) assessed as a score out of 10.	Mead (SD) appetite intensity improved from 6.5 (3.3) to 3.1 (3.7) in the dexamethasone group ($p<0.001$), and from 7.4 (3.1) to 4.1 (3.1) in the placebo group ($p<0.001$). Between group difference not significant.	Side effects similar between groups.

d. Evidence quality:

Very limited evidence – use seems to be guided largely by expert opinion.

No clear evidence regarding dose or duration of treatment, or to list specific indications/contraindications.

7. Alternative agents: none considered in this review.

EVIDENCE TO DECISION FRAMEWORK

<table>
<tr><th></th><th>JUDGEMENT</th><th>SUPPORTING EVIDENCE & ADDITIONAL CONSIDERATIONS</th></tr>
<tr><td>QUALITY OF EVIDENCE</td><td>What is the overall confidence in the evidence of effectiveness?

Confident ☐ Not confident [X] Uncertain ☐</td><td></td></tr>
<tr><td>BENEFITS & HARMS</td><td>Do the desirable effects outweigh the undesirable effects?
Benefits outweigh harms ☐ Harms outweigh benefits ☐ Benefits = harms or Uncertain [X]</td><td></td></tr>
<tr><td>THERAPEUTIC INTERCHANGE</td><td>Therapeutic alternatives available:
Yes ☐ No [X]

List the members of the group.

List specific exclusion from the group:</td><td>Rationale for therapeutic alternatives included:

References:

Rationale for exclusion from the group:

References:</td></tr>
<tr><td>VALUES & PREFERENCES /</td><td>Is there important uncertainty or variability about how much people value the options?
Minor ☐ Major ☐ Uncertain [X]

Is the option acceptable to key stakeholders?
Yes ☐ No ☐ Uncertain [X]</td><td></td></tr>
<tr><td>RESOURCE USE</td><td>How large are the resource requirements?

More intensive ☐ Less intensive ☐ Uncertain [X]</td><td>Cost of medicines/ month:
<table><tr><th>Medicine</th><th>Cost (ZAR)</th></tr><tr><td></td><td></td></tr><tr><td></td><td></td></tr></table>Additional resources:</td></tr>
</table>

EQUITY	**Would there be an impact on health inequity?** Yes ☐ No ☐ Uncertain ☒ X	
FEASIBILITY	**Is the implementation of this recommendation feasible?** Yes ☐ No ☒ X Uncertain ☐	Not feasible for general PHC use. Requires palliative care training.

Type of recommendation	We recommend against the option and for the alternative ☐	We suggest not to use the option or to use the alternative ☐	We suggest using either the option or the alternative ☐	We suggest using the option ☐	We recommend the option ☐

Recommendation:

Betamethasone is not considered appropriate for prescription at Primary Health Care level at this stage. It could be considered at hospital level, or for prescription by specially trained district palliative care teams (with access at certain PHC facilities via down-referral mechanisms if necesssary).

Rationale: Evidence of efficacy is limited and inconsistent. Although recommended in guidelines based on expert opinion, prescribing betamethasone for anorexia requires palliative care training, so it is not considered appropriate at a PHC setting at this stage.

Level of Evidence: III Expert opinion

Review indicator:

Evidence of efficacy	Evidence of harm	Price reduction
X	☐	☐

VEN status:

Vital	Essential	Necessary
☐	☐	☐

Monitoring and evaluation considerations

Research priorities

References:

1. Miller S, McNutt L, McCann MA, McCorry N. Use of corticosteroids for anorexia in palliative medicine: a systematic review. J Palliat Med. 2014;17(4):482-5.
2. Moertel CG, Schutt AJ, Reitemeier RJ, Hahn RG. Corticosteroid therapy of preterminal gastrointestinal cancer. Cancer. 1974;33(6):1607-9.
3. Bruera E, Moyano JR, Sala R, Rico MA, Bosnjak S, Bertolino M, et al. Dexamethasone in addition to metoclopramide for chronic nausea in patients with advanced cancer: a randomized controlled trial. Journal of pain and symptom management. 2004;28(4):381-8.