STEROIDS: USE OF IN PALLIATIVE CARE PATIENTS GUIDELINE ON MANAGEMENT

1. GUIDELINE STATEMENT:

This guideline is intended to promote the safe prescribing of corticosteroids (subsequently referred to as 'steroids') in patients with cancer. Steroids are one of the most common groups of drugs prescribed for patients seen by Specialist Palliative Care (SPC) teams[1] but have the potential for causing harm due to side effects.

2. RELATED INTERNAL HOSPICE POLICIES/PROCEDURES/DOCUMENTS:

- Medicines Management Standard Operating Procedures
- Medicines Management Policy and Guideline
- Malignant spinal cord compression (MSCC): guideline for the management of patients under the care of St Peter's hospice
- Variable dose chart for TTA
- Adrenal Insufficiency And Risk Of Adrenal Crisis Policy
- Diabetes Mellitus Management at the End of Life

3. SCOPE OF GUIDELINE:

This guideline relates to all patients under the care of the hospice (IPU, Day Hospice & Community) in whom steroids are considered. Medical staff and CNSs are expected to be aware of and adhere to this guideline.

4. KEY POINTS:

4.1 General principles

The following principles are embedded into the Corticosteroid template on EMIS, which should be completed when patients are started on steroids by SPH clinicians.

- There should be a clear clinical indication for the steroid, recorded in the notes and on the drug chart, and the starting dose should follow local clinical guidelines for that indication.

- A discussion should take place between the SPC team member recommending or prescribing steroids and the patient about their potential side effects. This should be recorded in the patient's notes.

- Risk of adrenal insufficiency should be considered when steroids are initiated and a Steroid Emergency Care issued when appropriate (see Adrenal Insufficiency and Risk of Adrenal Crisis Policy).

- **The clinical response to the steroid should be assessed approximately 5-7 days after commencement.** A plan for continuation, including weaning to the lowest dose necessary to achieve the desired effect, or stopping should then be agreed with the patient and documented.

- Patients taking ≥6mg of dexamethasone (or equivalent dose of prednisolone or hydrocortisone) should have a CBG check regularly (e.g. weekly)[2]. For more guidance on frequency of blood glucose monitoring. please refer to Appendices 2-3.

- Patients at risk of adrenal crisis (see Adrenal Insufficiency And Risk Of Adrenal Crisis Policy) should have the dose temporarily increased during significant intercurrent infection, trauma or surgery as they are at risk of adrenal crisis[3,4].

- It is recommended that steroids are taken before 14.00 in order to reduce the chance of steroids contributing to insomnia[5].

- Consider whether prophylaxis against osteoporosis (e.g. by calcium, vit D and oral bisphosphonates) is needed in patients on long-term steroids (>3 months) and/or a bone densitometry scan to assess risk[5].

- Doses may need to be increased if patients are also taking enzyme-inducers, e.g. phenytoin. In addition, phenytoin levels can be reduced by corticosteroids and doses may need to be adjusted[6].

4.2 Indications and doses[6]

The list of 'off-label' indications for systemic corticosteroids in advanced cancer is not exhaustive and the doses stated are usual, but not prescriptive, starting doses. For further information see the Palliative Care Formulary.[6]

Indication	**Steroid dose** (once daily or equivalent split bd dose)
Anorexia **Fatigue**	2-4mg
Malignant bowel obstruction **Nerve compression pain** **Liver capsule pain** **Nausea**	4-8mg
Lymphangitis carcinomatosis **Rapidly expanding bone mets** **Malignant spinal cord compression (MSCC)[7]** **Superior vena cava obstruction** **Large airway obstruction** **Intracerebral oedema**	8-16mg

4.3 Reduction/Discontinuation[8,9]

Symptom relief from dexamethasone reduces over time and undesirable effects increase. Thus, ideally the dose of dexamethasone should be reduced after one week and discontinued after 2-4 weeks. However, patients often experience recurrence of their symptoms as the dose of dexamethasone is decreased, thus it may be necessary to taper more slowly or continue a maintenance dose of dexamethasone indefinitely in some patients.

No clear evidence exists for specific tapering regimens, although it is clear that in many patients steroids should not be stopped abruptly[9] due to the risk of hypo-adrenal crisis. The following notes are therefore suggestions:

Abrupt withdrawal

Steroids may be stopped abruptly in those whose disease is unlikely to relapse AND have received treatment for <3 weeks AND are not in the groups below.

Gradual withdrawal

Gradual withdrawal of steroids is advised in patients who:

- Have received >3 weeks of treatment
- Have received dexamethasone 4-6mg (or equivalent) for > one week
- Have had a second dose in the evening
- Have received repeated treatments
- Are taking a short course within 1 year of stopping long-term treatment
- Have other possible causes of adrenal suppression

If a patient has taken dexamethasone for >3 weeks, reduction needs to be gradual and should be guided by whether the original indication is likely to relapse as steroids are reduced. If the latter is not likely to occur, suggest:

Dex >2mg daily – reduce dose by half every 3-5 days.
Dex < 2mg daily – reduce dose by 0.5mg every 5-7 days.

If relapse is a concern, reduce more slowly. If physiological stress occurs within 1 week of stopping the steroid, additional steroid cover should be prescribed to compensate for adrenal suppression.

4.4 Gastroduodenal protection

There is uncertainty about the need for gastroduodenal protection with use of corticosteroids. In a recent systematic review and meta-analysis, use of corticosteroids was associated with increased risk of gastrointestinal bleeding and perforation, however this increased risk was limited to hospitalized patients.[10] However, there is a 15 times increase in risk when corticosteroids are given concurrently with NSAIDs.

It is recommended that a proton pump inhibitor or H_2 antagonist should be prescribed for:

- all patients taking a combination of non-steroidal anti-inflammatory drugs and a corticosteroid[11,12]
- patients with two or more of the following risk factors:
  - anticipated cumulative dose of corticosteroid equivalent to or greater than 140mg dexamethasone
  - previous history of peptic ulcer disease
  - advanced malignancy[13]

Gastroduodenal protection with corticosteroids should also be considered in patients

- with concurrent use of SSRI/SNRIs, antiplatelet drugs and anticoagulants.
- with a starting dose of dexamethasone of 8mg or more.

4.5 At the end of life

If unable to take oral medications, consider the balance of benefits and burdens of subcutaneous injections versus possible steroid withdrawal reaction:

- If steroids have been essential in achieving good symptom control (e.g. headaches secondary to raised intracranial pressure) then the balance of benefits/burdens is more likely to be in favour of continuing steroids.
- Injection strength is 3.3mg/ml or 3.8mg/ml, depending on brand. (See appendix 1) Oral bioavailability of dexamethasone is ~80%[14]. For pragmatic reasons a 4mg PO dose can be considered roughly equivalent to 3.3mg or 3.8mg SC, depending on which preparation is available.
- Dexamethasone may be given as a single daily SC injection, preferably in the morning, if volume of injection is 2ml or less.
- Alternatively for higher doses dexamethasone can be administered via a syringe pump. It is incompatible with most other drugs so a second syringe pump is usually required.

Dose equivalence[6]

	Prednisolone	Dexamethasone
Approximate equivalent dose	5	0.5 -1
Anti-inflammatory potency	5	25-50
Oral bioavailability	75-85%	78%
Onset of action	No data	8-24 hours I.M.
Duration of action	12-36 hours	36-54 hours
Sodium retaining potency	0.25	<0.01
Daily dose above which adrenal suppression likely	7.5mg	1mg

Approximate equivalent anti-inflammatory doses of corticosteroids can be found in the Palliative Care Formulary[6]. Dexamethasone is 7 times more potent as an anti-inflammatory than prednisolone, i.e. 2mg dexamethasone is approximately equivalent to 15mg of prednisolone.

4.6 Side effects

Multiple and include diabetes mellitus, osteoporosis, avascular bone necrosis, mental disturbances – insomnia, paranoid psychosis, depression, euphoria, muscle wasting and weakness (typically proximal and after 3 months of dexamethasone >4mg daily although may occur sooner), peptic ulceration (if given with an NSAID), increased susceptibility to infection, sodium and water retention, potassium loss, hypertension and Cushing's syndrome.

4.7 Cautions

Prolonged courses of steroids increase susceptibility to infections and their severity. Clinical presentation may be atypical; the signs of infection may be masked.
In patients who have taken >10mg prednisolone (or equivalent) daily for 3 weeks, the occurrence of any significant intercurrent illness, trauma or surgical procedure necessitates a temporary increase in corticosteroid dose.

5. RESPONSIBILITY/ACCOUNTABILITY:

Ultimate Responsibility: Director of Patient Care/ Medical Director.

All health care professionals, who prescribe, administer or give advice about steroids should ensure they are aware of the content of these guidelines.

6. COMPLIANCE WITH STATUTORY REQUIREMENTS/REFERENCES:

References:

1. Shih A. Jackson KC. Role of corticosteroids in palliative care. Journal of Pain & Palliative Care Pharmacotherapy. 21(4):69-76, 2007

2. Pilkey et al. Corticosteroid-induced diabetes in palliative care. Journal of Palliative Medicine. 15(6):681-9, 2012

3. Peacey SR. Pope RM. Naik KS. Hardern RD. Page MD. Belchetz PE. Corticosteroid therapy and intercurrent illness: the need for continuing patient education. Postgraduate Medical Journal. 69(810):282-4, 1993

4. BNF (2011) Section 6.3.2 in: British National Formulary no 61. British Medical Association and the Royal Pharmaceutical Association of Great Britain, London

5. Extracted from: Glucocorticoid-induced osteoporosis: a concise guide for prevention and treatment. London: Royal College of Physicians, 2002. https://www.rcplondon.ac.uk/sites/default/files/documents/glucocorticoid-induced-osteoporosis-concise.pdf accessed 10/9/14

6. Twycross R, Wilcock A. Palliative Care Formulary 6th ed: 2017. Chapter 7

7. MSCC guidelines available at: http://publications.nice.org.uk/metastatic-spinal-cord-compression-cg75/guidance#treatment-of-spinal-metastases-and-mscc

8. CSM (committee on safety of medicines and medicines control agency) 1998: Withdrawal of systemic corticosteroids. Current problems in Pharmacovigilance. 24: 5-7

9. Margolin L. Cope DK. Bakst-Sisser R. Greenspan J. The steroid withdrawal syndrome: a review of the implications, etiology, and treatments. Journal of Pain & Symptom Management. 33(2):224-8, 2007

10. Narum S, Westergren T, Klemp M. Corticosteroids and risk of gastrointestinal bleeding: a systematic review and meta-analysis. *BMJ Open*. 2014;4(5):e004587. Published 2014 May 15. doi:10.1136/bmjopen-2013-004587

11. Piper JM, Ray WA, Daugherty JR, Griffin MR. Corticosteroid use and peptic ulcer disease: role of nonsteroidal anti-inflammatory drugs. Ann Intern Med 1991; 114:735.

12. Gabriel SE, Jaakkimainen L, Bombardier C. Risk for serious gastrointestinal complications related to use of nonsteroidal anti-inflammatory drugs. A meta-analysis. Ann Intern Med 1991; 115:787.

13. Ellershaw JE, Kelly MJ. Corticosteroids and peptic ulceration. Palliat Med 1994; 8(4): 313 – 319

14.Duggan D E et al (1975). Bioavailability of oral dexamethasone. Clinical Pharmacy and Therapeutics 18(2):205-209.

15. The Management of Glycaemic Control in Patients with Cancer, Sept 2021 JBDS JBDS_Oncology_Guideline_Final_Revised_September_2021.pdf (abcd.care)

16. Steroid use for Inpatients with diabetes, May 2021 Steroid use for inpatients with diabetes | ABCD (Diabetes Care) Ltd

EDUCATION & TRAINING:

Mandatory training as per agreed education plan which can be found on the education page of the intranet. Or follow the link here: Statutory and Mandatory Training Requirements

7. GUIDELINE MONITORING AND REVIEW:

This guideline will be reviewed every 3 years or as required if there are changes in national guidance, evidence or legislation. Clinical audit should be performed to ensure the guidelines are being followed.

TITLE:	**STEROIDS: USE OF IN PALLIATIVE CARE PATIENTS GUIDELINE ON MANAGEMENT**	**Version: 4**
Approved By: **Dr Anjali Mullick** **Signature:**		**Date of Approval:** **26th January 2022**
Guideline Owner: **Dr Anjali Mullick, Medical Director**		**Revision due by: Jan 2025**
Guideline Author: **Dr Bethany Wright, Consultant in Palliative Medicine**		**Committee: Clinical Services**

REVISION HISTORY:

Description	Date	Version	Author(s)
Guideline Originated	May 2015	1	Dr Bethany Wright
Guideline Updated – change of guideline name, was previously called Use of Steroids in Palliative Care Patients.	Nov 2015	2	Dr Bethany Wright
Guideline reviewed – additions made to most sections. Appendix 1 updated	Mar 2019	3	Dr Bethany Wright, Dr Beth Walker
Guideline reviewed – additions made in light of new corticosteroid EMIS template and new guideline in relation to adrenal insufficiency	Jan 2022	4	Dr Bethany Wright

Appendices:

Appendix 1 - Use of dexamethasone formulations at St Peter's Hospice

Appendix 2 - Pathway chart for blood glucose monitoring for patients on steroids in an Inpatient setting

Appendix 3 - Pathway chart for blood glucose monitoring for patients on steroids in a Community setting

APPENDIX 1

Use of dexamethasone formulations at St Peter's Hospice

Oral (PO) tablets are formulated as dexamethasone *base* and injectable formulations as dexamethasone *phosphate or sodium phosphate*. St Peter's hospice recommend **all dosing advice and prescribing should now be expressed in terms of dexamethasone *base*** to avoid confusion caused by recent labelling formulation changes, different injection strengths and brands available.
The injectable formulations available now contain either 3.3mg/mL (Hospira or Hameln) or 3.8mg/mL (Aspen) dexamethasone *base*. **St Peter's hospice will be using the injectable formulation 3.3mg/mL.**

When parenteral use is necessary in palliative care, dexamethasone is usually given subcutaneously (SC) rather than intramuscularly/intravenously (IM/IV). Traditionally, for ease of prescribing, conversion of PO to SC/IV dexamethasone was made on a 1:1 basis (e.g. 4mg PO = 4mg SC/IV). Continuing with an exact 1:1 conversion will lead to unnecessarily complex and wasteful use of the ampoules and vials. Therefore St Peter's Hospice adopts the *PCF* recommendation that:

- for pragmatic purposes, when converting between PO and SC/IV routes, both 3.3mg and 3.8mg **dexamethasone** *base* of the injectable formulations can be considered approximately equivalent to **dexamethasone** *base* 4mg PO.
- the SC/IV dose prescribed should take into account which injectable formulation is being used so as to avoid wasteful use of the vials/ampoules (Table 1).
- the dose should be subsequently titrated according to response.

Table 1 – Dexamethasone equivalent oral and subcutaneous doses

Dose of oral Dexamethasone prescribed (BASE)	Dose of Dexamethasone 3.3mg/mL injection prescribed (BASE)	Volume of Dexamethasone 3.3mg/mL injection administered (BASE)	
2mg	1.65mg	0.5 mL	Max stat dose is 2mL, so for higher volumes a syringe driver will be required
4mg	3.3mg	1mL	
6mg	4.95mg	1.5mL	
8mg	6.6mg	2 mL	
10mg	8.25mg	2.5mL	
12mg	9.9mg	3mL	
16mg	13.2mg	4mL	

When prescribing dexamethasone on the hospice inpatient unit, the PO and SC doses will need to be written as separate prescriptions, with the latter including strength and volume of injection (Table 2).

Table 2 Dexamethasone prescribing requirements

Drug	Dose	Route
Dexamethasone base	2mg	PO
Dexamethasone base (3.3mg/ml)	1.65mg (0.5ml)	SC

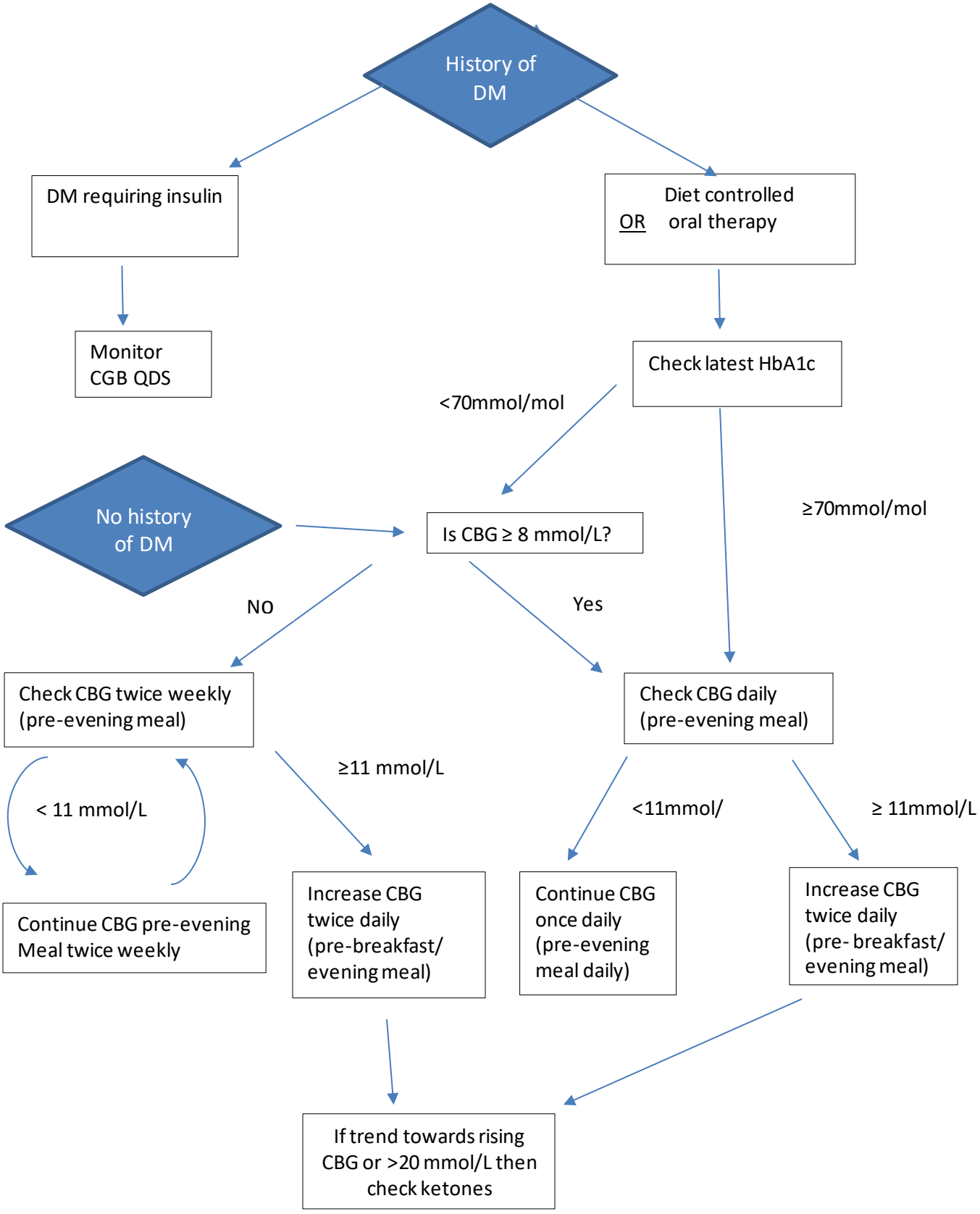
Syringe pump site reactions can sometimes be reduced by adding dexamethasone to the solution if compatability data permits. A dose of 660mcg = 0.2mL is recommended as being approximately equivalent to 1mg PO dexamethasone, as any smaller become difficult to accurately measure.

Further details:

Twycross et al. Palliative Care Formulary (6th edition).
MHRA (2014) Dexamethasone 4mg/mL injection (Organon Laboratories Limited: reformulation with changes in name, concentration, storage conditions, and presentation. *Drug Safety Update.* **3**. www.mhra.gov.uk/Safetyinformation
UK Medicines Information (2014) Dexamethasone injection. *In use product safety assessment report*. www.ukmi.nhs.uk.

Appendix 2 - Pathway for blood glucose monitoring for patients on steroids

In an Inpatient setting



Once steroid stopped, return to baseline monitoring if CBG within normal parameters over 2 days

Appendix 3 - Pathway for blood glucose monitoring for patients on steroids

In a Community setting

Key Points:

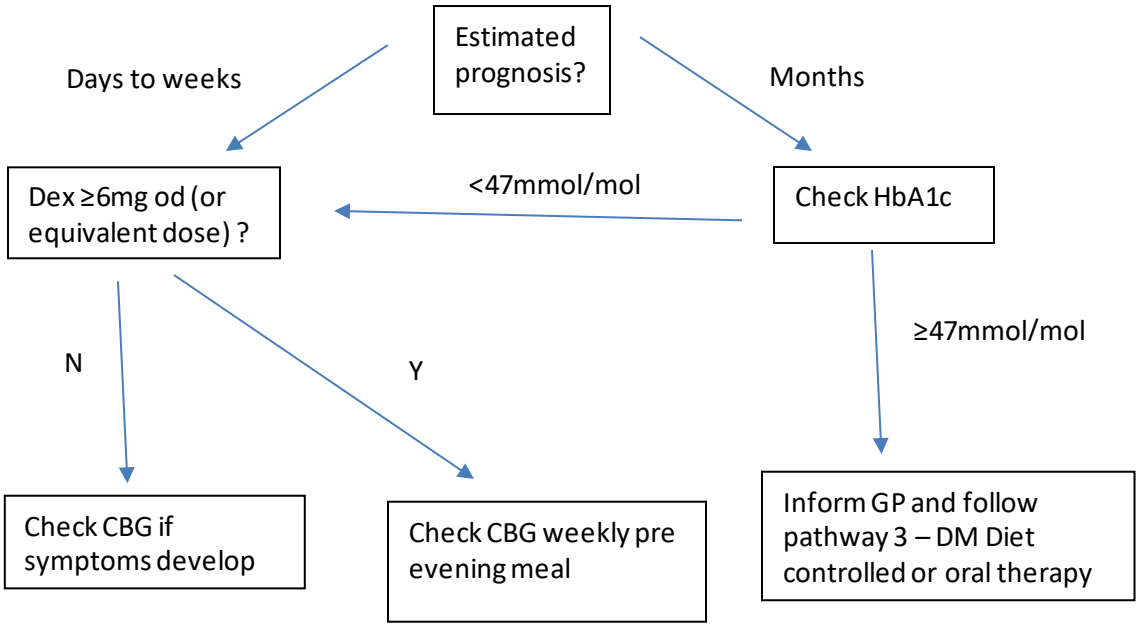
- Patients with HbA1c>47 mmol/mol/ 6.5% qualify for provision of a glucometer
- Patients not requiring insulin do not require blood glucose monitoring if dexamethasone (or equivalent) is limited to a 1week course of ≤4mg od
- The recommendations below are pragmatic in applying available national guidelines to care of patients in a community setting with a prognosis of less than one year.
- For patients with a longer prognosis, stricter blood glucose monitoring may be appropriate

1. DIABETES REQUIRING INSULIN

Monitor CBGs QDS
Once steroid stopped, return to baseline monitoring if CBG within normal range over 2 days

2. **NO HISTORY OF DIABETES**

- Request CBG if symptoms of hyperglycaemia develop or weekly whilst on dose of dex ≥6mg od or equivalent
- If prognosis likely to be months, also check HbA1c and follow DM diet controlled or oral therapy pathway if HbA1c>47 (i.e. implying diagnosis with DM)



3. DIABETES DIET CONTROLLED OR ORAL THERAPY