13.1 GENERAL PRINCIPLES

- Corticosteroids have been shown to be effective for a variety of uses in the palliative care setting. (see Table 13.1) As many as 50% of patients with advanced disease may be prescribed systemic corticosteroids during their illness.

| Table 13.1 Indications for systemic corticosteroids |
|-----------------------------------|---------------------------------|-------------------------------|
| Anorexia 2,3,4                     | GI obstruction 8,9              | Post radiotherapy 12          |
| Bone pain 5,6                      | Liver capsular pain 2           | Raised ICP 13, 14             |
| Dyspnoea 7                         | Lymphangitis carcinomatosis 10  | Spinal cord compression 15    |
| General well-being/weakness 2,4,6 | Nausea 2,7                      | SVCO/IVCO 16                  |
|                                   | Neuropathic pain 1, 5           | Tracheal obstruction 17       |

- The most commonly used systemic corticosteroids in clinical practice are prednisolone and dexamethasone. 40mg of prednisolone is equivalent to 6mg of dexamethasone.
- Topical and rectal preparations of corticosteroids are also available for treatment of local inflammation.

13.2 GUIDELINES

- Table 13.2 indicates suggested starting doses of systemic corticosteroids which are used in palliative care.

- It is important to limit the risk of inducing adrenal insufficiency. Therefore all patients prescribed corticosteroids should be given treatment for the shortest time using the lowest effective dose. 19 [Level 1+]

- The need for corticosteroids should be reviewed on a regular basis. 2,7 [Level 3]

- Corticosteroids should be discontinued if there has been no clinical response within 5–7 days. 5,7 [Level 4]

- Unless given in an emergency, corticosteroids should be administered once daily in the morning, or twice daily with the last dose before 2.00pm. This reduces suppression of the hypothalamic-pituitary-adrenal axis and may prevent corticosteroid-induced insomnia. 18, 19 [Level 1+]

- In the event of a deterioration in the patient’s symptom control, or the presence of an intercurrent illness, the corticosteroid dose may need to be increased for 5–7 days to maintain symptom control. Any subsequent reductions in dose may have to be made more slowly. 20,21 [Level 4]
All patients who are anticipated to require corticosteroids for longer than 3 weeks should be given a steroid card. 19 [Level 4]

<table>
<thead>
<tr>
<th>Suggested starting dose</th>
<th>Clinical indication</th>
<th>Mechanism of action</th>
<th>Additional notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>2mg-4mg</td>
<td>Anorexia</td>
<td>Uncertain</td>
<td>If patient has diabetes or a prognosis greater than 3 months, consider using megestrol acetate 160mg-320mg orally daily for appetite. 3, 8, 9</td>
</tr>
<tr>
<td></td>
<td>General well-being</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4mg-8mg</td>
<td>Nausea</td>
<td>Uncertain</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dyspnoea</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8mg</td>
<td>GI/GU obstruction</td>
<td>Reduction of tumour oedema/anti-inflammatory effect</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bone pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neuropathic pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Liver capsule pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Post-radiotherapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16mg</td>
<td>Spinal cord compression</td>
<td>Reduction of tumour oedema/anti-inflammatory effect</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Raised ICP</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>SVCO/IVCO</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tracheal obstruction</td>
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<td></td>
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<tr>
<td></td>
<td>Lymphangitis</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>carcinomatosis</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The need for gastroduodenal cover with systemic corticosteroids is uncertain. A proton pump inhibitor or H₂ antagonist should be co-prescribed with the corticosteroid for all patients taking NSAIDS 22 or those with two or more of the following risk factors. 23 [Level 2+]

- Advanced malignancy.
- Previous history of peptic ulcer disease.
- Anticipated cumulative dose of corticosteroid equivalent to or greater than 140mg dexamethasone.

It may also be worth considering gastric protection for the following patients: 23, 24 [Level 4]

- Concurrent use of SSRIs, aspirin, anticoagulants, bisphosphonates.
- Where the starting dose of corticosteroid is equivalent to or greater than 8mg dexamethasone.

If a patient is taking anti-epileptics such as phenytoin, carbamazepine or barbiturates there is a possibility of enzyme induction. Phenytoin in particular, has been shown to reduce the bioavailability of dexamethasone by as much as 75%. Patients may therefore require a 2-4 fold increase in their dexamethasone dose to achieve adequate symptom control. 25 Dexamethasone may also affect plasma phenytoin concentrations. 26 [Level 1-]
13.2.1 Corticosteroid Side Effects

- Side effects of corticosteroids include candida infection, weight gain, bruising, thinning of the skin, diabetes mellitus, proximal myopathy and cushingoid features. Patients on long-term corticosteroids should be maintained on the lowest possible corticosteroid dose and monitored for side effects. 12, 14, 23 [Level 3]

- Due to immunosuppression, patients on long-term corticosteroids also have an increased risk of developing new infections, or reactivating dormant infections such as TB or herpes zoster. Signs of infection may be masked by steroid use and patients should therefore be closely monitored. 21 [Level 4]

- If a patient develops a proximal myopathy secondary to the use of dexamethasone, it may be worth considering changing to a non-fluorinated corticosteroid (e.g. prednisolone), as these are thought to cause less myopathy. 27 [Level 3]

- Hyperglycaemia is a recognised side effect of corticosteroid therapy, in both diabetic and non-diabetic patients. 1, 2, 7, 28 It is therefore important to monitor glucose levels in all patients receiving corticosteroid therapy. Figure 13.1 gives guidelines for the monitoring and management of blood glucose in patients on corticosteroids. (see also Guidelines for the Management of Diabetes Palliative Care) [Level 4]

- Megestrol acetate may be an appropriate alternative for appetite stimulation in patients who develop hyperglycaemia or other toxicities due to corticosteroids. 3 [Level 4]

- Prolonged treatment with systemic corticosteroids is known to increase the risk of osteoporosis and fractures. This risk escalates rapidly within the first 3 months of treatment. Calcium and Vitamin D supplementation may be required for all patients taking corticosteroids with a deficient dietary intake. Bisphosphonates have been shown to be effective for the secondary prevention of fractures in some high-risk patients. Patients who are anticipated to require corticosteroids for longer than 3 months should be considered for prophylactic treatment with bisphosphonates at the time of commencing corticosteroids. Oral bisphosphonates may cause oesophageal/ gastric irritation. 29, 30, 31 [Level 4]

13.2.2 Withdrawal of Corticosteroids

- Corticosteroids should be discontinued once symptoms have resolved, or reduced to the lowest effective dose required to maintain symptom control. 19 [Level 1+]

- Any medications co-prescribed to prevent side effects should be stopped once corticosteroids have been discontinued. 24 [Level 4]

- The Committee on Safety of Medicines (CSM) has recommended that systemic corticosteroids should be gradually withdrawn in patients who have received treatment for longer than 3 weeks. 18, 19, 31 [Level 1+]

- Gradual withdrawal should also be considered in those patients who have received <3 weeks of treatment, but who are considered high-risk for developing adrenal insufficiency (see below). 18, 19, 31 [Level 4]

- The CSM has recommended that systemic corticosteroids may be stopped abruptly in those whose disease: 18, 19, 31 [Level 1+]
  1. is unlikely to relapse and
  2. who have received treatment for less than 3 weeks and
  3. who are not included in one of the high-risk groups (described below)

- Patients at high risk of developing adrenal insufficiency include the following: 18, 19, 31 [Level 4]
  1. Have recently received repeated courses of corticosteroids. (especially if taken for longer than 3 weeks)
  2. Are taking a short course of corticosteroids within one year of stopping long-term therapy.
3. Have other possible causes of adrenal suppression.
4. Have received more than prednisolone 40mg daily or the equivalent e.g. dexamethasone 4mg-6mg
5. Have received repeat doses in the evening.

- If stopping steroids gradually, the dose may be reduced rapidly if symptoms allow, until a physiological level (7.5mg prednisolone / 1mg dexamethasone) is reached. This may involve halving the dose daily. The dose should subsequently be reduced more slowly to allow the adrenals to recover and to prevent a hypo-adrenal crisis. During the withdrawal of corticosteroids it is important to monitor the patient for deterioration of symptoms. 18, 19, 31 [Level 4]

- At the present time, dexamethasone 0.5mg tablets are in limited supply in the UK.
- Dexamethasone liquid is a suitable alternative. 31 [Level 4]
- If steroids are administered continuously via a syringe driver, the patient is at greater risk of adrenal insufficiency if the steroids are discontinued abruptly. In these circumstances, unless the patient is in the dying phase, corticosteroids should be withdrawn gradually. 19, 24 [Level 4]

13.2.3 **Corticosteroids in the Last Days of Life**

- It is usually appropriate to discontinue corticosteroids in the dying phase unless they have been necessary in achieving good symptom control for the patient e.g. to treat: 18, 24 [Level 4]
  - headaches
  - seizures
  - pain

- For patients unable to take oral dexamethasone, doses <8mg may be given by bolus subcutaneous injection: 18, 31 [Level 4]

- If a continuous infusion is necessary, dexamethasone should be administered via a separate driver to prevent precipitation.
Figure 13.1  Guidelines for the monitoring and management of blood glucose in patients on corticosteroids [Level 4]

Patient commenced on corticosteroids

Non-diabetic

Capillary blood glucose (minimum) 2,7,14 days

CBG <7mmol  
CBG 7-15 mmol  
CBG >15 mmol

Patient asymptomatic  
Patient symptomatic

Review clinical need for steroid therapy

Consider fasting blood glucose to confirm diabetes (>7mmol/l)

Consider diet control/oral hypoglycaemics/referral to diabetic team. Monitor as required to optimise glycaemic control

Monitor CBG weekly

Diabetic

Monitor as per usual diabetic regimen (minimum 2,7,14 days)

CBG 7-15 mmol  
CBG >15 mmol

Patient asymptomatic  
Patient symptomatic

Consider monitoring as per usual diabetic regimen (minimum weekly)

Review clinical need for steroid therapy

Consider increasing diabetic medications/discuss with diabetic team. Monitor as required to optimise glycaemic control
13.3 **STANDARDS**

1. Corticosteroids should be given once daily in the morning, or twice daily with the last dose being given before 2.00 pm, unless there is an emergency situation.\(^\text{19}\) [Grade A]

2. All patients taking corticosteroids should be monitored for corticosteroid induced side effects and if identified they should be documented in the case notes.\(^\text{12, 14, 24}\) [Grade D]

3. Corticosteroids should be discontinued if the patient has shown no clinical response after 5–7 days.\(^\text{5, 7}\) [Grade D]

4. Patients should be maintained on the lowest effective dose of corticosteroid for the shortest possible time.\(^\text{19}\) [Grade A]

5. All patients who are anticipated to require corticosteroids for longer than 3 weeks should be given a steroid card.\(^\text{19}\) [Grade D]

6. An H\(_2\) antagonist or PPI should be co-prescribed with corticosteroids for all patients on NSAIDS and for patients with 2 or more of the following risk factors for gastro-intestinal bleeding.\(^\text{20}\) [Grade B]
   - Advanced malignancy.
   - History of peptic ulcer disease.
   - Anticipated cumulative dose of dexamethasone \(\geq 140\)mg.

13.4 **REFERENCES**


### 13.5 CONTRIBUTORS

**Lead Contributors**

Dr J Bellieu  
Specialist Registrar in Palliative Medicine  
Marie Curie Hospice  
Liverpool

Dr H Emms  
Consultant in Palliative Medicine  
St Johns Hospice  
Wirral

Dr A Murray  
Staff Grade Physician  
St Catherine’s Hospice  
Preston

**External Reviewer**

Dr T Rimmer  
Macmillan Consultant in Palliative Medicine  
East Cheshire Hospitals NHS Trust and  
Medical Director  
East Cheshire Hospice