# Dexamethasone - Palliative Care (Adults)

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## 1. Overview

### Purpose

This protocol outlines the administration, prescribing and monitoring of dexamethasone at Te Whatu Ora - Waitematā.

### Scope

All medical and nursing staff

⚠ This guideline is for use in the context of Palliative Care ONLY.

## 2. Presentation

Dexamethasone 0.5mg and 4mg tablets
Dexamethasone phosphate (as sodium) 4mg in 1ml glass ampoules*
Dexamethasone phosphate (as sodium) 8mg in 2ml glass ampoules*

**Dexamethasone injection is a clear, colourless solution*

## 3. Indications

### Licensed:

- Cerebral oedema (raised intracranial pressure)

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- Therapy for specific diseases including auto-immune, endocrine, pulmonary and blood disorders
- Treatment of allergy
- Adjunct treatment for shock[1]

### Unlicensed

- Nerve compression, spinal cord compression, superior vena cava obstruction, obstruction of hollow viscus (e.g. malignant obstruction of bowel or bronchus), bone pain, nausea and vomiting, prevention of inflammation at continuous subcutaneous infusion site, discharge from rectal tumour, paraneoplastic fever, dyspnoea, appetite stimulation, enhance sense of wellbeing, hypercalcaemia, liver capsule stretch pain, symptomatic radiation-induced oedema/inflammation, itch[2, 3, 4]

## 4. Contraindications and Precautions

### Contraindications[1]

- Known hypersensitivity to dexamethasone
- Concurrent immunotherapy (seek advice from medical oncology)
- Systemic infections*

**Dexamethasone can be considered in those with systemic infections in situations where they can be life threatening (e.g. seizures), can prevent/reverse severe morbidity (e.g. paraplegia) or if the patient is already on antibacterial/antiviral treatment for the systemic infection.*

⚠ The decision to administer corticosteroids in advanced disease must be weighed carefully between risk and benefit in a time-limited prognosis.

### Precautions[1, 7]

- Psychotic illness
- Diabetes mellitus
- Tuberculosis
- Congestive heart failure
- Recent myocardial infarction
- Hypertension
- Previous steroid myopathy
- Epilepsy and seizure disorders
- Myasthenia gravis
- Diverticulitis
- Liver failure
- Renal insufficiency
- Peptic ulcer and gastritis, gastrointestinal bleed

## 5. Mechanism of Action

- Dexamethasone prevents the development of the inflammatory process by suppression of neutrophil migration, decreased production of inflammatory mediators and reversal of increased capillary permeability. **This decreases oedema and inflammation around tumour.**[2, 3]
- Dexamethasone's mechanism of action as an antiemetic is unknown. It's been suggested that dexamethasone may deplete GABA stores in the medulla, reduce permeability of the blood-brain barrier and inhibit central prostaglandin release.[3]
- It is metabolised mainly by the CYP3A4 enzyme in the liver.[1, 3]

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## 6. Dose

**Doses can vary according to the individual patient and the indication.**[2, 3, 4]
In general, lower doses (2-4mg/day) are used for *non-specific indications*, while higher doses (>4mg) are used for *specific indications*. **See table below.**

| 0.5-1mg PO or SC/day | 2-4mg PO or SC/day | 4-8mg PO or SC/day | 8-16mg PO or SC/day |
|---|---|---|---|
| – To reduce irritation at the infusion site | <u>Non-specific indications</u><br>– increase appetite<br>– Co-analgesic<br>– Nausea and vomiting<br>– Weakness and fatigue<br>– Boost wellbeing | <u>Specific indications</u><br>– Co-analgesic in:<br>• nerve compression pain<br>• hepatomegaly<br>• other painful conditions<br>– Symptomatic radiation-induced oedema/ inflammation<br>– Malignant bowel obstruction | <u>Specific indications</u><br>– Raised intracranial pressure due to cerebral oedema (e.g. tumour induced)<br>– Spinal cord compression (16 mg daily)<br>– superior vena cava (SVC) obstruction<br>– Tumour induced airway obstruction<br>– Malignant bowel obstruction<br>– Prevention of chemo-emesis |
| **Note:** Consider use of a proton pump inhibitor (e.g. omeprazole) while on dexamethasone for frail and elderly patients and those on high dose treatment long-term[4, 5] | | | |
| The oral bioavailability of dexamethasone is 80% therefore the conversion ratio from oral(PO):subcut(SC)/intravenous(IV) is 1:1[3] | | | |

**Note:** Dexamethasone is often administered as a **single dose** in the morning to reduce the risk of insomnia and adrenal suppression.[4] However, it can also be administered via continuous subcutaneous infusion (CSCI) over 24 hours.

⚠ **Doses higher than 16mg dexamethasone daily are occasionally prescribed on Specialist advice.**

## 7. Principles of Use

- Consider a trial of 3 to 5 days to assess benefit before longer term plans are put in place; steroid effect is usually evident within 5 days
- A steroid plan should be well documented and communicated, including indications, duration of course, review intervals and down titration
- The patient and steroid dose should be reviewed ***at least*** weekly and instructions documented clearly
- Aim for the shortest course possible to obtain benefit or prevent morbidity; some patients may require courses longer than 3 weeks or remain on maintenance therapy to control symptoms or prevent morbidity e.g. seizure activity

### Reducing dose[2, 4]

- Dexamethasone may be stopped abruptly if used:
  - at doses up to 4mg daily for less than 3 weeks
  - at doses up to 12mg daily for no longer than 5-7 days

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- **If used for longer than 3 weeks** or repeated courses are given, reduce dose slowly to avoid adrenal insufficiency due to adrenal suppression.
- Reducing dose slowly also allows time at new level to assess response and symptoms, especially if there is deterioration:
    - Dexamethasone dose above 4mg daily
        - reduce by 2mg every 5-7 days until reaching 2mg, then by 0.5mg every 5-7 days
        - assess for symptoms before each dose reduction
    - Dexamethasone dose of 4mg or less
        - reduce by 0.5mg every 5-7 days
    - If rapid reduction is required, consider dose reduction every 3-4 days

### End of life considerations

- If dexamethasone is considered to still be beneficial to the patient's well-being and maintenance of symptom management, do not stop abruptly especially if used for specific indications (see section 6)
- If the deteriorating patient is unable to swallow consider switching the route of administration from oral to subcutaneous (1:1 ratio)
- If the dying patient has been on dexamethasone for 3 weeks or longer or has required repeated courses, consider a dose reduction and a switch to subcutaneous route; do not stop abruptly unless the patient become unconscious and is very close to dying
- Consider up-titration of other medications (e.g. analgesics for pain, benzodiazepines for seizures) to allow for steroid reduction or abrupt withdrawal if necessary (e.g. if steroid is considered to be contributing to terminal agitation) while maintaining symptom management
  *Seek advice from the palliative care team*

## 8. Administration

**Note:** Dexamethasone is only licensed for oral and intravenous administration. Despite, this the subcutaneous route is a commonly used route of administration in the context of Palliative Care.

### 8.1 Subcutaneous bolus/IV

- For subcutaneous bolus / IV administration dexamethasone does not need to be diluted
- It is long acting and can be given once daily as a bolus injection[2]
- Avoid giving more than 2ml (8mg) as single stat subcutaneous dose. For doses greater than 8mg, give as separate injections (e.g. if 12mg is prescribed, administer as 2 bolus doses of 6mg at different injection sites).

### 8.2 Diluent

#### Continuous subcutaneous infusion

- When added to a syringe driver the recommended diluent is water for injection. Sodium chloride 0.9% should be considered if there is potential for inflammation at the injection site
- Dexamethasone should be **added last** to an already dilute combination of drugs in order to reduce the risk of precipitation. It is advisable to use a 30ml BD Plastipak Luer-Lock® syringe for this purpose.[2]

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## 8.3 Administration Procedure

### Subcutaneous

- Should be injected through a Saf-T-Intima
- The Saf-T-Intima should be flushed with 0.2 ml of water for injection after administration of medication
- Can be administered via a continuous subcutaneous infusion pump (Niki T34).

## 8.4 Additional Equipment

- Subcutaneous Saf-T-Intima single lumen [ADM140] (*See Te Whatu Ora – Waitematā policy Palliative Care - Subcutaneous Site Selection and Insertion of BD Saf –T- Intima Cannula*)
- Continuous subcutaneous infusion pump (Niki T34) if required.

## 8.5 Compatibility

### Compatible with

- Water for injection, 0.9% sodium chloride, morphine sulfate, morphine tartrate, tramadol, methadone, metoclopramide, clonazepam, oxycodone, hyoscine hydrobromide, hyoscine butylbromide.[2, 3, 4]

### Concentration dependent compatibility with

- Cyclizine, haloperidol, promethazine, levomepromazine, midazolam, octreotide[2, 3, 4]
    - Mixing these with dexamethasone should be avoided if possible
    - If used, the solution must be carefully checked for precipitation at least once a shift.

**Note:** If dexamethasone is to be mixed with other medications in a syringe driver, add as much diluent as possible before adding the dexamethasone last.[3]

⚠ Do not use if the solution is cloudy or a precipitate is present.

# 9. Observation and Monitoring

- Patient may require monitoring of blood sugars depending on clinical scenario[2]
- Observe for any psychiatric disturbances[2]
- Monitor for oral candida
- Monitor for signs of proximal myopathy[4]
- Observe for headaches in susceptible patients when reducing the dose[2]
- Monitor for any signs of gastrointestinal symptoms/gastritis.

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## 10. Adverse Effects

| Immediate (within 24 to 72 hours) | Short to medium term (days to short weeks) | Medium to long term (weeks to short months) | Long term (months to years) |
|---|---|---|---|
| • Increased appetite<br>• Hyperactivity/ restlessness<br>• Psychological changes (e.g. depression, insomnia, agitation, behavioural changes, paranoid psychoses)<br>• Hyperglycaemia<br>• Oral candidiasis | • Suppression of hypothalamic-pituitary-adrenal axis<br>• Increased susceptibility to infection due to immunosuppression<br>• Oedema<br>• Fluid and electrolyte disturbances (e.g. hypokalaemia)<br>• Hypertension<br>• Peptic ulcer with perforation<br>• Oesophageal ulceration | • Cushing's syndrome (moon face, truncal obesity, skin changes)<br>• Proximal myopathy<br>• Increased susceptibility to infection due to immunosuppression<br>• Skin changes (e.g. acne, bruising, impaired wound healing, hirsutism, striae) | • Cataracts<br>• Glaucoma<br>• Osteoporosis<br>• Avascular osteonecrosis of femoral head<br>• Joint pains |

## 11. Interactions

- Dexamethasone plasma levels are reduced by CYP3A4 inducers (e.g. rifampicin, carbamazepine, phenobarbital and phenytoin). Higher doses will be necessary to treat patients receiving these antiepileptics.[1, 2]
- Dexamethasone can increase or decrease the plasma levels of phenytoin. This is important when changing the dose of dexamethasone when a patient is at risk of seizures. Phenytoin levels should be monitored.[2]
- CYP3A4 inhibitors (e.g. ketoconazole, ciclosporin, ritonavir, itraconazole, erythromycin) may increase the effects of dexamethasone[1, 2]
- The action of anticoagulants may be reduced or less often enhanced by dexamethasone. Monitor INR closely (at least weekly) in patients taking warfarin.[1, 7]
- Increased risk of bleeding with medications that can pre-dispose patients at risk of bleeding (e.g. non-steroidal anti-inflammatories, antiplatelets, anticoagulants)
- Dexamethasone antagonises the effects of oral hypoglycaemics and insulin, antihypertensive and diuretics.[2]
- Increased risk of hypokalaemia when administered with potassium-depleting diuretics (e.g. bendrofluazide, furosemide) and beta-2 agonists (e.g. salbutamol).[2]

## 12. References


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