# Prednisolone
## Newborn Use Only

**2024**

| | |
|---|---|
| **Alert** | Routine use of prednisolone for prevention of chronic lung disease is not recommended. |
| **Indication** | Treatment of severe bronchopulmonary dysplasia ≥36 weeks gestation |
| **Action** | • Predominantly glucocorticoid effects with minimal mineralocorticoid effects<br>• Decreases inflammation by suppression of migration of polymorphonuclear leukocytes and reversal of increased capillary permeability.<br>• suppresses the immune system by reducing activity and volume of the lymphatic system |
| **Drug Type** | Synthetic glucocorticoid. |
| **Trade Name** | Redipred<br>Predmix (not first choice due to propylene glycol content) |
| **Presentation** | Liquid: 5mg/mL (recommended)<br><br>Note: Prednisolone tablets may be used if there is stock availability issues of the liquid products. Contact local pharmacy department for appropriate preparation using tablets. |
| **Dose** | **NOTE: It is highly recommended to consult paediatric respiratory specialist before commencing prednisolone therapy.**<br><br>**14-day ORAL regimen course[1]**<br>Day 1 to Day 5 (5 days): 1 mg/kg/dose 12 hourly,<br>Day 6 to Day 8 (3 days): 1 mg/kg/dose 24 hourly,<br>Day 10 – Day 14 (6 days): 1 mg/kg/dose 48 hourly |
| **Dose adjustment** | Therapeutic hypothermia – Not applicable.<br>ECMO- Not applicable.<br>Hepatic impairment – Metabolised in liver, but no specific dose adjustment is suggested.<br>Renal impairment – No dose adjustment. |
| **Route** | Oral/OGT/NGT |
| **Preparation** | N/A |
| **Administration** | Administer undiluted with feeds |
| **Monitoring** | Blood pressure, weight, BGL, electrolytes, bone mineral density, haemoglobin, signs of infection |
| **Contraindications** | Uncontrolled infections<br>Systemic fungal infections<br>Known hypersensitivity to prednisolone or prednisone |
| **Precautions** | Adrenal suppression<br>Immunosuppression<br>Metabolic bone disease |
| **Drug Interactions** | Phenobarbital increases prednisolone's metabolism and may reduce its activity |
| **Adverse Reactions** | Vomiting, abdominal distension, diarrhoea<br>Increased appetite<br>Agitation<br>Hyperglycaemia<br>Hypokalaemia<br>Hypertension<br>Reduced growth (long term treatment)<br>Osteopenia (long term treatment)<br>Reduced wound healing<br>Sodium and water retention |
| **Overdose** | For further information, contact the Poisons Information Centre on 131 126 (Australia). |
| **Compatibility** | Not applicable. |
| **Incompatibility** | Not applicable. |
| **Stability** | Discard commercial liquids 4 weeks after opening |
| **Storage** | Redipred brand store at room temperature below 25°C<br>Predmix brand store refrigerated at 2–8°C |

| | |
|---|---|
| **Excipients** | Redipred: Sorbitol solution (70%) non-crystallising, disodium edetate, monobasic sodium phosphate, dibasic sodium phosphate, methyl hydroxybenzoate, propyl hydroxybenzoate, nature identical raspberry flavour 08-3326 and water-purified.<br><br>Predmix: Propylene glycol, methyl hydroxybenzoate, propyl hydroxybenzoate, dibasic sodium phosphate dodecahydrate, monobasic sodium phosphate, disodium edetate and water-purified. |
| **Special Comments** | Immunise one month before starting or at least one month after ceasing corticosteroids. |
| **Evidence** | **Background**<br>Bronchopulmonary dysplasia (BPD) in preterm infants is associated with delayed brain maturation and diffuse white matter anomalies that are associated with increased risk of neurodevelopmental impairment.[2] Dexamethasone has been acknowledged in multiple trials as a long-acting glucocorticoid that can be used to prevent or treat developing BPD. Methylprednisolone and prednisolone are alternate steroids, and there is emerging evidence to support their use in some infants at high risk of BPD or established BPD. Both prednisolone and methylprednisolone have been safely used for other pulmonary diseases, primarily within the paediatric asthma population, but there is a paucity of available evidence for their use in the neonatal population.<br>**Efficacy**<br>There are no published studies on commencement of dexamethasone for treatment of BPD in preterm infants beyond 36 weeks gestation. There are 3 retrospective studies reporting on the efficacy of prednisolone/methylprednisolone for severe BPD in preterm neonates beyond 36 weeks corrected gestation.<br>A single centre retrospective cohort study by Bhandari et al, assessed 385 infants of whom 131 (34%) received oral prednisolone to support weaning from oxygen at 36 weeks postmenstrual age.[1] 63% of these infants were deemed responsive to oral prednisolone therapy and able to be weaned from oxygen, with lower pulmonary acuity scores than those infants non-responsive to treatment. Predictive responsiveness to oral prednisolone therapy identified a capillary PCO2 value of < 48.5 mmHg had a sensitivity of 50% and specificity of 89.7%, with positive and negative predictive values of 89.1% and 51.8%, respectively. The dose of oral prednisolone used in Bhandari regimen was 2 mg/kg/day in 2 divided doses for 5 days, then 1 mg/kg/day daily for 3 days, and then 1 mg/kg/dose every other day for 3 doses. It was noted however that many of this group may also have received treatment with dexamethasone prior to commencement of prednisolone.<br>A single-centre retrospective cohort study by Linafelter et al, identified 43 infants with a mean gestational age of 26 weeks, who were treated with an extended course (≥ 30 days) of prednisolone for severe BPD, using pulmonary severity score (PSS) as a primary outcome measure. The average age at start of prednisolone treatment was 42.5 ± 5.9 weeks; while the median duration and median cumulative dose of prednisolone therapy were 67 (IQR 57–107) days and 61.3 (IQR 39.9–93.3) mg/kg, respectively.[3] PSS decreased after 1 week of prednisolone therapy (mean difference, 0.19; 95% Cl, 0.01 to 0.37; p = 0.03). No further reduction in PSS was noted despite continued treatment. Length z-scores decreased after 4 weeks of continued treatment (mean difference 0.6; 95% CI 0.01 to 1.1; P = 0.04), while weight and head circumference did not change.[3]<br>Another retrospective study by Liviskie et al, described the use of prednisolone for late treatment of pulmonary disease in infants with established BPD, after the first month of life. This study identified 34 patients where prednisolone treatment was initiated at a mean postmenstrual age of 41.7 weeks. Typically, 1-2 mg/kg/d and weaned by 0.5 every 5-7 days (>30 day course). A significant decrease in PSS was observed (p<0.001) without rebound following discontinuation of treatment.[4] This study, conversely, did not identify any significant impact on anthropometric measures.<br>**Safety of dexamethasone versus prednisolone or methylprednisolone**<br>A secondary analysis of a multi-centre randomised controlled trial (Preterm Erythropoietin Neuroprotection – PENUT trial) reported 2-year neurodevelopmental outcomes in extremely preterm infants treated with dexamethasone, methylprednisolone, and prednisolone. The study identified an association between reduced BSID III scores and > 14 days treatment with dexamethasone. The median (IQR) start day was 29 (20-44) days for dexamethasone and 53 (30-90) days for prednisolone or methylprednisolone. The median (IQR) total days of exposure was 10 (5-15) days for dexamethasone and 13 (6-25) days for prednisolone or methylprednisolone. The median (IQR) cumulative dose of |

dexamethasone was 1.3 (0.9-2.8) mg/kg. After adjusting for potential confounders, treatment with dexamethasone for longer than 14 days was associated with worse neurodevelopmental outcomes. The same finding was not identified in the methylprednisolone and prednisolone group however the numbers in this cohort were small (n=99) and brains were more mature at the time of exposure.[5] This subgroup analysis of the PENUT trial demonstrated no long term neurologic complications from prednisolone use starting on average at day 50 of life and continued for an average of 13 days. There were also some benefits on neurodevelopment for the infants treated with 8 to 14 days of prednisolone.[5]

**ANMF consensus:** Secondary analysis of PENUT trial reported worse neurodevelopmental outcomes with long courses of dexamethasone and no such effect was seen with short courses of either prednisolone or methylprednisolone. However, subgroup analyses of RCTs carry limitations such as poor definitions, low statistical power, and inflated type I error due to multiple hypotheses testing. Similarly a long course (>30 days) of prednisolone was shown to decrease length z-scores.[3] A short course of oral prednisolone may be considered in weaning off respiratory support in preterm infants closer to term or post term with severe bronchopulmonary dysplasia. It is highly recommended to consult paediatric respiratory specialist before commencing prednisolone therapy.

**Pharmacokinetics**

Prednisolone is readily absorbed from the gastrointestinal tract. It is mostly metabolised in liver and excreted in urine.

**Safety**

No specific adverse events have been reported with short courses of prednisolone in the above mentioned studies. However, extended course of prednisolone>30 days was associated with reduced length z scores.[3]

**Vaccines post prednisolone:** Australian Immunisation handbook has made the following recommendations for infants and children weighing ≤10 Kg:[6]

| Prednisone-equivalent dose | Duration of therapy | Potential timing of vaccination |
|---|---|---|
| <1 mg/kg/day | <30 days | Anytime during therapy |
| <2 mg/kg/day | <14 days | Anytime during therapy |
| <2 mg/kg/day | 14-28 days | Immunise 1 month before starting corticosteroids or at least 1 month after stopping corticosteroids. Alternatively, person may be able to receive live vaccines at any time during therapy, but only after seeking expert advice. |
| ≥2 mg/kg/day | <14 days | Immunise 1 month before starting corticosteroids or any time after stopping corticosteroids. |
| ≥2 mg/kg/day | 14-28 days | Immunise 1 month before starting corticosteroids or at least 1 month after stopping corticosteroids. |

**Note: 1 mg prednisone = 1 mg prednisolone = 0.1 mg dexamethasone.**

**Practice points**

**References**

1. Bhandari A, Schramm CM, Kimble C, Pappagallo M, Hussain N. Effect of a short course of prednisolone in infants with oxygen-dependent bronchopulmonary dysplasia. Pediatrics. 2008;121(2):e344-e9.
2. Anderson PJ, Doyle LW, editors. Neurodevelopmental outcome of bronchopulmonary dysplasia. Semin Perinatol; 2006: Elsevier.
3. Linafelter A, Cuna A, Liu C, Quigley A, Truog WE, Sampath V, et al. Extended course of prednisolone in infants with severe bronchopulmonary dysplasia. Early human development. 2019;136:1-6.
4. Liviskie C, Vesoulis Z, Zeller B, Rao R, McPherson C. Respiratory effects of prolonged prednisolone use in infants with evolving and established Bronchopulmonary dysplasia. Early Human Development. 2021;156:105344.

| | |
|---|---|
| | 5. Puia-Dumitrescu M, Wood TR, Comstock BA, Law JB, German K, Perez KM, et al. Dexamethasone, prednisolone, and methylprednisolone use and 2-year neurodevelopmental outcomes in extremely preterm infants. JAMA Network Open. 2022;5(3):e221947-e.<br>6. Australian Immunisation Handbook. Accessed online on 7 March 2024. |


| Version/Number | Date |
|---|---|
| Original 1.0 | 28/03/2024 |
| Review | 28/03/2029 |

**Authors of the current version**

| | |
|---|---|
| Original author/s | Srinivas Bolisetty, Rebecca Barzegar |
| Evidence Review | Srinivas Bolisetty, Rebecca Barzegar |
| Expert review | Louisa Owens, Saikiran Gopalakaje |
| Nursing Review | Bryony Malloy, Eszter Jozsa |
| Pharmacy Review | Rebecca O'Grady, Michelle Jenkins |
| ANMF Group contributors | Nilkant Phad, Bhavesh Mehta, Rebecca Barzegar, Martin Kluckow, Mohammad Irfan Azeem, Thao Tran, Susanah Brew, Simarjit Kaur, Helen Huynh, Stephanie Halena, Benjamin Emerson-Parker, Renae Gengaroli, Kerryn Houghton |
| Final editing | Srinivas Bolisetty |
| Electronic version | Thao Tran, Helen Huynh, Cindy Chen, Ian Callander |
| Facilitator | Srinivas Bolisetty |

**Citation for the current version**

Bolisetty S, Barzegar R, O'Grady R, Jenkins M, Malloy B, Jozsa E, Azeem MI, Phad N, Mehta B, Kluckow M, Tran T, Huynh H, Halena S, Brew S, Kaur S, Houghton K, Srnic N, Gengaroli R, Chen C, Owens L, Gopalakaje S, Callander I. Prednisolone. Consensus formulary by the Australasian Neonatal Medicines Formulary group. Version 1, dated 28 March 2024. www.anmfonline.org