BuDESONide
Newborn use only

2022

Alert	Protect infant's face and eyes during drug administration
Indication	Chronic lung disease
Action	Inhaled glucocorticoid bronchodilator
Drug type	Corticosteroid
Trade name	Pulmicort Respules
Presentation	500 microgram/2 mL and 1000 microgram/2 mL Respules nebulising suspension
Dose	**500 micrograms twice daily up to 14 days** (ANMF consensus).*[1-3] Variation to the dose and duration is at the discretion of the treating NICU team and/or in consultation with paediatric respiratory team.
Dose adjustment	Therapeutic hypothermia – No information. ECMO – No information. Renal impairment – No dose adjustment. Hepatic impairment – No dose adjustment.
Maximum dose	600 micrograms twice daily.[2]
Total cumulative dose	
Route	Inhalation via nebuliser
Preparation	May be given undiluted or dilute with 2 mL of sodium chloride 0.9% to give a total volume of 4mL.
Administration	Place an eye mask over infant's eyes to avoid drug entering the eyes. Nebulise for 10 minutes and discard remaining contents. Post-inhalation - wipe face and eyes
Monitoring	
Contraindications	Known hypersensitivity to budesonide or any other ingredients
Precautions	Neonates with fungal and viral infections in the airways.Neonates who are being transferred from oral corticosteroids to budesonide, consider weaning oral steroids slowly. Do not cease oral steroid therapy suddenly.
Drug interactions	
Adverse reactions	Mild irritation in the throat, candida infection in the oropharynx at high doses, facial skin irritation, bronchoconstriction (rare), gastrointestinal (nausea and vomiting), suppression of the pituitary-adrenal axis, posterior subcapsular cataracts.
Compatibility	N/A
Incompatibility	N/A
Stability	Unused Respules should be discarded three months after opening of foil packs.
Storage	Stored below 30°C. Do not refrigerate.
Excipients	Disodium edetate, sodium chloride, polysorbate 80 (E433), citric acid (E330), sodium citrate dihydrate (E331) and water for injections.
Special comments	There is data indicating the benefit of inhaled steroids in chronic lung disease but the dosage schedule is somewhat arbitrary. The effect on growth and adrenal function has not yet been studied in newborn infants, though there is favourable topical to systemic effect ratio.
Evidence	**Efficacy** **<u>Chronic lung disease (CLD)</u>** Inhaled steroids are used to prevent chronic lung disease (CLD) in the hope that they would have fewer adverse effects than systemic corticosteroids. However, the outcomes reported in the systemic reviews/trials are variable.[3-6] **Inhaled corticosteroids (IC) for prevention or treatment of BPD:** Shinwell 2016 meta-analysis of RCTs of ICs versus placebo for either prevention or treatment of BPD found that ICs were associated with a significant reduction in death or BPD at 36 weeks' postmenstrual age (RR = 0.86, 95% CI 0.75 to 0.99). BPD was significantly reduced (RR = 0.77, 95% CI 0.65 to 0.91), although there was no effect on death (RR = 0.97, 95% CI 0.42 to 2.2). The clinical significance of this outcome is uncertain noting that the upper CI limit for the combined outcome of BPD or death was 0.99.[6]

	Early inhaled corticosteroids (within first 2 weeks of life): The 2017 Cochrane Review included 10 trials with 1,644 neonates.[7] Early inhaled steroids reduced CLD at 36 weeks among survivors (RR 0.76, 95% CI 0.63–0.93) and the combined outcome of death or CLD at 36 weeks among all randomised neonates (RR 0.86, 95% CI 0.75–0.99; typical RD −0.06, 95% CI −0.11 to −0.00). Whilst there is statistical significance, the clinical relevance is of question as the upper CI limit for the outcome of death or CLD at 36 weeks' PMA is infinity. Moreover, one of the trials included in this review (NEUROSIS trial) found a trend towards increased mortality, but this was not confirmed by this Cochrane Review or another 2016 meta-analysis.[6] NEUROSIS trial published their long term outcomes in 2018 and found that the rate of neurodevelopmental disability at 2 years did not differ significantly among surviving preterm infants who received early inhaled budesonide in comparison to placebo group.[8] The current expert recommendation is that early routine inhaled corticosteroids (first week of life) cannot be recommended until further studies/reviews have been performed.[9] **Late inhaled corticosteroids (≥ 7 days of life):** A 2017 Cochrane review included 8 trials with 232 preterm infants. The meta-analysis showed a reduced extubation failure at 7 days (RR 0.80, 95% CI 0.66 to 0.98; 5 studies, 79 infants), but clinical significance of this outcome is uncertain noting the upper CI limit is 0.98. There was no impact on the total duration of mechanical ventilation or oxygen dependency. The review concluded that inhaled corticosteroids initiated at ≥ 7 days of life for preterm infants cannot be recommended.[3] **Dose regimens for CLD:** Neurosis trial used budesonide 400 micrograms BD in the first 14 days of life and 200 micrograms BD from day 15.[4, 8] Arnon et al used budesonide 600 micrograms twice daily for 7 days or until extubation.[2] Jonsson et al used budesonide 500 micrograms twice daily for a total of 14 days.[1] In Arnon trial, budesonide was delivered into small volume spacer, and filled with oxygen without a rubber flap valve. Distal end of spacer was directly connected onto the endotracheal tube.[2] In Jonsson trial, drug was delivered using a jet nebuliser, delivering the aerosol during the inspiration but not the expiration phase of mechanical breaths. In spontaneously breathing infants, a Laerdal mask modified to fit to the inhalator nozzle was used.[1] Device/s for nebulisation: In NEUROSIS trial and trial by Arnon et al, budesonide was administered by means of a metered-dose inhaler connected to a spacer.[2, 4] In trial by Jonsson et al, budesonide was delivered by an electronic jet nebuliser.[1] **<u>Safety</u>** Inhaled corticosteroids used for the prevention/treatment of CLD in preterm infants were generally well tolerated.[1-6, 10] The NEuroSIS trial reported a significant decrease in the incidence of CLD but a non-significant trend to increased mortality. This trend was not noted in subsequent meta-analysis.[3, 4, 6] NEuroSIS trial did not find any increased risk of sepsis or pneumonia.[10] A prospective study in children with asthma found that inhaled corticosteroids was not associated with posterior subcapsular cataract or ocular hypertension.
Practice points	
References	1. Jónsson B, Eriksson M, Söder O, Broberger U, Lagercrantz H. Budesonide delivered by dosimetric jet nebulization to preterm very low birthweight infants at high risk for development of chronic lung disease. Acta Paediatrica. 2000;89(12):1449-55. 2. Arnon S, Grigg J, Silverman M. Effectiveness of budesonide aerosol in ventilator-dependent preterm babies: a preliminary report. Pediatric pulmonology. 1996;21(4):231-5. 3. Onland W, Offringa M, Van Kaam A. Late (≥ 7 days) inhalation corticosteroids to reduce bronchopulmonary dysplasia in preterm infants. Cochrane Database of Systematic Reviews. 2017;2017(8). 4. Bassler D, Plavka R, Shinwell ES, Hallman M, Jarreau P-H, Carnielli V, et al. Early Inhaled Budesonide for the Prevention of Bronchopulmonary Dysplasia. New England Journal of Medicine. 2015;373(16):1497-506. 5. Shah SS, Ohlsson A, Halliday HL, Shah VS. Inhaled versus systemic corticosteroids for preventing bronchopulmonary dysplasia in ventilated very low birth weight preterm neonates. Cochrane Database of Systematic Reviews. 2017(10). 6. Shinwell ES, Portnov I, Meerpohl JJ, Karen T, Bassler D. Inhaled Corticosteroids for Bronchopulmonary Dysplasia: A Meta-analysis. Pediatrics. 2016;138(6):e20162511.

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