Inhaled Budesonide (Pulmicort® Turbuhaler)

What is it?

- A corticosteroid with potent glucocorticoid and weak mineralocorticoid activity. When inhaled, it provides a local anti-inflammatory effect which may benefit individuals with mild symptoms of COVID-19.

Health Canada Indication:	Maintenance therapy for bronchial asthma.

At this time, inhaled budesonide is not being pursued for approval by Health Canada for the indication of COVID-19. [1]

Nova Scotia Health recommends budesonide be considered for use on a case-by-case basis in adults ≥18 years of age with mild symptoms of COVID-19 (i.e. not requiring new or additional supplemental oxygen, intravenous fluids, or physiological support) within 14 days of symptom onset.

Evidence:

- Key support comes from the primary analysis of the **PRINCIPLE** trial[2] which involved 2530 adult outpatients with confirmed COVID-19 and symptom onset within the past 14 days and who were at high risk for complications, i.e. either advanced age ≥ 65 years or ≥ 50 years with comorbidities (CVD, HTN, asthma/lung disease, DM, hepatic impairment, stoke or neurological problems, weakened immune system, obesity/BMI ≥ 35 kg/m^2). Patients (mean age 64.2 years [SD 7.6], 81% with comorbidities, median 6 days since symptom onset), were randomized to receive either 1) budesonide dry powder inhaler 800 mcg inh BID x 14 days + usual care (n = 787) or 2) usual care alone (n = 1069). The trial was stopped early when pre-specified superiority criteria were met:

PRINCIPLE: multi-centre, open-label RCT based out of primary care centres in the UK (enrolled April 2020-March 2021)

- **Quicker time to self-reported recovery [median days (95% Bayesian credible interval)]**
  - 11.8 days (10.0 – 14.1) budesonide recipients versus 14.7 days (12.3 – 18.0) usual care recipients; HR 1.21 (1.08 – 1.36), probability of superiority >0.999*
- **No difference in composite of hospital admission or death at 28 days [absolute rate (95% Bayesian credible interval)]**
  - 6.8% (4.1 – 10.2) budesonide recipients versus 8.8% (5.5 – 12.7) usual care recipients; OR 0.75 (0.55 – 1.03), probability of superiority 0.963**
- **Serious adverse events (SAEs):**
  - Recorded in 2 budesonide recipients (hospitalization for lower limb fracture, alcohol-induced pancreatitis) and 4 usual care recipients (hospitalization for cholelithiasis, atrial fibrillation, heart valve surgery, and appendicitis)

*Threshold for superiority pre-specified at 0.99; **Threshold for superiority pre-specified at 0.975

- The **STOIC** trial[3], a phase 2 open-label RCT, investigated the role of inhaled budesonide versus usual care alone for reducing urgent care visits (emergency department assessments or hospitalization) in adult outpatients with early, mild COVID-19 (n = 146). In this overall young and healthy population (median age 45, 5% diabetes, 9% cardiovascular disease, mean BMI 26-27 kg/m^2), there were statistically significantly fewer urgent care visits in budesonide recipients [2/73 (3%)] versus usual care [11/73 (15%)]; difference in proportion 0.123 (95% CI 0.033 – 0.213); p = 0.009.

The use of inhaled budesonide for COVID-19 is not addressed by the World Health Organization (WHO), the National Institute of Health (NIH), nor the Infectious Diseases Society of America (IDSA) guidelines at this time.[4-6]

Practical Considerations

- Forceful inhalation required to receive budesonide dose through Turbuhaler dry powder inhaler (DPI) device.
- Nebulized budesonide is NOT recommended as an alternative to the dry powder inhaler as nebulization is an aerosol-generating medical procedure (AGMP). Systemic corticosteroids and other steroid inhalers (e.g. fluticasone, ciclesonide) are also inappropriate alternatives to budesonide DPI.
- Rinsing mouth after inhaler use may reduce risk of adverse events (oral thrush, hoarseness, throat irritation) and systemic absorption.

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References:

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