Department of Health & Social Care | The Scottish Government Riaghaltas na h-Alba | Llywodraeth Cymru Welsh Government | Department of Health | An Roinn Sláinte | Männystrie O Poustie | NHS

Interim Position Statement

Interim Position Statement: Inhaled budesonide for adults (50 years and over) with COVID-19

12 April 2021

Interim position

The PRINCIPLE trial has reported a 3-day median benefit in self-reported recovery for patients with COVID-19 in the community setting who received inhaled budesonide. The impact on hospitalisation rates or mortality has not been established, but the evaluation is ongoing, so recommendations may change as more data become available. At this point in time, inhaled budesonide is not being recommended for routine use, but can be considered to be prescribed by healthcare professionals on a case-by-case basis using the information described in this Interim Position Statement and the interim results from the PRINCIPLE trial (pre-print). This is an off-label use of a licensed medicine, the meaning of which should be discussed with the patient.

The eligibility and exclusion criteria for this Interim Position Statement have been drawn from those used in the PRINCIPLE trial and the Summary of Product Characteristics (SmPC) for inhaled budesonide. Healthcare professionals are encouraged to check the SmPC carefully.

Key messages from PRINCIPLE trial

- The trial included people in the community with COVID-19 at higher risk of complications from COVID-19 who are either 65 years or over or 50-64 years with comorbidities.
- Time to first self-reported recovery was shorter in the budesonide group (n=751) compared to usual care (n=1028) with an estimated median benefit of 3 days in patients with a positive SARS-CoV-2 test.
- There was no statistically significant improvement in COVID-19-related hospitalisation or deaths within 28 days of follow-up.
- There was benefit in self-reported early sustained recovery at 28 days.
- 79.7% of participants randomised to budesonide reported taking budesonide for at least 7 days.
- Results from the STOIC trial have been published, reporting a benefit from using inhaled budesonide in the community for people with COVID-19 within a smaller phase 2 trial.

Implementation

Eligibility criteria

Patients are eligible to be considered for treatment with inhaled budesonide when **all** of the following criteria are met:

- Patients with onset of symptoms[1] of COVID-19 within the past 14 days, and symptoms are ongoing.
- COVID-19 confirmed by PCR test within the past 14 days.
- 65 years and over OR 50-64 years with a comorbidity consistent with a long-term health condition from the flu list[2].

Exclusion criteria

Budesonide should not be administered in the following circumstances:

- Known hypersensitivity to budesonide or other inhaled corticosteroids.
- Patient admitted to hospital with COVID-19 before onset of treatment with budesonide.
- Almost recovered (generally much improved and symptoms now mild or almost absent).
- Any known contraindication to inhaled corticosteroids (as per SmPC: patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine. Lactose, the excipient in the product, contains small amount of milk proteins and can therefore cause allergic reactions).
- Patient currently prescribed inhaled or systemic corticosteroids.
- Unable to use an inhaler (even with assistance or reasonable adjustments).

Dose

The PRINCIPLE trial used inhaled budesonide (Pulmicort Turbohaler® 400 micrograms), 800 micrograms twice daily for up to 14 days or until all doses of the inhaler are used (whichever comes first). Supplementary information for patients on the use of a budesonide inhaler is available here.

The following alternative devices for delivering budesonide may be considered[3]:

1. Pulmicort Turbohaler® 200 micrograms
2. Budelin Novolizer® 200 micrograms
3. Easyhaler Budesonide® 400 micrograms
4. Easyhaler Budesonide® 200 micrograms

Healthcare professionals should consider whether the use of inhaled budesonide should be continued if admission to hospital is required due to deteriorating symptoms of COVID-19.

[1] Symptoms listed within the PRINCIPLE trial protocol include, but are not limited to: shortness of breath, general feeling of being unwell, muscle pain, diarrhoea and vomiting

[2] https://www.nhs.uk/conditions/vaccinations/flu-influenza-vaccine/), which differs from the PRINCIPLE trial eligibility criteria.

[3] The device used should be best suited to the patient

Co-administration

Largely, there is no restriction to concomitant medications using inhaled budesonide. The SmPC states that concomitant treatment with ketoconazole, HIV protease inhibitors or other potent CYP3A inhibitors may increase systemic budesonide levels, but that this is of little clinical significance for a short-term treatment of 14 days.

Safety reporting

Any suspected adverse drug reactions (ADRs) for patients receiving budesonide should be reported directly to the MHRA via the Yellow Card reporting site at: https://yellowcard.mhra.gov.uk/

Marketing authorisation

The use of inhaled budesonide in COVID-19 is off-label.

Governance

Off-label use of medication

There is no licensed alternative for this indication. The use of inhaled budesonide to treat COVID-19 is off-label. Prescribers should follow the principles of personalised care (including a shared decision making approach with the patient) to prescribe inhaled budesonide. Guidance on the prescribing of off-label medicines can be found here:

- https://www.gov.uk/drug-safety-update/off-label-or-unlicensed-use-of-medicines-prescribers-responsibilities

Effective from

This Interim Position Statement will be in effect from the date of publication.

Position review date

This is an Interim Position Statement based on pre-publication evidence. Further data from the PRINCIPLE trial is expected when the full cohort of patients completes their 28-day follow-up period. Published data from other trials may also require this Interim Position Statement to be reviewed. The full process of policy production has been abridged. Development of a clinical commissioning policy would replace this Interim Position Statement.