Evaluation of appropriateness of inhaled corticosteroid (ICS) therapy in COPD and guidance on ICS withdrawal

This guide provides an algorithm to identify people with chronic obstructive pulmonary disease (COPD) who might benefit from ICS treatment and those in whom it may not be appropriate, and an approach to withdrawing ICS in patients in whom it is not needed.

- In symptomatic patients with COPD at low risk of exacerbation, bronchodilation should be the first-line treatment. [GOLD 2017]. In symptomatic patients on monotherapy, treatment can be stepped up to a combination long-acting β2-agonist plus long acting muscarinic antagonist (LABA+LAMA), and for patients with severe breathlessness (CAT score 10 or MRC grade 2) initial therapy with LABA+LAMA may be considered [GOLD 2017].
- In patients with symptoms (CAT score <10 or MRC grade <2) at high risk of an exacerbation, R E S P I R A T O R Y  S O C I E T Y  U K  P R I M A R Y  C A R E

### History/examination

- Does the patient have asthma?
  - Documented history of asthma, with or without atopy (note: consider diagnoses made in people under 40 more likely to be correct)
  - A large degree of reversibility of airflow limitation (>15% and 400 mL in post-bronchodilator FEV1)
  - Does the patient have elevated blood eosinophils (>600 cells/mm3)

### Biomarker

- Does the patient have a high exacerbation risk?
  - >2 exacerbations or >1 exacerbation leading to hospitalisation in the previous 12 months?
  - AND Does the patient have elevated blood eosinophils?
    - >400 cells/mm3?

### Treatment at assessment consultation

- ICS+LABA
- ICS+LABA+LAMA (Triple Therapy)

### Continue ICS and titrate to the lowest dose to prevent airways exacerbations and / or asthma symptoms

- Monitor for potential ICS-related adverse events; continued exacerbation despite biomarker may indicate lack of efficacy of ICS or need for additional therapy

### For people with COPD who don’t need ICS

- Remove ICS or switch to lower-dose ICS in separate inhaler
  - Low/Medium-dose* ICS → stop ICS
  - Switch to LABA/LAMA (optimised bronchodilation)
- Interim call with patient (approx. 2 weeks) to check compliance and ensure stability

### Consultation with monitoring clinician including assessment of pulmonary function using spirometry

- If stable or improved continue with LABA/LAMA (optimised bronchodilation)
- If stable or improved continue with LABA/LAMA (optimised bronchodilation) stop ICS in separate inhaler
- Reassess need for ICS use if:
  - moderate or severe exacerbations
  - airflow limitation worsening (FEV1 decrease >100 mL)
  - Optional (blood eosinophil count >400)

### Follow-up with monitoring clinician for full clinical review

- See the patient:
  - twice yearly during the first year of ICS withdrawal,
  - followed by an annual review if the patient’s COPD is stable and exacerbation-free

* See next figure * ICS that is not in a combination inhaler is not licensed for treatment of COPD

Note: Whilst the use of LAMA and LABA+LABA combinations are recommended as options by GOLD for patients at risk of exacerbation, the licensed indications are as maintenance bronchodilator treatments to relieve symptoms in adult patients with COPD.
the recommended first-line treatment is a LAMA (stepping up to LABA+LAMA if necessary) or a LABA+LAMA. In more symptomatic high-risk patients, combination LABA+LAMA is the preferred first-line treatment, with LAMA or ICS+LABA given as alternative options [GOLD 2017]. If exacerbations persist on LABA+LAMA, patients can be stepped up to LABA+LAMA+ICS (triple therapy).

- Long-term ICS use is associated with a significant risk of pneumonia [Yawn 2013; Suissa 2013; Kew & Seniukovich 2014], and systemic effects [Price 2012]; therefore ICS-containing regimens are not recommended in low-risk patients, and should only be considered for high-risk patients with features of asthma, or as triple therapy if exacerbations persist despite treatment with a LABA+LAMA [GOLD 2017].

- Discontinuing ICS rapidly decreases the risk of serious pneumonia [Suissa 2015].

- Despite years of guidance on the limited role of ICS in COPD [GOLD 2001], there is evidence of inappropriate use of ICS in COPD patients who are at low risk of exacerbation [Vestbo 2014; Price 2014].

- Recent studies have indicated that ICS can be withdrawn in both low- and high-risk patients, provided adequate bronchodilator therapy is in place [Rossi 2014a; Rossi 2014b; Magnussen 2014]. Withdrawal of ICS only increased exacerbation rates in patients with both raised eosinophils and a history of frequent exacerbations [Calverley 2016].

### ICS dose switch guidance

<table>
<thead>
<tr>
<th>Current treatment</th>
<th>Switch to</th>
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<tbody>
<tr>
<td>Fluticasone/salmeterol - 250/50µg 1 puff twice daily</td>
<td>LABA/LAMA</td>
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<tr>
<td>Beclomethasone/formoterol - 100/6µg 2 puffs twice daily</td>
<td>LABA/LAMA</td>
</tr>
<tr>
<td>Fluticasone/vilanterol - 92/22µg 1 puff once daily</td>
<td>LABA/LAMA</td>
</tr>
<tr>
<td>Budesonide/formoterol - 400/12µg 1 puff twice daily</td>
<td>LABA/LAMA</td>
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<tr>
<td>- 200/6µg 2 puffs twice daily</td>
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<tr>
<td>Budesonide/formoterol - 400/12µg 1 puff twice daily</td>
<td>LABA/LAMA</td>
</tr>
<tr>
<td>Fluticasone/salmeterol - 500/50µg 1 puff twice daily</td>
<td>LABA/LAMA plus - budesonide 200µg 2 puffs twice daily</td>
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<tr>
<td>- fluticasone 250µg 1 puff twice daily</td>
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The following fixed ICS/LABA combination brands are licensed in COPD: Seretide Accucap, AirFluSal Forspiro, Relvar Ellipta, Symbicort, DuoResp Spiromax, FosterMDI and Foster NEXThaler, Fobumix Easyhaler.

### References


- Rossi A, Guerriero M, Carado A. Withdrawal of inhaled corticosteroids can be safe in COPD patients at low risk of exacerbation: a real-life study on the appropriateness of treatment in moderate COPD patients (OPTIMO). Respir Res 2016;17:77


