**HERTFORDSHIRE MEDICINES MANAGEMENT COMMITTEE (HMMC)**

**FLUTICASONE/FORMOTEROL (FLUTIFORM) FOR ASTHMA AND COPD - RECOMMENDED FOR RESTRICTED USE**

<table>
<thead>
<tr>
<th>Name:</th>
<th>What it is</th>
<th>Indications</th>
<th>Date Decision last revised</th>
<th>Decision Status</th>
<th>NICE / SMC Guidance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluticasone/formoterol (Flutiform®)</td>
<td>Inhaled twice daily fixed-dose combination of an inhaled corticosteroid (ICS) and a long-acting beta-2 agonist (LABA)</td>
<td>Asthma and COPD</td>
<td>April 2013</td>
<td>Final</td>
<td>NICE - No Guidance SMC – accepted for use for asthma</td>
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**HMMC Recommendation:** RECOMMENDED FOR RESTRICTED USE:

**ASTHMA:** as a treatment option for new patients or existing uncontrolled patients when a LABA/ICS fixed dose combination is indicated and a MDI is an appropriate delivery device.
- Advice for all patients with asthma:
  - Many patients with asthma may be over-treated, and may be receiving excessive doses of potent ICS and LABA:
    - Patients should be regularly reviewed and before starting a new drug or stepping up treatment, adherence with existing therapies, inhaler technique, and appropriate elimination of trigger factors should be confirmed.
    - Therapy should be stepped down once asthma is controlled. Reductions in ICS dose should be considered every 3 months, decreasing the dose by approximately 25–50% each time.
    - The dose of ICS should be titrated to the lowest dose at which effective control is maintained.

**COPD:** Flutiform® 250 micrograms/10 micrograms (2 puffs twice daily) is recommended as a third line treatment option when a LABA/ICS is indicated and patients are unable to use budesonide/formoterol (Symbicort 400/12 Turbohaler®) and fluticasone/salmeterol (Seretide 500 Accuhaler®) DPI devices but a MDI would be an appropriate delivery device.
- No LABA/ICS combination MDI is licensed for use in COPD and use for this indication would be ‘off label’.

**EFFICACY**
- Evidence from non-inferiority studies in patients with asthma indicate that Flutiform® is non-inferior to a comparable dose of fluticasone plus formoterol in separate inhalers, and non-inferior to a fluticasone/salmeterol combination inhaler in terms of effect on lung function.
- The individual drug components in Flutiform® have been available in separate inhalers for a number of years and there is evidence supporting their use in the treatment of asthma.
- COPD – refer to Assessment Against Ethical Framework, Evidence of Clinical Effectiveness.

**SAFETY**
- Limited long-term safety data.
- In key studies, the side-effect profiles of Flutiform® and the separate inhalers and fluticasone/salmeterol combination inhaler comparators appeared similar.
- Side-effects of LABAs and ICSs are well known.
- MHRA has advised that the prolonged use of high dose ICS carries a risk of systemic side effects.

**COST**
- Cost per patient per year = £219-554 depending on strength.
- Current costs – lower than Seretide® MDI (medium and high strength) and lower than Symbicort® (all strengths)
- The patent expiry for fluticasone propionate/salmeterol xinafoate (Seretide®) is 06/09/2013 and lower cost generics may then become available.

**PATIENT FACTORS**

**Flutiform® Background Information**
- Flutiform® is licensed for people whose asthma is not adequately controlled on an ICS and an ‘as required’ inhaled short-acting beta-2 agonist (SABA), or for people whose asthma is adequately controlled on both an ICS and a LABA.
- Flutiform® is available in 3 strengths: fluticasone/formoterol 50/5 micrograms, 125/5 micrograms and 250/10 micrograms, using a regimen of 2 puffs twice daily. The low and medium strengths are licensed for people aged 12 years and over; the high strength for people aged 18 years and over.
- Flutiform® is administered via a CFC-free aerosol in a pressurised metered dose inhaler (MDI)
- Potency of fluticasone in Flutiform® is approximately double beclometasone (except Qvar® & Fostair® devices) or budesonide.
This HMMC recommendation is based upon the evidence available at the time of publication. The recommendation will be reviewed upon request in the light of new evidence becoming available.

Assessment against Ethical Framework

Evidence of Clinical Effectiveness

Asthma

- Refer to efficacy and safety boxes.
- The primary outcomes of the 2 key studies in asthma reported that Flutiform is non-inferior in terms of effect on lung function to a comparable dose of fluticasone plus formoterol in separate inhalers (at week 8 mean change in pre-morning dose FEV1: 0.346 litres for Flutiform vs 0.267 litres for separate inhalers) and non-inferior to a fluticasone/salmeterol combination inhaler (at week 12 mean pre-dose FEV1: 2.402L for Flutiform vs 2.463L for fluticasone/salmeterol).
- Published studies are relatively short & small and primary outcomes used disease rather than patient orientated outcomes.
- Limited experience in patients with less severe asthma and no published studies in children under 18 years.
- No published head to head trials of high dose Flutiform® vs high dose Seretide® or Symbicort®.

COPD

- Both Flutiform® 250/10 micrograms and Seretide 250 Evohaler® (fluticasone/salmeterol 250//25 micrograms) are not licensed for use in COPD:
  - A dose of 2 puffs twice daily of these inhalers deliver the equivalent total daily dose of fluticasone that is delivered by Seretide 500 Accuhaler® (1 inhalation twice daily) which is licensed for COPD.
  - Some patients are unable to use the licensed DPI devices and an MDI device may be an appropriate delivery device.
  - Local specialists have indicated that they already use Seretide 250 Evohaler® ‘off-label’ for COPD and would be prepared to use Flutiform® 250/10 micrograms 'off-label' for COPD instead of Seretide 250 Evohaler®.

Cost of treatment and Cost Effectiveness

- No published NHS cost-effectiveness analysis is available.
- Refer to cost box and table below (costs of relevant comparators per year):

<table>
<thead>
<tr>
<th></th>
<th>Low strength*</th>
<th>Medium strength*</th>
<th>High strength*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flutiform® MDI</td>
<td>50/5 micrograms</td>
<td>125/5 micrograms</td>
<td>250/10 micrograms</td>
</tr>
<tr>
<td>(fluticasone/formoterol)</td>
<td>2 puffs twice daily: £219</td>
<td>2 puffs twice daily: £356</td>
<td>2 puffs twice daily: £554</td>
</tr>
<tr>
<td>Fostair® MDI</td>
<td>Not available</td>
<td>100/6 micrograms</td>
<td>Not available</td>
</tr>
<tr>
<td>(budesonide/formoterol)</td>
<td>2 puffs twice daily: £219</td>
<td>2 puffs twice daily: £357</td>
<td></td>
</tr>
<tr>
<td>Seretide® MDI (Evohaler)</td>
<td>50/25 micrograms</td>
<td>125/25 micrograms</td>
<td>250/25 micrograms</td>
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<tr>
<td>(fluticasone/salmeterol)</td>
<td>2 puffs twice daily: £219</td>
<td>2 puffs twice daily: £426</td>
<td>2 puffs twice daily: £724</td>
</tr>
<tr>
<td>Seretide® DPI (Accuhaler)</td>
<td>100/50 micrograms</td>
<td>250/50 micrograms</td>
<td>500/50 micrograms</td>
</tr>
<tr>
<td>(fluticasone/salmeterol)</td>
<td>1 puff twice daily: £219</td>
<td>1 puff twice daily: £426</td>
<td>1 puff twice daily*: £498</td>
</tr>
<tr>
<td>Symbicort® DPI (Turbohaler)</td>
<td>100/6 micrograms</td>
<td>200/6 micrograms</td>
<td>400/12 micrograms</td>
</tr>
<tr>
<td>(budesonide/formoterol)</td>
<td>2 puffs twice daily: £402</td>
<td>2 puffs twice daily or</td>
<td>2 puffs twice daily: £925</td>
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<tr>
<td></td>
<td></td>
<td>400/12 micrograms</td>
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</table>

Drug Tariff March 2013 and dmRd - Doses shown are for general comparison only and do not imply therapeutic equivalence.

* Asthma: Low strength - beclometasone (BDP) equivalent 400 micrograms per day (adult step 3)  
Medium strength - BDP equivalent 800-1000 micrograms per day (adult step 3)  
High strength - BDP equivalent 1600-2000 micrograms per day (adult step 4)  

The needs of the population

The needs of the community

Current costs for Flutiform® are lower than Seretide® MDI (medium and high strength) and Symbicort®. There is therefore the potential for short term cost savings for the local health economy. However, the patent expiry for Seretide® is 06/09/2013 and costs may then decrease if generic products become available.

Policy Drivers

- SIGN/BTS guidelines on asthma.
- NICE guidance on ICS for asthma recommends that if a combination device is chosen, then the least costly device that is suitable for the individual is recommended (evaluation did not include Flutiform® & Fostair® as launched after publication).
- Local COPD treatment guidelines & NICE Clinical Guidelines. No LABA/ICS combination MDI is licensed for use in COPD

Equity

No impact anticipated

Implementability

No issues identified

References