Response to public comments received on the ‘Inventory of paediatric therapeutic needs – Respiratory’ (EMA/244726/2016)

<table>
<thead>
<tr>
<th>Start of public consultation</th>
<th>11 May 2016</th>
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<tbody>
<tr>
<td>End of consultation (deadline for comments)</td>
<td>11 July 2016</td>
</tr>
</tbody>
</table>

Comments from:

Name of organisation or individual

(1) GSK
1. General comments

<table>
<thead>
<tr>
<th>Stakeholder number</th>
<th>General comment (if any)</th>
<th>Outcome (if applicable)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1)</td>
<td>GSK welcomes the opportunity to comment on the Guideline on <em>Inventory of paediatric therapeutic needs for Respiratory</em> prepared by EMA. Below and in the attached appendices, we have identified where data are available that may address some of the needs described in the inventory.</td>
<td>NA</td>
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### 2. Specific comments on text

<table>
<thead>
<tr>
<th>Line number(s) of the relevant text</th>
<th>Stakeholder number</th>
<th>Comment and rationale; proposed changes</th>
<th>Outcome</th>
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<tbody>
<tr>
<td><strong>Inhaled corticosteroids:</strong></td>
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<tr>
<td>Fluticasone propionate</td>
<td>1</td>
<td>Data on PK, efficacy and safety in children &lt; 4 years of age in the treatment of asthma</td>
<td>The comment is noted and this medicine will be removed from the inventory.</td>
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<tr>
<td></td>
<td></td>
<td>Comment: <strong>PK and Clinical data in children &lt; 4 years of age in the treatment of asthma have been published</strong> (see Appendix 1 below for citations).</td>
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<td></td>
<td></td>
<td><strong>FP MDI is approved for use in children aged 1-4 years for asthma across several countries in the EU.</strong></td>
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<tr>
<td><strong>Intranasal corticosteroids</strong></td>
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<tr>
<td>Fluticasone furoate</td>
<td>1</td>
<td>Data on PK, efficacy and safety in the treatment of allergic rhinitis and hypertrophic adenoids, particularly in children &lt; 6 years of age</td>
<td>As the authorisation status of this product does not cover the EU paediatric patients, it is considered relevant for this medicine to remain in the inventory.</td>
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<td></td>
<td></td>
<td>Comment: <strong>PK and Clinical data in children &lt; 6 years of age in the treatment of allergic rhinitis have been published</strong> (see Appendix 2 below for citations).</td>
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<td></td>
<td><strong>Intranasal FF is approved for use in children 2 &lt; 6 years in the treatment of allergic rhinitis in countries outside of the EU, including the US.</strong></td>
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<tr>
<td>Line number(s) of the relevant text</td>
<td>Stakeholder number</td>
<td>Comment and rationale; proposed changes</td>
<td>Outcome</td>
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<tr>
<td><strong>Combination therapy</strong>&lt;br&gt; Inhaled corticosteroids and long-acting Beta 2-agonists&lt;br&gt;Salmeterol + fluticasone propionate</td>
<td>1</td>
<td><strong>Data on PK, efficacy and safety in children &lt;5 years of age in the treatment of asthma</strong>&lt;br&gt;<strong>Comment:</strong> PK and Clinical data in children aged 4 years and above in the treatment of asthma have been published (see Appendix 3 below for citations).&lt;br&gt;Inhaled Salmeterol/FP is approved for children in the treatment of asthma from the age of 4 in the EU.&lt;br&gt;Data on safety in long-term use&lt;br&gt;<strong>Comment:</strong> Data from an ongoing study (200860) in Japanese subjects 6 months – 4 years of age with bronchial asthma will be submitted under Article 46 in due course.</td>
<td>The first comment is noted and the change will be implemented accordingly (i.e. &quot;Data on PK, efficacy and safety in children &lt;4 years of age in the treatment of asthma&quot;).&lt;br&gt;Regarding the second comment, as the safety data have not yet been submitted, no change at this point in time will be made. Of note, updates of the inventory list are foreseen in the future.</td>
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Appendix 1: Inhaled Fluticasone Propionate

Data on PK, efficacy and safety in children < 4 years of age in the treatment of asthma

1. Effectiveness of montelukast administered as monotherapy or in combination with inhaled corticosteroid in pediatric patients with uncontrolled asthma: A prospective cohort study

2. Bérubé D et al. Allergy, Asthma and Clinical Immunology 2014 10:1 Article Number 21

3. Salmeterol and fluticasone in young children with multiple-trigger wheeze


5. Bioavailability of inhaled fluticasone propionate via chambers/masks in young children


7. Evaluation of fluticasone propionate and fluticasone propionate/salmeterol combination on exercise in pediatric and adolescent patients with asthma


9. Effectiveness of fluticasone propionate and rare adverse effects in preschoolers with asthma

10. Bajraktarevic A et al. Allergy: European Journal of Allergy and Clinical Immunology 2011 66 SUPPL. 94 (584)

11. Combination therapy salmeterol/fluticasone versus doubling dose of fluticasone in children with asthma


13. Comparison of effectiveness between beclomethasone dipropionate and fluticasone propionate in treatment of children with moderate asthma


15. Salmeterol/fluticasone propionate vs. double dose fluticasone propionate on lung function and asthma control in children


17. Add-on salmeterol compared to double dose fluticasone in pediatric asthma: A double-blind, randomized trial (VIAPAED)
19. Fluticasone propionate/salmeterol and exercise-induced asthma in children with persistent asthma
21. Effect of inhaled fluticasone on lung function in infants with recurrent wheezing: a randomised controlled trial
23. Preemptive use of high-dose fluticasone for virus-induced wheezing in young children
25. Fluticasone or montelukast for preschool children with asthma-like symptoms: Randomized controlled trial
27. Inhaled corticosteroids in asthmatic children: Are they as safe in infants and preschoolers as in older children? A review
29. Fluticasone propionate in children and infants with asthma
31. Efficacy and safety of fluticasone propionate hydrofluoroalkane inhalation aerosol in pre-school-age children with asthma: A randomized, double-blind, placebo-controlled study
33. The efficacy and safety of fluticasone propionate in very young children with persistent asthma symptoms
35. Fluticasone improves pulmonary function in children under 2 years old with risk factors for asthma
37. Efficacy of fluticasone propionate on lung function and symptoms in wheezy infants
39. Effects of Inhaled Fluticasone Propionate in Children Less Than 2 Years Old with Recurrent Wheezing
41. Persistent wheezing in infants with an atopic tendency responds to inhaled fluticasone
42. Chavasse R.J et al. Archives of Disease in Childhood 2001 85:2 (143-147)
43. Safety of inhaled corticosteroid therapy in young children with asthma
44. Turktas I et al. Annals of Allergy, Asthma and Immunology 2001 86:6 (649-654)
45. The effect of inhaled fluticasone propionate in the treatment of young asthmatic children: A dose comparison study
47. Comparison of fluticasone propionate and sodium cromoglycate for the treatment of childhood asthma (an open parallel group study)
Appendix 2: Intranasal Fluticasone Furoate

Data on PK, efficacy and safety in the treatment of allergic rhinitis and hypertrophic adenoids, particularly in children < 6 years of age

1. Safety and efficacy of fluticasone furoate nasal spray in Japanese children 2 to <15 years of age with perennial allergic rhinitis: a multicentre, open-label trial
3. Efficacy and safety of once-daily fluticasone furoate nasal spray in children with seasonal allergic rhinitis treated for 2 wk
4. Meltzer E.O et al. Pediatric Allergy and Immunology 2009 20:3 (279-286)
5. HPA axis safety of fluticasone furoate nasal spray once daily in children with perennial allergic rhinitis
6. Tripathy I et al. Pediatric Allergy and Immunology 2009 20:3 (287-294)
7. Growth velocity reduced with once-daily fluticasone furoate nasal spray in prepubescent children with perennial allergic rhinitis
Appendix 3: Inhaled Salmeterol + Fluticasone Propionate

Data on PK, efficacy and safety in children < 5 years of age in the treatment of asthma.

Data on safety in long-term use.

1. Salmeterol and fluticasone in young children with multiple-trigger wheeze
3. Components of asthma control and treatment response of individual control criteria in children: Analysis of the PEACE study
5. Evaluation of fluticasone propionate and fluticasone propionate/salmeterol combination on exercise in pediatric and adolescent patients with asthma
7. Device type and real-world effectiveness of asthma combination therapy: An observational study
9. Combination therapy salmeterol/fluticasone versus doubling dose of fluticasone in children with asthma
11. Fluticasone propionate/salmeterol combination in children with asthma: Key cardiac and overall safety results
12. Li J.S et al. Clinical Research and Regulatory Affairs 2010 27:3 (87-95)
13. Step-up therapy for children with uncontrolled asthma receiving inhaled corticosteroids
15. Salmeterol/fluticasone propionate vs. double dose fluticasone propionate on lung function and asthma control in children
17. Fluticasone propionate/salmeterol and exercise-induced asthma in children with persistent asthma

19. A 6-month safety and benefit study of inhaled fluticasone propionate/salmeterol combination versus inhaled fluticasone propionate in the treatment of subjects 4-11 years old with persistent asthma.