



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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

<b>Start of public consultation</b>	11 May 2016
<b>End of consultation (deadline for comments)</b>	11 July 2016

### Comments from:

Name of organisation or individual

(1) GSK



## 1. General comments

Stakeholder number	General comment (if any)	Outcome (if applicable)
(1)	<p>GSK welcomes the opportunity to comment on the Guideline on <i>Inventory of paediatric therapeutic needs for Respiratory</i> prepared by EMA.</p> <p>Below and in the attached appendices, we have identified where data are available that may address some of the needs described in the inventory.</p>	NA

## 2. Specific comments on text

Line number(s) of the relevant text	Stakeholder number	Comment and rationale; proposed changes	Outcome
<b>Inhaled corticosteroids:</b> Fluticasone propionate	1	Data on PK, efficacy and safety in children < 4 years of age in the treatment of asthma  Comment: <b>PK and Clinical data in children &lt; 4 years of age in the treatment of asthma have been published (see Appendix 1 below for citations).</b>  <b>FP MDI is approved for use in children aged 1-4 years for asthma across several countries in the EU.</b>	The comment is noted and this medicine will be removed from the inventory.
<b>Intranasal corticosteroids</b> Fluticasone furoate	1	Data on PK, efficacy and safety in the treatment of allergic rhinitis and hypertrophic adenoids, particularly in children <6 years of age  Comment: <b>PK and Clinical data in children &lt; 6 years of age in the treatment of allergic rhinitis have been published (see Appendix 2 below for citations).</b>  <b>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.</b>	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.

Line number(s) of the relevant text	Stakeholder number	Comment and rationale; proposed changes	Outcome
<p><b>Combination therapy inhaled corticosteroids and long-acting Beta 2-agonists</b></p> <p>Salmeterol + fluticasone propionate</p>	1	<p>Data on PK, efficacy and safety in children &lt;5 years of age in the treatment of asthma</p> <p>Comment: <b>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).</b></p> <p><b>Inhaled Salmeterol/FP is approved for children in the treatment of asthma from the age of 4 in the EU.</b></p> <p>Data on safety in long-term use</p> <p>Comment: <b>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.</b></p>	<p>The first comment is noted and the change will be implemented accordingly (i.e. “Data on PK, efficacy and safety in children &lt;4 years of age in the treatment of asthma”).</p> <p>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.</p>

## 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
4. Mäkelä M.J et al. *Annals of Allergy, Asthma and Immunology* 2012 109:1 (65-70)
5. Bioavailability of inhaled fluticasone propionate via chambers/masks in young children
6. Blake K et al. *European Respiratory Journal* 2012 39:1 (97-103)
7. Evaluation of fluticasone propionate and fluticasone propionate/salmeterol combination on exercise in pediatric and adolescent patients with asthma
8. Murray J.J et al. *Open Respiratory Medicine Journal* 2011 5:1 (11-18)
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
12. Vaessen-Verberne A.A.P.H et al. *American Journal of Respiratory and Critical Care Medicine* 2010 182:10 (1221-1227)
13. Comparison of effectiveness between beclomethasone dipropionate and fluticasone propionate in treatment of children with moderate asthma
14. Ahmadiafshar A et al. *World Allergy Organization Journal* 2010 3:10 (250-252)
15. Salmeterol/fluticasone propionate vs. double dose fluticasone propionate on lung function and asthma control in children
16. De Blic J et al. *Pediatric Allergy and Immunology* 2009 20:8 (763-771)
17. Add-on salmeterol compared to double dose fluticasone in pediatric asthma: A double-blind, randomized trial (VIAPAED)

18. Gappa M et al. *Pediatric Pulmonology* 2009 44:11 (1132-1142)
19. Fluticasone propionate/salmeterol and exercise-induced asthma in children with persistent asthma
20. Pearlman D et al. *Pediatric Pulmonology* 2009 44:5 (429-435)
21. Effect of inhaled fluticasone on lung function in infants with recurrent wheezing: a randomised controlled trial
22. Mallo J et al. *Allergologia et Immunopathologia* 2009 37:2 (57-62)
23. Preemptive use of high-dose fluticasone for virus-induced wheezing in young children
24. Ducharme F.M et al. *New England Journal of Medicine* 2009 360:4 (339-353)
25. Fluticasone or montelukast for preschool children with asthma-like symptoms: Randomized controlled trial
26. Kooi E.M.W et al. *Pulmonary Pharmacology and Therapeutics* 2008 21:5 (798-804)
27. Inhaled corticosteroids in asthmatic children: Are they as safe in infants and preschoolers as in older children? A review
28. Garcia-Marcos L et al. *Current Drug Safety* 2008 3:1 (35-45)
29. Fluticasone propionate in children and infants with asthma
30. Marchac V et al. *Archives de Pediatrie* 2007 14:4 (376-387)
31. Efficacy and safety of fluticasone propionate hydrofluoroalkane inhalation aerosol in pre-school-age children with asthma: A randomized, double-blind, placebo-controlled study
32. Qaqundah P.Y et al. *Journal of Pediatrics* 2006 149:5 (663-670.e1)
33. The efficacy and safety of fluticasone propionate in very young children with persistent asthma symptoms
34. Carlsen K.C.L et al. *Respiratory Medicine* 2005 99:11 (1393-1402)
35. Fluticasone improves pulmonary function in children under 2 years old with risk factors for asthma
36. Teper A.M et al. *American Journal of Respiratory and Critical Care Medicine* 2005 171:6 (587-590)
37. Efficacy of fluticasone propionate on lung function and symptoms in wheezy infants

38. Hofhuis W et al. American Journal of Respiratory and Critical Care Medicine 2005 171:4 (328-333)
39. Effects of Inhaled Fluticasone Propionate in Children Less Than 2 Years Old with Recurrent Wheezing
40. Teper A.M et al. Pediatric Pulmonology 2004 37:2 (111-115)
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
46. Bisgaard H et al. American Journal of Respiratory and Critical Care Medicine 1999 160:1 (126-131)
47. Comparison of fluticasone propionate and sodium cromoglycate for the treatment of childhood asthma (an open parallel group study)
48. Price J.F et al. Respiratory Medicine 1995 89:5 (363-368)

## 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
2. Okubo K et al. Allergology international: official journal of the Japanese Society of Allergology 2015 64:1 (60-65)
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
8. Lee L.A et al. J Allergy Clin Immun Pract 2014; 2(4): 421-7



## **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
2. Mäkelä M.J et al. Annals of Allergy, Asthma and Immunology 2012 109:1 (65-70)
3. Components of asthma control and treatment response of individual control criteria in children: Analysis of the PEACE study
4. Pedersen S et al. Pediatric Pulmonology 2011 46:12 (1182-1188)
5. Evaluation of fluticasone propionate and fluticasone propionate/salmeterol combination on exercise in pediatric and adolescent patients with asthma
6. Murray J.J et al. Open Respiratory Medicine Journal 2011 5:1 (11-18)
7. Device type and real-world effectiveness of asthma combination therapy: An observational study
8. Price D et al. Respiratory Medicine 2011 105:10 (1457-1466)
9. Combination therapy salmeterol/fluticasone versus doubling dose of fluticasone in children with asthma
10. Vaessen-Verberne A.A.P.H et al. American Journal of Respiratory and Critical Care Medicine 2010 182:10 (1221-1227)
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
14. Lemanske Jr. R.F et al. New England Journal of Medicine 2010 362:11 (975-985)
15. Salmeterol/fluticasone propionate vs. double dose fluticasone propionate on lung function and asthma control in children
16. De Blic J et al. Pediatric Allergy and Immunology 2009 20:8 (763-771)
17. Fluticasone propionate/salmeterol and exercise-induced asthma in children with persistent asthma

18. Pearlman D et al. *Pediatric Pulmonology* 2009 44:5 (429-435)
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.
20. DA Stempel et al. Abstract 2427 and poster 2016 presented at the European Academy of Allergy and Clinical Immunology, Austria, 11-15 June 2016.  
Available at: <http://www.professionalabstracts.com/eaaci2016/iplanner/> Accessed 14 June 2016