

SUMMARY REMARKS

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WHY ARE WE HERE?

Joint Pulmonary-Allergy Drugs Advisory
Committee, Drug Safety and Risk
Management Advisory Committee, and
Pediatric Advisory Committee Meeting
December 10-11, 2008

Pediatric Advisory Committee Meeting 2007

Requested that AC be
convened to address benefit-
risk questions regarding use
of LABAs in children

FDA Meta-analysis of LABA-associated risks

Preparation for discussion at AC: age-specific analysis of risks of LABAs

- pediatric data in context of adult data
- framing of data to be analyzed done before analysis began:
 - FDA requested patient- and trial-level data on LABA trials from sponsors of LABAs
 - Studied indication: asthma
 - Parallel placebo and/or active controlled trials with and without ICS use
 - Approved dose and product in U.S.

Summary findings of meta-analysis

- Quantified risk of LABAs
 - Including data outside SMART study
- Found overall age trend with younger age associated with higher risk
- Could not draw distinctions regarding individual LABAs and how they might differ with respect to risk

Benefit data summary comments

- Risk data put in context of benefits: derived from review of the pivotal trials for drug approval
- Comparison of OSE review with others; “benefit”:
 - Interpretation of spirometric endpoints consistent with other analyses
 - OSE focused only on pivotal trials for drug approval
 - Interpretation of secondary benefits may vary: generally, trials were not powered to assess “quality of life” data

Given these findings:

What is the age-specific risk-benefit profile of LABAs for the asthma indication?

FDA's Questions for the Joint Advisory Committee on Long- Acting Beta-2 Agonists

December 10-11, 2008

We would like you to discuss and answer the questions below. We have structured Questions 1-4 by active LABA ingredient and by age group. If there are issues that you believe are relevant for the entire LABA class, please state so in your discussion. Note that Questions 5-8, which concern individual LABA-containing products, require voting.

1. Discuss the benefits of using salmeterol for the treatment of asthma in patients not adequately controlled on other asthma-controller medications (eg, low- to medium-dose inhaled corticosteroids) or whose disease severity clearly warrants initiation of treatment with two maintenance therapies, in each of the following age groups:

- in adults [\geq 18 years of age]
- in adolescents [12-17 years of age]
- in children [4-11 years of age]

2. Discuss the benefits of using formoterol for the treatment of asthma in patients not adequately controlled on other asthma-controller medications (eg, low- to medium-dose inhaled corticosteroids) or whose disease severity clearly warrants initiation of treatment with two maintenance therapies, in each of the following age groups:

- in adults [\geq 18 years of age]
- in adolescents [12-17 years of age]
- in children [5-11 years of age]

3. Discuss the risks of using salmeterol for the treatment of asthma in patients not adequately controlled on other asthma-controller medications (eg, low- to medium-dose inhaled corticosteroids) or whose disease severity clearly warrants initiation of treatment with two maintenance therapies, in each of the following age groups:

- in adults [\geq 18 years of age]
- in adolescents [12-17 years of age]
- in children [4-11 years of age]

4. Discuss the risks of using formoterol for the treatment of asthma in patients not adequately controlled on other asthma-controller medications (eg, low- to medium-dose inhaled corticosteroids) or whose disease severity clearly warrants initiation of treatment with two maintenance therapies, in each of the following age groups:

- in adults [\geq 18 years of age]
- in adolescents [12-17 years of age]
- in children [5-11 years of age] (Note that Symbicort is not indicated in this age group.)

5. Do the benefits of Serevent (salmeterol xinafoate) outweigh its risks for the maintenance treatment of asthma in patients not adequately controlled on other asthma-controller medications (eg, low- to medium-dose inhaled corticosteroids) or whose disease severity clearly warrants initiation of treatment with two maintenance therapies, in the following age groups:

- in adults [≥ 18 years of age] (Voting question)
- in adolescents [12-17 years of age] (Voting question)
- in children [4-11 years of age] (Voting question)

6. Do the benefits of Foradil (formoterol fumarate) outweigh its risks for the maintenance treatment of asthma in patients not adequately controlled on other asthma-controller medications (eg, low- to medium-dose inhaled corticosteroids) or whose disease severity clearly warrants initiation of treatment with two maintenance therapies, in the following age groups:

- in adults [\geq 18 years of age] (Voting question)
- in adolescents [12-17 years of age] (Voting question)
- in children [5-11 years of age] (Voting question)

7. Do the benefits of Advair (fluticasone propionate; salmeterol xinafoate) outweigh its risks for the maintenance treatment of asthma in patients not adequately controlled on other asthma-controller medications (eg, low- to medium-dose inhaled corticosteroids) or whose disease severity clearly warrants initiation of treatment with two maintenance therapies, in the following age groups:

- in adults [\geq 18 years of age] (Voting question)
- in adolescents [12-17 years of age] (Voting question)
- in children [4-11 years of age] (Voting question)

8. Do the benefits of Symbicort (budesonide and formoterol fumarate dihydrate) outweigh its risks for the maintenance treatment of asthma in patients not adequately controlled on other asthma-controller medications (eg, low- to medium-dose inhaled corticosteroids) or whose disease severity clearly warrants initiation of treatment with two maintenance therapies, in the following age groups:

- in adults [\geq 18 years of age] (Voting question)
- in adolescents [12-17 years of age] (Voting question)

9. Based on your discussion and votes above, are there further labeling changes or risk mitigation strategies for individual LABA products, or the class as a whole, that would be advisable?

10. What further studies, if any, would clarify important unanswered questions of safety and efficacy for individual LABA products or the class as a whole?