

Errata

FDA Briefing Package

Date: 12/04/08

To: Joint Meeting of the Pulmonary-Allergy Drugs Advisory Committee, Drug Safety and Risk Management Advisory Committee and Pediatric Advisory Committee on December 10-11, 2008

Subject: Risks and Benefits of Long-Acting Beta Adrenergic Agonists in the Treatment of Asthma

Drug Name (NDA numbers): Advair (021254, 021077)
Foradil (020831, 021279, 021592)
Serevent (020236, 020692)
Symbicort (021929)

Application Type: NDA

Applicant/sponsor: GlaxoSmithKline
Novartis
Astrazeneca

Summary of Changes

Office of Surveillance and Epidemiology

Section III. B. Summary of results and concepts stemming from review of pivotal trials leading to drug approval

Page 17, Table 8: Pivotal controlled trials of formoterol versus albuterol in patients age 13 years or older

Replace current Table 8 with the new version below. The numbers are changed based on data submitted by the sponsor, and do not change the overall assessment and conclusions of the review.

Table 8. Pivotal controlled trials of formoterol versus albuterol in patients age 13 years or older.				
Product	Formoterol 12 µg bid (Aerolizer)		Formoterol 10 µg bid (MDDPI Certihaler)	
Study	040	041	2302	2303
Comparator	Albuterol qid	Albuterol qid	Albuterol qid	Albuterol qid
N exposed to F	136	139	86	80
1° efficacy				
Δ 12° FEV ₁ ¹	0.3	0.3		
Δ 12° AUC FEV ₁ ² (L/hr)			1.49	1.64
2° efficacy				
Δ nocturnal asthma score ³	-0.3	0	-0.06	0.41 ⁹
Δ combined asthma score ⁴	-0.2	-0.1		
Δ % nights Awakened ⁵	-15	-13		
Δ % nights using rescue meds ⁶	-12	-8		
Δ rescue med use ⁷ (puffs/d)			-0.27	0.55
Δ asthma QOL ⁸			-0.01	0.25

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¹Difference in Forced Expiratory Volume-1 (FEV-1) between patients taking Formoterol versus patients taking Albuterol at 12 hours after the first dose.

²Difference in area under the curve of Forced Expiratory Volume-1 (FEV-1) comparing patients receiving Formoterol and those receiving Albuterol between 0 and 12 hours after the first dose.

³ A negative number would be in the direction of less severe asthma symptoms in Foradil treated patients, with a total of a 5 point scale (Appendix).

⁴A negative number would be in the direction of less severe asthma symptoms in Foradil treated patients.

⁵A decrease in this measure would be in the direction of less severe asthma symptomatology in Foradil treated patients.

⁶Decrease in this number would be in the direction of less need for rescue medication in Foradil treated patients.

⁷A decrease in puffs per day of rescue medication would be in the direction of greater symptomatic improvement in Foradil treated patients.

⁸Standardized validated questionnaire (Appendix). A decrease on this questionnaire would be in the direction of more severe symptomatology from asthma in Foradil treated patients.

⁹This value was submitted by the sponsor, but has not been independently reviewed by the Office of Surveillance and Epidemiology.

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Page 19, Table 9: Pivotal controlled trials of formoterol versus albuterol, or formoterol versus placebo in patients age 5-12 years.

Replace current Table 9 with the new version below. The numbers are changed based on data submitted by the sponsor, and do not change the overall assessment and conclusions of the review.

Table 9. Pivotal controlled trials of formoterol versus albuterol, or formoterol versus placebo in patients age 5-12 years.			
Product	Formoterol 12 µg bid (Aerolizer)		Formoterol 10 µg bid (MDDPI Certihaler)
Study	049	DP/PD2	604
Comparator	Placebo	Albuterol qid	Placebo
N exposed to F	171	77	127
1° efficacy			
Δ 12° AUC FEV ₁ ¹ (L/hr)	0.15		0.95
Δ PEF ² (L/min)		13.4	
2° efficacy			
Δ AM PEF ³ (L/min)	12		-8
Δ AM asthma score ⁴ (0-3)	-0.07	-0.12	-0.05 ¹²
Δ PM asthma score ⁵ (0-4)	-0.09	-0.07	-0.05
Δ sleep disturbance Score ⁶		-0.01	-0.07 ¹²
Δ AM rescue med use ⁷ (puffs/d)	-0.06	-0.14	0.11 ¹²
Δ PM rescue med use ⁸ (puffs/night)	-0.09	-0.08	0.06 ¹²
Δ % using no rescue ⁹		5	
Δ rescue med use ¹⁰ (puffs/24 hr)			-0.16
Δ % with exacerbation ¹¹	1.8		

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¹Difference in area under the curve of Forced Expiratory Volume-1 (FEV-1) comparing patients taking formoterol and patients taking albuterol between 0 and 12 hours after the first dose.

²Difference in peak flow rate in individuals receiving formoterol versus comparator.

³Change in morning peak flow rate in patients receiving formoterol versus comparator.

⁴ A negative number would be in the direction of less severe asthma symptoms in formoterol treated patients, with a total of a 4 point scale (Appendix).

⁵A negative number would be in the direction of less severe asthma symptoms in formoterol treated patients, with a 5 point scale.

⁶A negative number would be in the direction of less severe asthma symptoms in formoterol treated patients.

⁷⁻⁸A decrease in puffs per day of rescue medication would be in the direction of less severe asthma symptoms in formoterol treated patients.

⁹Increase in this number would be in the direction of less severe asthma symptomatology in formoterol treated patients.

¹⁰A decrease in puffs per day of rescue medication would be in the direction of less severe asthma symptomatology in formoterol treated patients.

¹¹Increase in percent with asthma exacerbation would be in the direction of more severe asthma symptomatology in formoterol treated patients.

¹²These values were submitted by the sponsor, but have not been independently reviewed by the Office of Surveillance and Epidemiology

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Page 25, Table 12: Pivotal controlled trials comparing formoterol/budesonide vs. budesonide in patients age 12 years and older.

Replace current Table 12 with the new version below. The numbers are changed based on data submitted by the sponsor, and do not change the overall assessment and conclusions of the review.

Table 13. Pivotal controlled trials comparing formoterol/budesonide vs. budesonide in patients age 12 years and older.		
Study	716	717
Formoterol dose	9 mg bid	9 mg bid
Budesonide dose	160 mg bid	320 mg bid
N exposed	123	124
1° efficacy		
Δ % 12° FEV ₁ ¹ (L)	0.18	0.20
Δ % pre-dose FEV ₁ ² (L)	0.14	0.12
2° efficacy (data obtained from sponsor)		
Δ % awakening-free nights ³	1.5	-2.1 (favors budesonide)
Δ rescue inhalations/day ⁴	-0.5	-0.7
Δ % of patients with exacerbations ⁵	-2.8	-14.2
Δ Asthma Quality of Life Questionnaire ⁶	0.2	0.3

¹Difference in percent Forced Expiratory Volume-1 (FEV-1) between patients taking Symbicort versus patients taking Budesonide at 12 hours after therapy.

²Difference in percent pre-dose Forced Expiratory Volume-1 (FEV-1) between patients taking Symbicort versus patients taking Budesonide.

³Increase in the percent of nights without nocturnal awakening would be in the direction of an improvement in asthma symptomatology.

⁴A decrease in daily rescue medication use would be in the direction of symptomatic improvement.

⁵Decrease in percent with asthma exacerbations would be in the direction of a decrease in asthma symptomatology.

⁶A difference of 0.5 points is considered clinically meaningful (see Symbicort labeling)