



## Therapeutic Class Review<sup>SM</sup>

### Respiratory – arformoterol (Brovana<sup>®</sup>)

July 2007

**New Product for Review:**

arformoterol (Brovana<sup>®</sup>) [Sepracor]

**Dossier Provided by Manufacturer:**

**Dossier Evaluation: (2)**

- 1- dossier w/missing components
- 2- all components present, except pharmacoeconomic model
- 3- all components present (comprehensive)

**Available Therapeutic Alternatives:**

Preferred/Formulary	Non-preferred/non-formulary
formoterol (Foradil <sup>®</sup> Aerolizer <sup>®</sup> ) [Schering] (dry powder inhaler)	arformoterol nebulizer solution (Brovana <sup>®</sup> ) [Sepracor]
salmeterol (Serevent <sup>®</sup> Diskus <sup>®</sup> ) [GSK] (dry powder inhaler)	formoterol nebulizer solution (Perforomist <sup>®</sup> ) [Dey] available fall 2007

**Executive Summary**

- Arformoterol (Brovana<sup>®</sup>) is a long acting  $\beta_2$ -agonist (LABA), and is dosed at 15mcg twice daily.
- Arformoterol (Brovana) is indicated for use in chronic obstructive pulmonary disease (COPD).
- Chronic obstructive pulmonary disease (COPD) causes more than 500,000 hospitalizations and more than 100,000 deaths in the United States each year. The treatment options available are limited, and no pharmacologic therapy slows the progressive loss of lung function that occurs.<sup>10</sup>
- Smoking cessation slows the decline in FEV<sub>1</sub>, but the sustained quit rates attained by intensive smoking cessation interventions are low. Long-term oxygen therapy is the only other treatment that has been shown to improve survival. However, oxygen appears to extend life by less than 2 years in patients with advanced disease.<sup>10</sup>
- Marketing – the manufacturer has:
  - expanded its sales force by 25%.
  - significant spending on physician and direct-to-consumer advertising.
  - years of experience in detailing levalbuterol (Xopenex<sup>®</sup>) to respiratory specialists and primary care physicians.
- There is no good comparative evidence for efficacy or safety.
- The place in therapy for a nebulized LABA is yet to be defined. Populations in which it might potentially be used include patients without the inspiratory drive or manual dexterity to activate a dry powder inhaler.

- Arformoterol (Brovana) is similar in action and safety to other LABA medications.
  - It is the most costly option of the branded LABA products available.
  - It is more expensive than the generic short acting  $\beta_2$  agonists available.

## Evidence

- There is no useful evidence to demonstrate the value of arformoterol (Brovana) relative to other LABAs:
  - Of the 16 studies on arformoterol (Brovana), 14 are pharmacokinetic studies.
  - In the two pivotal trials of 1,456 patients, only 288 (20%) received the FDA approved dose.
  - The two identical trials were only 12 weeks in duration.
- There is a risk that arformoterol (Brovana) may be used in patients with asthma, and there is no evidence to support its efficacy outside of COPD.
  - There have been no trials identified to date in asthma.
  - It is a nebulizer item, so it does decrease the risk of over-utilization. However, it is being promoted by a large known sales force (same manufacturer as Xopenex).

## Safety

- As a nebulized medication, there is a theoretical risk that someone might administer Brovana as a rescue medication.
- Arformoterol (Brovana) should be used with caution in patients with hepatic impairment because drug accumulation may occur.
- Like other LABAs, Brovana has the same black box warning for a potential increased risk of asthma-related death.

## *Considerations in subpopulations:*

- **Pediatrics** - The safety and effectiveness of arformoterol (Brovana) in pediatric patients has not been established.
- **Geriatrics**: No overall differences in safety or effectiveness were observed between subjects 65 years and over and younger subjects.
- **Gender**: No dosage adjustment is necessary based on gender.
- **Race, ethnicity**: No dosage adjustment is necessary based on race or ethnicity.

## Conclusion

Arformoterol (Brovana) is non-preferred/non-formulary because:

- Its place in therapy is not clear.
  - It provides another treatment option for COPD.
  - It has unclear value from an economic perspective.
  - It has an inconvenient dosage form requiring refrigeration.

- There is insufficient evidence to favor one long-acting bronchodilator over others.<sup>9</sup>

## Products

Drug Products	FDA approval <sup>a</sup>	Patent Expiration(s) <sup>c</sup>	FDA approved indications	Usual Dose/Route	Cost <sup>b</sup>	Potential Off-label Uses <sup>d</sup>
arformoterol (Brovana)	10/2006	3/2012	COPD, including chronic bronchitis and emphysema	nebulizer	\$172.80	Asthma, EIB*
formoterol (Foradil <sup>®</sup> )	2/2001	12/2016	Asthma, EIB*, COPD	Dry powder inhaler	\$122.56	
salmeterol (Serevent <sup>®</sup> discus)	9/1997	8/2008	Asthma, EIB, COPD, nocturnal asthma	Dry powder inhaler	\$136.45	Cystic Fibrosis, extrinsic asthma; prophylaxis,, high altitude pulmonary edema, occupational asthma
Formoterol (Perforomist)	5/2007 expected launch is fall 2007	5/2010	COPD, including chronic bronchitis and emphysema	nebulizer	Not Available	

<sup>a</sup> Date applies to approval date for the original brand name medication where there are now generics available.

<sup>b</sup> Cost estimate based on AWP (average wholesale price) listed in First Data Bank or MAC (maximum allowable cost) as of March 2007 for 1 month of therapy.

<sup>c</sup> Based on patents listed in Orange Book as of 03/29/2007.

<sup>d</sup> As listed in © 1974 - 2007 Thomson MICROMEDEX database or as referenced.

\*EIB (exercise induced bronchospasm)

## References

1. Brovana<sup>®</sup> (arformoterol nebulized solution) Prescribing Information. 2006. Sepracor Inc. Marlborough, MA.
2. Sepracor 2005 Annual Report accessed November 20, 2006 [http://library.corporate-ir.net/library/90/901/90106/items/190778/SEPR\\_05AR.pdf](http://library.corporate-ir.net/library/90/901/90106/items/190778/SEPR_05AR.pdf)
3. Sepracor page on the internet, press release: <http://phx.corporate-ir.net/phoenix.zhtml?c=90106&p=irol-newsArticle&ID=913184&highlight=> accessed November 2006.
4. Product Dossier: Brovana<sup>®</sup> (arformoterol nebulized solution). Sepracor Inc. Marlborough, MA. Reviewed 1/24/2007.
5. Foradil<sup>®</sup> (formoterol fumarate inhalation powder) Prescribing Information. June 2006. Novartis Pharma AG, Basle Switzerland.
6. Serevent<sup>®</sup> (salmeterol xinafoate inhalation powder) Prescribing Information. March 2006. GlaxoSmithKline, Research Triangle Park, NC.
7. Thomson Micromedex © 1974-2007. Micromedex<sup>®</sup> Healthcare Series USP DI<sup>®</sup> and Advice for the Patient<sup>®</sup>.

8. Appleton S, Poole P, Smith B, Veale A, Lasserson TJ, Chan MM, Cates CJ. Long-acting beta2-agonists for poorly reversible chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews* 2006, Issue 3. Art. No.: CD001104. DOI:10.1002/14651858.CD001104.pub2.
9. From the Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2006. Available from: <http://www.goldcopd.org>. accessed March 27, 2007.
10. Croxton TL, Weinmann GG, Senior RM, Wise RA, Crapo JD, and Buist AS. Clinical Research in Chronic Obstructive Pulmonary Disease Needs and Opportunities. 2003. *Am J Respir Crit Care Med*, Vol 167. pp 1142–1149.
11. Drug Class Review on Beta2-Agonists Final Report November 2006 (pdf) from the OHSU Evidence-based Practice Center.
12. Baumgartner RA, Hanania NA, Calhoun WJ, Sahn SA, Sciarappa K and Hanrahan JP. Nebulized arformoterol in patients with COPD: A 12-week, multicenter, randomized, double-blind, double-dummy, placebo- and active-controlled trial. 2007 *Clin Ther*, Vol 29 (2) 261-278.