

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**21-912**

**PROPRIETARY NAME REVIEW(S)**

**CONSULTATION RESPONSE**

**DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT  
OFFICE OF SURVEILLANCE AND EPIDEMIOLOGY  
(DMETS; WO22, Mail Stop Room 4447)**

<b>DATE RECEIVED:</b> April 13 2006	<b>DESIRED COMPLETION DATE:</b> August 4, 2006	<b>OSE REVIEW #:</b> 06-0051-1
<b>DATE OF DOCUMENT:</b> March 31, 2006	<b>PDUFA DATE:</b> October 12, 2006	
<b>TO:</b> Badrul Chowdhury, MD Director, Division of Pulmonary and Allergy Products HFD-570		
<b>THROUGH:</b> Linda Kim-Jung, PharmD, Team Leader Denise Toyer, PharmD, Deputy Director Carol Holquist, RPh, Director Division of Medication Errors and Technical Support		
<b>FROM:</b> Kristina C. Arnwine, PharmD, Safety Evaluator Division of Medication Errors and Technical Support		
<b>PRODUCT NAME:</b> Brovana (Arformoterol Tartrate Inhalation Solution) 15 mcg		
<b>NDA#:</b> 21-912		
<b>NDA SPONSOR:</b> Sepracor, Inc.		
<b>RECOMMENDATIONS:</b> <ol style="list-style-type: none"><li>1. DMETS has no objections to the use of the proprietary name, Brovana. This is considered a final decision. However, if the approval of the NDA is delayed beyond 90 days from the signature date of this document, the name with its associated labels and labeling must be re-evaluated. A re-review of the name before NDA approval will rule out any objections based upon approvals of other proprietary and/or established names from the signature date of this document.</li><li>2. DMETS recommends implementation of the label and labeling revisions outlined in ODS Consult 06-0051 dated June 27, 2006 to minimize potential errors with the use of this product.</li><li>3. DDMAC finds the proprietary name, Brovana, acceptable from a promotional perspective.</li></ol> <p>DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Diane Smith, project manager, at 301-796-0538.</p>		

Division of Medication Errors and Technical Support (DMETS)  
White Oak Bldg 22, Mail Stop Room 4447  
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: July 12, 2006  
NDA#: 21-912  
NAME OF DRUG: Brovana (Arformoterol Tartrate Inhalation Solution)  
NDA HOLDER: Sepracor, Inc.

I. INTRODUCTION:

This consult was written in response to a request from the Division of Pulmonary and Allergy Products (HFD-570), for assessment of the proprietary name Brovana, regarding potential name confusion with other proprietary or established drug names. Additionally, the sponsor submitted an independent name analysis on the proposed proprietary name, Brovana, for review and comment. The study was conducted by Drug Safety Institute (DSI), a subsidiary of the Brand Institute. Please refer to ODS Consult 06-0051 dated June 27, 2006 for DMETS' recommendations on the container labels, carton and insert labeling.

PRODUCT INFORMATION

Brovana is being developed for the indication of long-term maintenance treatment of bronchoconstriction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema. The usual dose of Brovana is 15 mcg inhaled by mouth via nebulizer twice daily. Brovana is supplied as a 2 mL sterile solution in unit-dose, low-density polyethylene (LDPE) vials individually overwrapped in foil in cartons of thirty vials.

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## II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of several standard published drug product reference texts<sup>1,2</sup> as well as several FDA databases<sup>3,4</sup> for existing drug names which sound-alike or look-alike to Brovana to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted<sup>5</sup>. The Saegis<sup>6</sup> Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

### A. EXPERT PANEL DISCUSSION (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name Brovana. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. DDMAC finds the name Brovana acceptable from a promotional perspective.
2. The Expert Panel identified five proprietary names that were thought to have the potential for confusion with Brovana. These products are listed in table 1 (see page 4), along with the dosage forms available and usual dosage.

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<sup>1</sup> MICROMEDEX Integrated Index, 2005, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.

<sup>2</sup> Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.

<sup>3</sup> AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 98-05, and the electronic online version of the FDA Orange Book.

<sup>4</sup> Phonetic and Orthographic Computer Analysis (POCA)

<sup>5</sup> WWW location <http://www.uspto.gov/tmdb/index.html>.

<sup>6</sup> Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at [www.thomson-thomson.com](http://www.thomson-thomson.com)

Table 1: Potential Sound-Alike/Look-Alike Names Identified by DMETS Expert Panel

Product Name	Dosage form(s), Established name	Usual adult dose	Other
Brovana	Azelnidone Inhalation Solution 5 mg/5 mL	15 mg by mouth via nebulizer twice daily	
Brovon	Adrenaline 0.9%, Papaverine 0.9% and Atropine 0.14% Inhalant 20 mL and 50 mL	Inhale by mouth three times daily.	LA/SA
Boniva	Ibandronate Sodium Tablets: 2.5 mg and 150 mg Injection: 5 mg	Oral: 2.5 mg by mouth once daily; or 150 mg by mouth once a month Injection: 3 mg intravenously every 3 months	LA
Arava	Leflunomide Tablets 10 mg, 20 mg, and 100 mg	100 mg by mouth daily for 3 days, then 10 mg to 20 mg by mouth once daily	LA
Provera	Medroxyprogesterone Tablets 2.5 mg, 5 mg, and 10 mg	5 mg or 10 mg daily for 5 to 10 days, beginning day 16 or 21 of the menstrual cycle or 5 mg or 10 mg daily for 12 to 14 consecutive days per month, beginning on day 1 or 16 of the cycle	SA/LA
Brovex	Brompheniramine Suspension, 12 mg/5 mL	1 to 2 tablets or 1 to 2 teaspoons by mouth twice daily.	LA
Brovex CT	Brompheniramine Chewable Tablets, 12 mg		
Brovex HC	Brompheniramine/Pseudoephedrine/ Hydrocodone Suspension 2.5 mg/30 mg/3 mg/5mL		
Brovex D	Brompheniramine/Phenyleprine Suspension, 12 mg/20 mg/5 mL		

\*Frequently used, not all-inclusive.

\*\*L/A (look-alike), S/A (sound-alike).

## B. PRESCRIPTION ANALYSIS STUDIES

### 1. Methodology:

Three separate studies were conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of Brovana with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. These studies employed a total of 119 health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. An inpatient order and outpatient prescriptions were written, each consisting of a combination of marketed and unapproved drug products and a prescription for Brovana (see page 5). These prescriptions were optically scanned and one prescription was delivered to a random sample of the participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via e-mail to the medication error staff.

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
<p><u>Outpatient RX:</u>            Brovana            H<sub>1</sub>            shake well and inhale            1 puff BID</p>	<p>“Next prescription is for Brovana. She’s to shake it well and inhale one puff twice a day. And she’s to have one of those.”</p>
<p><u>Inpatient RX:</u>            Brovana, shake well and inhale 1 puff bid</p>	

2. Results:

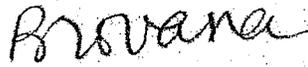
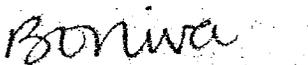
Three respondents in the verbal study misinterpreted the name as “Provana”. Provana can sound similar to the marketed drug product, Provera.

C. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name, the primary concerns relating to look-alike and sound-alike confusion with Brovana are Brovon, Boniva, Arava, Provera, and Brovex. Upon review of these names, the name Brovon was not reviewed further because it is an over-the-counter foreign product and it is unlikely that it will be prescribed in the U.S. Furthermore, the two products differ with regard to product strength, dosage form, and dosing frequency.

Additionally, DMETS conducted prescription studies to simulate the prescription ordering process. In this case, there was no confirmation that the proposed name could be confused with any of the aforementioned names. The majority of misinterpretations were misspelled/phonetic variations of the proposed name, Brovana. However, negative findings are not predicative as to what may occur once the drug is widely prescribed, as these studies have limitations primarily due to a small sample size.

1. Boniva was identified as a name that looks similar to Brovana. Boniva is a biphosphonate indicated for the treatment and prevention of osteoporosis in postmenopausal women. Brovana and Boniva both begin with the letter “B” and end with the letter “a” which are the primary contributors to the look-alike characteristics of the names. Additionally, both names contain the letters “o,” “v” and “n” in the middle portion of each name, however they are presented in different positions in each name, which may help to distinguish the two names from each other (see below).

With regard to product characteristics, Brovana and Boniva are taken orally, and both have the numeral “15” in their usual dose and product strength strength (15 mcg vs. 150 mg). However, the dosing frequency associated with those doses differs greatly (twice daily vs. once monthly). Boniva is also available in a 2.5 mg tablet that is taken once daily and a 5 mg injection that is administered every three months, unlike Brovana, which is an inhalation solution taken twice

daily. Overall, the orthographic differences in the middle portion of each name along with the differing dosage forms and dosing frequencies help to decrease the potential for confusion between Brovana and Boniva.

2. Arava was identified as a name that looks similar to Brovana. Arava is an antirheumatic agent indicated for the treatment of active rheumatoid arthritis in adults. The middle portion of Brovana (rova) can look similar to the ending of Arava (rava) which is the principal contribution to the look-alike characteristics of each name. However, the beginning letters of each name (B vs. A) differ along with the fact that Brovana contains two additional letters at the end of the name (-na) which help to distinguish the two names from each other (see below).

Brovana  
Arava

With regard to product characteristics, Brovana and Arava are both taken orally. However, the route of administration is the only product characteristic commonality that they share. Brovana is an inhalation solution, available in 15 mcg vials, with a usual dose is 15 mcg twice daily. Conversely, Arava is a tablet, available in 10 mg, 20 mg, and 100 mg tablets, with a usual dose of 100 mg daily for three days, then 10 mg to 20 mg once daily. The orthographic differences between the beginning and ending of each name, along with the differing usual dose, product strength, and dosing frequency decrease the potential for confusion between Brovana and Arava.

3. Provera was identified as a name that looks and sounds similar to Brovana. Additionally, there were three respondents in the verbal study who misinterpreted the name as "Provana," which may sound similar to Provera. Provera is a progestin indicated for the treatment of secondary amenorrhea and abnormal uterine bleeding as well as to reduce the incidence of endometrial hyperplasia. The beginnings of each name (Brovs. Prov) can sound similar and can also look similar depending on how they are scripted (see page 6). Additionally, the ending of each name (ana vs. era) may also look-alike when scripted. However, the endings of each name differ phonetically, which may help to distinguish the name pair.

Provera  
Brovana

Although Brovana and Provera may share orthographic characteristics, the two products do not share many commonalities with regard to product characteristics. Brovana and Provera are both taken orally. However, Brovana is supplied as 15 mcg inhalation solution with a usual dose of 15 mcg twice daily, unlike Provera which supplied as 2.5 mg, 5 mg and 10 mg tablets, with a usual dose of 5 mg or 10 mg once daily. Although it is possible to achieve a 15 mg dose with the product strengths of Provera, and thus both products can potentially have overlapping numerals (15), the dosing frequency differs, which should help to distinguish the two products from one another. Brovana is taken twice daily and Provera is taken only once daily for five to ten days or twelve to fourteen days on certain days of a woman's menstrual cycle, depending on the indication. Thus, prescription orders for Provera will most likely contain explicit instructions with regard to when and how long to take the medication (e.g. Provera, 5 mg once daily for 12 to 14 days, beginning on day one of menstrual cycle. Despite some orthographic similarities, the

differing product characteristics including dosage form, usual dose, dosing frequency, and context of use decrease the potential for name confusion between Brovana and Provera.

4. The Brovex product line was identified as a name that looks similar to Brovana. Brovex is a line of products containing brompheniramine alone (Brovex and Brovex CT) or in combination with phenylephrine (Brovex D) or pseudoephedrine and hydrocodone (Brovex HC). Brovana and the root name Brovex both begin with the letters "Brov" which is the principal contribution to the look-alike similarities of the names. However, the endings of each name (ana vs. ex) differ orthographically, which should help to distinguish the two names from each other. Additionally, since there is more product in the Brovex line, if a prescriber desires anything other than Brovex (e.g. Brovex HD), they must include the modifier in the prescription. Thus, when included in prescription orders, the modifiers used in conjunction with Brovex (CT, D, and HC) should help to further distinguish Brovex from Brovana.

Brovana

Brovex

With regard to product characteristics, Brovana and each of the products in the Brovex line are taken orally twice daily. Additionally, since Brovana and all of the products in the Brovex line are supplied in only one strength, the product strength may not be included in a prescription. However, Brovana is supplied as 15 mcg inhalation solution, and Brovex is either supplied as a suspension (Brovex, Brovex D, and Brovex HD) or a chewable tablet (Brovex CT). Thus, in addition to the orthographic differences between the names, the dosage form, if included on prescription, may help to further distinguish the two products from each other. Additionally, it is likely that prescribers will include the instructions "via nebulizer" on prescriptions for Brovana, which should also help to further distinguish orders for the two products. Overall, the orthographic differences between the ending of each name, along with the Brovex modifiers, and differing dosage forms, and context of use, should help to decrease the potential for confusion between the name pair.

D.   Name Review

1. Proprietary Name Promotional Assessment

Sepracor employed the   to b(4)  
evaluate whether the proprietary name Brovana makes claims that are misleading, exaggerated, or inappropriate. — conducted a research study utilizing an Internal Expert Panel and a total of 190 health care professionals that included physicians, nurses, and pharmacists. — concludes that Brovana was not found to be exaggerated, misleading, or inappropriate.

**DMETS Comment:** DMETS does not comment on the promotional nature of proprietary names. However, the Division of Drug Marketing, Advertising, and Communications (DDMAC) finds the name acceptable from a promotional perspective.

## 2. Proprietary Name Safety Assessment

Sepracor employed the [ ] to evaluate whether the proprietary name Brovana is confusingly similar in sound or appearance to proprietary or non-proprietary names in the United States. b(4)

### a. Internal Expert Panel Discussion

A — Internal Expert Panel identified the names Avandia, Boniva, Bravelle, Brevibloc, Diovan, Invanz, Movana, Survanta, and Trovan as names having similar sound and/or appearance to Brovana. After product profiles of the aforementioned names were compared to that of Brovana, minimal significant overlapping characteristics were identified that were regarded as an apparent issue for the prescribing/dispensing of Brovana. b(4)

#### *DMETS Comment*

DMETS identified the name Boniva as having similar appearance to Brovana. DMETS did not identify the names Avandia, Bravelle, Brevibloc, Diovan, Invanz, Movana, Survanta, or Trovan. However, upon analysis of these names, DMETS does not think they pose a risk due to minimal overlapping orthographic and/or phonetic similarities in addition to differing product characteristic such as indication, dosage form, prescription status, and context of use.

### b. Rx Studies

In the verbal prescription study for Brovana, one respondent misinterpreted Brovana as Provera. None of the remaining responses were misinterpretations for any other existing brand or generic drug name — concluded that due to the differing dosage forms, route of administration, frequency of administration, dosage strength, usual dose, and indication, the risk of confusion leading to an actual medication error is extremely low. b(4)

Additionally, the surveyed healthcare providers identified the names Boniva and Mylanta as having similar sound and appearance to Brovana, and the name Bonine as having similar sound to Brovana. After analysis with [ ] [ ] concluded that Boniva, Mylanta, and Bonine did not exceed their product characteristic, phonetic and/or orthographic thresholds for similarity with Brovana. b(4)

— staff conducted a search to identify any additional drug names that were not mentioned by the above survey respondents that might be considered similar to the proposed proprietary name. — identified the names Barobag, Brolade, Bromaline, Bromalix, Bomanate, Bromatane, Bromatap, Bromatapp, Brombay, Bromtapp, Bronkaid, Brotane, Dermovan, Frova, Povan, Procan, Proval, Proval #3, Provatene, Provera, and Truvada. After analysis with [ ] [ ] concluded that although [ ] [ ] Bromaline, Bromalix, Bromanate, Bromanyl, Bromatane, Bromatap, Bromatapp, Brombay, Bromtapp, Bronkaid, Brotane, Dermovan, Povan, Procan, [ ] [ ] Proval #3, Provatene, and Truvada exceed either phonologic and/or orthographic thresholds for similarity with Brovana, they share minimal overlapping product profile characteristics. Therefore, the likelihood of a medication error occurring due to confusion is minimal. b(4)

— also identified the name Brovon as a “Foreign Name Near-Identical to Brovana.” — concluded that when the product profiles of these two products are compared, there are significant differences in dosage strength and frequency of administration, thus reducing the likelihood of a medication error.

b(4)

*DMETS Comment*

DMETS identified the proprietary names Provera, Brovon, and Boniva as having similar sound and appearance to Brovana. DMETS did not identify the names Bonine or Mylanta. DMETS acknowledges DSI's conclusion that the potential for confusion between Brovana and Provera, Boniva, Bonine, Brovon, Mylanta, in addition to all of the names identified by the — staff, is decreased due to differing product characteristics in conjunction with phonetic and/or orthographic differences.

b(4)

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Attachment A

Verbal	Inpatient Written	Outpatient Written
Brivana	Brovama	Brevana
Brovana	Brovana	Brevancer
Brovana	Brovana	Brevara
Brovana	Brovana	Brevara
Brovanna	Brovana	Brovana
Brovanna	Brovana	Brovance
Brovanna	Brovarra	Brovance
Provana	Brovarra	
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	Brovarra	

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/s/

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DRUG SAFETY OFFICE REVIEWER  
Also signing for Kristina Arnwine 8/28/06.

Denise Toyer  
8/28/2006 03:20:56 PM  
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Also signing for Carol Holquist, DMETS Director, in her  
absence