CENTENE Corporation

MEDICAL NECESSITY GUIDELINE

DEPARTMENT: Pharmacy	**DOCUMENT NAME:** levalbuterol MDI/Inhalation Solution (Xopenex®)
PAGE: 1 of 6	**REFERENCE NUMBER:** NH.PMN.07
EFFECTIVE DATE: 09/06	**REPLACES DOCUMENT:**
RETIRED:	**REVIEWED:** 11/09, 02/14, 02/15, 4/16, 12/16, 10/17
PRODUCT TYPE: All	**REVISED:** 05/08, 04/10, 02/11, 02/12, 02/13, 02/14

IMPORTANT REMINDER

This Clinical Policy has been developed by appropriately experienced and licensed health care professionals based on a thorough review and consideration of generally accepted standards of medical practice, peer-reviewed medical literature, government agency/program approval status, and other indicia of medical necessity.

The purpose of this Clinical Policy is to provide a guide to medical necessity. Benefit determinations should be based in all cases on the applicable contract provisions governing plan benefits ("Benefit Plan Contract") and applicable state and federal requirements, as well as applicable plan-level administrative policies and procedures. To the extent there are any conflicts between this Clinical Policy and the Benefit Plan Contract provisions, the Benefit Plan Contract provisions will control.

Clinical policies are intended to be reflective of current scientific research and clinical thinking. This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

Description: Levalbuterol is a short-acting beta-agonist. It is the optically pure (R)-isomer of racemic albuterol. Levalbuterol is known to be responsible for the bronchodilator effects of the racemate, while the (S)-isomer is considered to be biologically inert.

Brand: levalbuterol (Xopenex HFA®): Aerosol; inhalation: 45mcg per actuation (as tartrate)
levalbuterol (Xopenex® inhalation solution): 0.31, 0.63, 1.25 mg/3ml

FDA Labeled Indications: Treatment or prevention of bronchospasm in adults and children 4 years of age and older (HFA) and greater than 6 years of age (nebulizer solution) with reversible obstructive airway disease.

Centene Medical Policy Statements represent technical documents developed by the Medical Management Staff. Questions regarding interpretation of these policies for the purposes of benefit coverage should be directed to a Medical Management Staff person.

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NOTE: No age limits will be applied to Xopenex® approval criteria.

Criteria for Approval:

A. Xopenex® approval requires documented congenital heart disease, cardiac arrhythmia, or other cardiac anomaly **OR**
B. Severe side effects from albuterol use documented in submitted office progress notes. Increased heart rate, tremor, agitation and many other side effects that accompany episodes of reversible reactive airway disease exacerbations make these physical signs difficult to attribute to albuterol exposure and
C. No reported allergy/hypersensitivity to albuterol, levalbuterol or any component of the specific dosage formulation (e.g., urticaria, rash, angioedema)

NOTE: The National Asthma Education and Prevention Program guidelines state that Xopenex®, at half the dose of albuterol, produces similar bronchodilation and side effects as albuterol. Current data do not support routine use of Xopenex® over albuterol.

Approval:

Initial Approval: 3 months.

Continued Approval: 12 months (based on resolution of adverse effects as compared with prior treatment with albuterol).

Special Instructions
➢ 2 inhalations (90 mcg) repeated every 4 to 6 hours; in some patients, 1 inhalation every 4 hours may be sufficient. More frequent administrations or a larger number of inhalations is not routinely recommended. It is

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recommended to prime the inhaler before using for the first time and in cases where the inhaler has not been used for more than 3 days by releasing 4 test sprays into the air, away from the face.
- Administered 3 times/day by nebulization.
- Increasing use of a short-acting beta agonist (using SABA >2 days/week) or the use of more than one canister a month indicates inadequate control of asthma and the need for initiating or intensifying anti-inflammatory therapy.
- Some trials have shown increased efficacy of levalbuterol over racemic albuterol while other trials have failed to detect any advantage.
- Levalbuterol has not been shown to have fewer systemic beta-adrenergic adverse effects (tremor, nervousness) than albuterol.
- Pregnancy Category C.

References:

1. Xopenex® HFA prescribing information. AccessedDecember 2012. http://www.xopenex.com/files/Xopenex-HFA-PI-900875R05.pdf
2. Xopenex® nebulizer solution prescribing information. AccessedDecember, 2012. http://www.xopenex.com/files/XopenexUDV-PI-400437R07.pdf
3. National Heart, Lung and Blood Institute: Expert Panel Report 3 (EPR3): Guidelines for the Diagnosis and Management of Asthma, 2007, Section 3, Component 4 – Medication, Accessed December, 2012. http://www.nhlbi.nih.gov/guidelines/asthma/07_sec3_comp4.pdf
4. Nelson HS, Bensch G, Pleskow WW et al. Improved bronchodilation with levalbuterol compared with racemic albuterol in patients with asthma. *J Allergy Clin Immunol.* 1998;102: 943-952.

5. Gawchik SM,Consuelo SL, Noonan M, et al. The safety and efficacy of nebulized levalbuterol compared with racemic albuterol and placebo in the treatment of asthma in pediatric patients. *J Allergy Clin Immunol* 1999; 103:615-21
6. Xopenex Monograph, Clinical Pharmacology. Accessed December 2012.

Revision Log	
Revision	**Date**
Separate Xopenex and Xopenex HFA guidelines. Xopenex HFA a Medical Necessity Guideline; Xopenex a Prior Authorization Guideline.	05/08
Updated References to reflect current literature search.	05/08
Change "FDA Labeled Indications" section from adolescents age 6 years to adolescents age 4 years.	05/08
Remove the following two items from the "Criteria for Approval" section "a. Patient has failed a maximum dose of nebulized alternate preferred albuterol for at lease one week or documented intolerance to beta-adrenergic side effects; **and** b. Patient currently compliant on a regimen of anti-inflammatory asthma therapy".	05/08
Added the following to "Criteria for Approval" "…[Documented trial and failure of Albuterol HFA formulations] due to lack of efficacy. Noted that levalbuterol has not been shown to have fewer systemic beta-adrenergic adverse effects (tremor, nervousness) than albuterol and this will not be considered criteria for approval."	05/08
Add the following to the "Approval" section "Reauthorization for 12 months if documentation submitted showing improved symptoms and no adverse events."	05/08
Remove the following from "Special Instructions" section:	05/08

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Xopenex was recently approved for treatment in children as young as 6years of age. A double-blind, multi-center, placebo-controlled trial randomized 338 pediatric patients to tid nebulizations of 0.31mg or 0.63mg of levalbuterol, 1.25mg or 2.5mg of albuterol, or placebo. After 21 days of treatment FEV scored for all active treatments were significantly improved ($p<0.05$) in comparison to placebo. Levalbuterol 0.31mg demonstrated bronchodilation equivalent to that associated with albuterol 2.5mg and was indistinguishable from placebo for most β_2-adrenoceptor-mediated side effects. The 0.31mg strength of levalbuterol is the starting dose recommended for children aged 6 to 11 years of age.	
Remove the following from "Special Instructions" section: Dosing: Children aged 6-11 years: 0.31mg tid, not to exceed 0.63mg tid. Adults and children aged > 12 years: 0.63mg administer tid every 6 to 8 hours, to a maximum of 1.25mg tid.	05/08
Add the following to the "Special Instructions" section: Adults and children 4 years of age and older: 2 inhalations (90 mcg) repeated every 4 to 6 hours; in some patients, 1 inhalation every 4 hours may be sufficient. More frequent administrations or a larger number of inhalations is not routinely recommended. It is recommended to prime the inhaler before using for the first time and in cases where the inhaler has not been used for more than 3 days by releasing 4 test sprays into the air, away from the face.	05/08
Add the following to the "Special Instructions" section: Some trials have shown increased efficacy of levalbuterol over racemic albuterol while other trials have failed to detect any advantage.	05/08
Updated Reference section to reflect current literature search and reference documents.	11/09

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Combined Xopenex nebulizer and HFA into an MN criteria document with P&T approved retirement of the nebulizer PA document and removal from the PDL. Updated Reference section to reflect current literature search.	04/10
Removal of age limits based on P&T Review.	04/10
Revision of a definition of adverse effects attributable to albuterol use. Initial approval decreased from 12 months to 3 months for an evaluation of differential resolution of adverse effects with Xopenex vs. albuterol treatment.	02/11
References updated.	02/12
Added criteria "C" in the "Criteria for Approval" section.	02/13
Added "using SABA >2 days per week" in "Special Instructions".	02/13
Updated Reference section to reflect current literature search and reference documents.	02/13
No Changes.	02/14
No Changes.	02/15
Removed "as presented in submitted office progress notes" from criterion A.	6/15
Annual Review, No Changes	12/16
Annual Review, No Changes	10/17

POLICY AND PROCEDURE APPROVAL

Pharmacy & Therapeutics Committee: Approval on file

V.P., Pharmacy Operations: Approval on file

Sr. V.P., Chief Medical Officer: Approval on file