



Therapeutic Class ReviewSM

Antihistamine – levocetirizine (Xyzal[®])

December 2007

New Product for Review:

Levocetirizine (Xyzal[®]) [UCB]

Dossier Provided by Manufacturer:

Dossier Evaluation: (2)

- 1 - Dossier missing significant clinical trial(s).
- 2 - Mfg. provided all relevant trials; Missing pharmacoeconomic model.
- 3 - Mfg. provided all relevant trials and information.

Available Therapeutic Alternatives:

Preferred/Formulary	Non-Preferred/Non-Formulary
fexofenadine (Allegra [®]) [various]	cetirizine (Zyrtec [®]) [UCB]
	desloratadine (Clarinet [®]) [Schering]
	loratadine (Claritin [®]) [Schering Plough]

* Covered with prior authorization

Executive Summary

- Levocetirizine (Xyzal), a stereoisomer of cetirizine (Zyrtec), is a second generation antihistamine indicated for the treatment of PAR, SAR, and CIU.
 - Allergic rhinitis affects more than 30% of adults and up to 40% of children in the U.S.
 - CIU is a skin condition that appears as flares and wheals resulting from activation of the histamine pathway.

- Current market status of second-generation antihistamines includes:

Product	Prescription only	Over-the-counter	Generic availability
cetirizine (Zyrtec)	X	anticipated late 2007	anticipated late 2007
desloratadine (Clarinet)	X		
fexofenadine (Allegra)	X		X
levocetirizine (Xyzal)	X		
loratadine (Claritin)		X	X

- National and international treatment guidelines for the treatment of allergic rhinitis make no distinction between the available second-generation antihistamine alternatives.
- Intranasal corticosteroids are the first line therapy for the treatment of allergic rhinitis.
- Over-the-counter antihistamine products have not historically been covered under the prescription benefit at Regence.

Evidence

- The evidence for levocetirizine (Xyzal) is of uncertain validity. Available evidence includes:
 - Three studies in patients with SAR.
 - Six studies in patients with PAR.
 - Two studies in patients with CIU.
- There is no evidence supporting superiority of levocetirizine (Xyzal) over other second-generation antihistamine products in the treatment of SAR, PAR, or CIU.
- There is no current evidence comparing levocetirizine (Xyzal) to intranasal corticosteroids.^[2,3,4,5,6]
- There is no direct evidence of differences in harms between levocetirizine (Xyzal) and other second-generation antihistamines.

Considerations in subpopulations

- Pediatrics - Safety and effectiveness of levocetirizine (Xyzal) was studied in pediatrics 6 years of age and older.
- Geriatrics – There were not sufficient numbers of patients 65 years of age and older enrolled in levocetirizine (Xyzal) clinical trials to determine whether they respond differently than younger subjects.
- Gender, race, and ethnicity – no information was reported.

Product Value

Levocetirizine (Xyzal) provides:

- another treatment choice for antihistamine therapy in patients with allergic rhinitis and urticaria;
- a competitive alternative for desloratadine (Clarinx) and fexofenadine (Allegra).

Conclusion

Levocetirizine (Xyzal) is non-preferred/non-formulary because there is no useful evidence demonstrating any additional benefits over currently available medications in the treatment of seasonal or perennial allergic rhinitis or chronic idiopathic urticaria.

Products

Drug Products	FDA Approval ^a	Patent Expiration(s) ^c	FDA approved indications	Usual Dose/Route	Cost ^b	Potential Off-label Use ^d
cetirizine (Zyrtec)	12/95	12/07	<ul style="list-style-type: none"> Seasonal allergic rhinitis (SAR) in patients 2 years of age and older Perennial allergic rhinitis (PAR) in patients 6 months of age and older Chronic idiopathic urticaria in patients 6 months of age and older 	5 mg PO QD 10 mg PO QD	\$83.25 \$83.25	<ul style="list-style-type: none"> Allergic cough Asthma; Adjunct Atopic dermatitis Drug induced rash, antiretroviral related, prophylaxis Excessive vomiting in pregnancy Food Allergy Motion sickness Urticaria, acute
desloratadine (Clarinet)	12/01	10/07	<ul style="list-style-type: none"> Seasonal allergic rhinitis (SAR) in patients 2 years of age and older Perennial allergic rhinitis (PAR) in patients 6 months of age and older Chronic idiopathic urticaria in patients 6 months of age and older 	5 mg PO QD	\$103.80	<ul style="list-style-type: none"> Urticaria, acute
fexofenadine (Allegra)	7/96	11/06 Expired	<ul style="list-style-type: none"> Seasonal allergic rhinitis (SAR) in patients 6 years of age and older Chronic idiopathic urticaria in patients 6 years of age and older 	60 mg PO BID 180 mg PO QD	\$48.00 \$39.00	<ul style="list-style-type: none"> Hymenoptera immunology, pretreatment Motion sickness Perennial allergic rhinitis Solar urticaria
levocetirizine (Xyzal)	5/07	5/10	<ul style="list-style-type: none"> Seasonal allergic rhinitis (SAR) in patients 6 years of age and older Perennial allergic rhinitis (PAR) in patients 6 years of age and older Chronic idiopathic urticaria in patients 6 years of age and older 	5 mg PO QHS	\$84.40	n/a
loratadine (Claritin)	4/93	12/02 Expired	<ul style="list-style-type: none"> Seasonal allergic rhinitis (SAR) in patients 2 years of age and older Chronic idiopathic urticaria in patients 2 years of age and older 	10 mg PO QD	\$12.30	<ul style="list-style-type: none"> Asthma Cough, chronic Eosinophilic nonallergic rhinitis Exercise-induced asthma Insect bite; prophylaxis

^a Date applies to approval date for the original brand name medication where there are now generics available.

^b Cost estimate based on AWP (average wholesale price) listed in First Data Bank as of 9/6/2007, for 30 days of therapy.

^c Based on patents listed in Orange Book as of 06/28/07.

^d As listed in © 1974 - 2007 Thomson MICROMEDEX database or as referenced.

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