



Therapeutic Class ReviewSM

Pain – cyclobenzaprine (Amrix[®])

April 2008

New Product for Review:

cyclobenzaprine ERC (Amrix[®]) [Cephalon]

Dossier Provided by Manufacturer: Yes

Dossier Evaluation: (Dossier ranked 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.

Executive Summary

- The U.S. Food and Drug Administration (FDA) approved cyclobenzaprine ERC (Amrix) in February 2007. It was launched in October 2007.
- Cyclobenzaprine ERC (Amrix) is indicated as an adjunct to rest and physical therapy for relief of muscle spasm associated with acute, painful musculoskeletal conditions.
- Use of cyclobenzaprine ERC (Amrix) for periods longer than two or three weeks is not recommended.^[1]
- Cyclobenzaprine ERC (Amrix) capsules should not be opened, crushed or chewed, as doing so may alter the absorption and systemic exposure.
- There is a 35% increase in cyclobenzaprine levels when cyclobenzaprine ERC (Amrix) is given with food.
- Cyclobenzaprine ERC (Amrix) should not be used in elderly patients or in patients with impaired hepatic function.
- There is no evidence comparing the efficacy and safety of cyclobenzaprine ERC (Amrix) to preferred/formulary options.
- The evidence does not support any conclusions about the comparative safety or efficacy of any of the skeletal muscle relaxants.^[3]

Evidence

- The evidence from two randomized, controlled trials (RCTs) in patients with muscle spasms associated with acute painful musculoskeletal conditions is not useful.
- 174 (34.5%) of the 504 ITT patients did not complete 14 days of treatment with study drug.

Decision

Cyclobenzaprine ERC (Amrix) is non-preferred/non-formulary because:

- There is no evidence of its superiority over other skeletal muscle relaxants.
- There are safety concerns with this product, including:

- It is contraindicated in patients over 65;
- It is contraindicated in patients with any level of hepatic impairment; and
- There is a 35% increase in drug levels when taken with food.
- There are less expensive generic and preferred/formulary brand alternatives available.

Products

Drug Products	FDA approval ^a	Patent Expiration(s) ^c	FDA approved indications	Usual Dose/Route	Potential Off-label Uses ^d
carisoprodol	4/1959	N/A	Musculoskeletal conditions	1 PO QID	
carisoprodol compound (w ASA +/- codeine)	11/1983	N/A		1-2 PO QID	
chlorzoxazone	8/1958	N/A	Musculoskeletal conditions	250-500mg PO 3-4 times a day	
cyclobenzaprine hydrochloride	8/1977	N/A	Muscle spasm	5-10mg PO TID	fibromyalgia
cyclobenzaprine ERC (Amrix [®])	02/2007	02/2010	Muscle spasm	15-30mg PO QD	
diazepam	11/1963	N/A	Muscle relaxant	2 to 10 mg 3 or 4 times/day	
metaxalone 800mg (Skelaxin [®])	8/1962	12/2021	adjunct to rest, physical therapy, and other measures for the relief of discomforts associated with acute, painful musculoskeletal conditions.	1 tab tid-qid	
methocarbamol	7/1957	N/A	Musculoskeletal conditions:	4-8 G/day (max) divided, 3 or 4 times daily	
orphenadrine (Norflex [®]) various	6/1998	N/A	Musculoskeletal conditions	100mg PO BID	
orphenadrine compound various	10/1982	N/A	Musculoskeletal conditions	1-2 PO 3-4 times/day	

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

^c Based on patents listed in Orange Book as of 01/30/2008.

^d As listed in © 1974 - 2008 Thomson MICROMEDEX database or as referenced.

References

1. Amrix[™] (Cyclobenzaprine Hydrochloride Extended-Release Capsules) Prescribing Information. September 2007. Cephalon, Inc., Frazer, PA:
2. Amrix[™] Fact Sheet available at http://www.cephalon.com/newsroom/assets/amrix_fact_sheet_010308.pdf accessed January 11, 2008.
3. Oregon Health Resources Commission: Drug Class Review on Skeletal Muscle Relaxants Updated Final Report #2. May 2005. http://www.oregon.gov/OHPPR/HRC/docs/HRC_Reports/SMR_HRC.pdf accessed January 31, 2008.
4. Cyclobenzaprine Hydrochloride tablets Prescribing Information. March 2006. Watson Laboratories, Inc. Corona, CA:
5. Skelaxin (Metaxalone) Tablets Prescribing Information. April 2007. King Pharmaceuticals, Inc., Bristol, TN

6. Browning R, Jackson J L, O'Malley P G. Cyclobenzaprine and back pain: a meta-analysis. *Archives of Internal Medicine*. 2001;161(13):1613-1620.
7. Koes B and van Tulder M. Low back pain (acute) Clinical Evidence Review. Available at: <http://clinicalevidence.bmj.com/ceweb/conditions/msd/1102/1102-get.pdf>. Accessed February 1, 2008.
8. Thomson Micromedex © 1974-2008. Micromedex[®] Healthcare Series USP DI[®] and Advice for the Patient[®].
9. Drug Facts and Comparisons. Drug Facts and Comparisons 4.0 [online]. 2008. Available from Wolters Kluwer Health, Inc. at: <http://online.factsandcomparisons.com/index.aspx?> Accessed January 8, 2008.
10. Methocarbamol Tablets USP Prescribing Information. June 2006. Watson Laboratories, Inc. Corona, CA.
11. Product Medication Information for Amrix (cyclobenzaprine Hydrochloride Extended-Release Capsules). Cephalon, Inc., Frazer, PA.