



Therapeutic Class ReviewSM

Selegiline transdermal system (Emsam[®])

July 2006

New Product for Review:

Selegiline transdermal system (Emsam[®])

Dossier Provided by Manufacturer:

Dossier Evaluation: 1

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

Executive Summary

- There is possibly useful evidence showing modest efficacy of selegiline transdermal system (Emsam) in achieving a clinically relevant response in major depressive disorder over six to eight weeks.
- There is no useful evidence that selegiline transdermal system (Emsam) provides more clinical advantages than other formulary alternatives in major depressive disorder.
- There is no useful evidence that selegiline transdermal system (Emsam) is safer in the treatment of major depressive disorder than other formulary alternatives.
- Considerations in Subpopulations:
 - Pediatrics: There is no useful evidence to establish the safety and efficacy of selegiline transdermal system (Emsam) in pediatric patients.
 - Geriatrics:
 - Current clinical experience with selegiline transdermal system (Emsam) indicates no overall differences in effectiveness between younger and older (> 65 years of age) patients.
 - In short-term, placebo-controlled depression trials, patients age 50 and older appeared to be at higher risk for rash.
 - Race, ethnicity, and/or gender: Current clinical experience with selegiline transdermal system (Emsam) has not identified differences in safety or efficacy based on race, ethnicity or gender.

Decision

- Selegiline transdermal system (Emsam) is non-preferred/non-formulary because there is:
 - No useful evidence for improved efficacy over existing formulary agents.
 - No useful evidence for improved safety over existing formulary agents.
 - Substantially higher cost relative to other formulary agents.

Products

Drug Products	FDA approval ^a	FDA approved indications	Usual Dose/Route	Potential Off-label Uses ^c
Serotonin/Norepinephrine Reuptake Inhibitors (SNRIs)				
duloxetine (Cymbalta [®])	8/2004	Major depressive disorder, Pain associated with diabetic peripheral neuropathy	60mg po QD 60mg po QD/BID	Pain management Stress urinary incontinence Fibromyalgia
venlafaxine (Effexor [®]) (Effexor XR [®])	12/2003 10/1997	Major depressive disorder, Generalized Anxiety disorder, Social Anxiety disorder	150mg po daily	Atypical facial pain, Post-mastectomy pain syndrome, Colonic sensorimotor functions, Obsessive-compulsive disorder, Diabetic peripheral neuropathy Painful polyneuropathy ¹ , Bipolar depression, Premenstrual dysphoric disorder, Management of hot flushes, diabetic neuropathic pain, ⁴¹ Fibromyalgia ⁴⁹
Selective Serotonin Reuptake Inhibitors (SSRIs)				
citalopram	7/1998	Depression	20mg po daily	Headache Panic disorder
escitalopram (Lexapro [®])	8/2002	Depression, Generalized anxiety disorders	10mg po daily	Anxiety with depression
fluoxetine Prozac Weekly [®]	12/1987 02/2001	Depression, Bulimia nervosa, Obsessive-compulsive disorder, Panic disorder, Premenstrual dysphoric disorder	20mg po daily 90mg po QWk	Body dysphoric disorder, fibromyalgia, post-traumatic stress disorder, Raynaud's phenomenon
fluvoxamine	12/1994	Obsessive-compulsive disorder	200mg po daily	Depression, Autism, Panic disorder, Social anxiety disorder
paroxetine	12/1992	Same as sertraline (Zoloft) and generalized anxiety disorder	20mg po daily	Pathological gambling
sertraline (Zoloft [®])	12/1991	Depression, obsessive-compulsive disorder, panic disorder, posttraumatic stress disorder, premenstrual dysphoric disorder, social anxiety disorder	100mg po daily	dysthymia
Tricyclic Antidepressants (TCAs)				
amitriptyline	4/1961	Depression w/ anxiety	25mg po TID	polyneuropathy, diabetic neuropathic pain, fibromyalgia
desipramine	10/1964	Depression	150mg po daily	Attention deficit disorder, Diabetic neuropathic pain
imipramine	5/1984	Depression Enuresis (children)	100mg po daily	Panic disorder, diabetic neuropathic pain, urinary incontinence
Dopamine reuptake inhibitors				
bupropion bupropion SR Wellbutrin XL	12/1985 10/1996 8/2003	Depression, smoking cessation	100mg po TID 150mg po BID 300mg po QD	
Monoamine Oxidase Inhibitors (MAOI's)				
isocarboxazid (Marplan)	7/1959	Depression	20mg po BID	Dyskinesia, eating disorder, exogenous obesity, orthostatic hypotension, trichotillomania
phenelzine sulfate (Nardil)	6/1961	Depression	15mg po TID	Agoraphobia, Bulimia nervosa, Crohn's disease, Globus hystericus, Headache, Narcolepsy, Obsessive-compulsive disorder, Orthostatic hypotension, Panic disorder, Posttraumatic stress disorder, Social phobia
tranylcypromine sulfate (Parnate)	2/1961	Depression	10mg po TID	Panic disorder, Dysmorphophobia, Obsessive-compulsive disorder, Seasonal affective disorder, Social phobia, Subcortical leukoencephalopathy
Selegiline transdermal system (Emsam)	02/2006	Depression	6mg to 12mg applied QD	Smoking cessation, HIV-associated cognitive impairment, cocaine addiction, ADHD

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

^c As listed in © 1974 - 2005 Thomson MICROMEDEX database or as referenced.

References

1. Klasco RK (Ed): DRUGDEX® System (electronic version). Thomson Micromedex, Greenwood Village, Colorado, USA. Available at: <http://www.thomsonhc.com> (cited: 01/15/06).
2. Emsam® [package insert]. Tampa, FL: Somerset Pharmaceuticals Inc.; February 2006
3. Bodkin JA, Amsterdam JD. Transdermal selegiline in major depression: a double-blind, placebo-controlled, parallel-group study in outpatients. *Am J Psychiatry*. 2002 Nov;159(11):1869-75.
4. Amsterdam JD. A double-blind, placebo-controlled trial of the safety and efficacy of selegiline transdermal system without dietary restrictions in patients with major depressive disorder. *J Clin Psychiatry*. 2003 Feb;64(2):208-14.
5. Study S9303-P0052 – Short term trial. Clinical Study Report Synopsis. Product Dossier: Emsam® (selegiline transdermal system). Somerset Pharmaceuticals Inc.; Tampa, FL. page 35 Reviewed 5/3/2006.
6. 52 – Week Pivotal, Double-Blind, Relapse Prevention Trial. Clinical Study Report Synopsis. Product Dossier: Emsam® (selegiline transdermal system). Somerset Pharmaceuticals Inc.; Tampa, FL. page 38 Reviewed 5/3/2006.
7. Sacktor N, Schifitto G, McDermott MP, Marder K, McArthur JC, Kieburtz K. Transdermal selegiline in HIV-associated cognitive impairment: pilot, placebo-controlled study. *Neurology*. 2000 Jan 11;54(1):233-5.
8. Product Dossier: Emsam® (selegiline transdermal system). Somerset Pharmaceuticals Inc.; Tampa, FL. Reviewed 5/3/2006.
9. Butler R, Carney S, Cipriani A, Geddes J, Hatcher S, Price J, et al. Depressive disorders. *Clinical Evidence* [online] 2005 [cited 5/3/2006]. URL: <http://www.clinicalevidence.com/ceweb/conditions/meh/1003/1003.jsp>.
10. American Psychiatric Association: Practice guideline for the treatment of patients with major depressive disorder, 2nd edition. 2000; pp. 1-71. (accessed June 26, 2005).
http://www.psych.org/psych_pract/treatg/pg/Practice%20Guidelines8904/MajorDepressiveDisorder_2e.pdf.
11. National Institute of Mental Health. CGI: Clinical Global Impressions. In: Guy W, Bonato RR, eds. *Manual for the ECDEU Assessment Battery.2*. Rev ed. Chevy Chase, MD: National Institute of Mental Health; 1970:12-1-12-6.
12. Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry* 1960;23:56-63.
13. Montgomery SA, Asberg MA. A new depression scale designed to be sensitive to change. *Br J Psychiatry* 1979;134:382-9.