



Therapeutic Class ReviewSM

Duloxetine (Cymbalta[®])

July 2005

New Product(s) for Review

duloxetine (Cymbalta) [Eli Lilly & Co]

Dossier Provided by Manufacturer: Yes

Quality of Dossier: 3

1-Low quality (dossier w/missing components)

2-Medium quality (all components, except pharmacoeconomic model)

3-High quality (all components, well done)

Available Therapeutic Alternative(s) –

	Status	Depression	Diabetic Peripheral Neuropathic Pain	Fibromyalgia
Selective/Norepinephrine Reuptake Inhibitors (SNRIs)				
venlafaxine (Effexor [®] /Effexor XR [®]) [Wyeth]	F	√	√	√
Selective Serotonin Reuptake Inhibitors (SSRIs)				
citalopram (generics)	F	√		
fluoxetine (generics)	F	√		√
fluvoxamine (generics)	F	√		
paroxetine (generics)	F	√		
paroxetine (Paxil [®] CR) [GSK]	NF	√		
sertraline (Zoloft [®]) [Pfizer-Roerig]	NF	√		
escitalopram (Lexapro [®]) [Forest]	NF	√		
fluoxetine (Prozac [®] Weekly) [Eli Lilly]	NF	√		
Tricyclic antidepressants (TCAs)				
amitriptyline, desipramine, imipramine (generics)	F	√	√	√ _{amitriptyline}
Dopamine reuptake inhibitor				
bupropion, bupropion SR (generics)	F	√		
bupropion XL (Wellbutrin XL [®]) [GSK]	NF	√		
Antiepileptic medications				
gabapentin, carbamazepine, phenytoin (generics)	F		√	
topiramate (Topamax [®]) [McNeil]	F		√	
Narcotic analgesics				
tramadol +/- acetaminophen (generics)	F		√	√
oxycodone (generics)	F		√	
Muscle relaxants				
cyclobenzaprine (generics)	F			√
Others				
levocarnitine (generics)	F		√	
capsaicin	OTC		√	

Executive Summary

Depression

- There is possibly useful evidence that duloxetine (Cymbalta[®]) has efficacy over placebo in achieving a clinically relevant response.
- Duloxetine (Cymbalta[®]) was inconsistent in achieving a remission.
- There is no evidence that duloxetine (Cymbalta[®]) provides clinical advantages over selective serotonin reuptake inhibitors (SSRIs) or serotonin-norepinephrine reuptake inhibitors (SNRIs).
- Claims that duloxetine (Cymbalta[®]) decreases painful physical symptoms associated with depression are unsubstantiated.

Diabetic Neuropathic Pain & Fibromyalgia

- The evidence is weak for the efficacy and safety of duloxetine (Cymbalta[®]) in diabetic neuropathic pain or fibromyalgia. These studies have:
 - Major design flaws.
 - Conclusions not supported by study results.
- There is no evidence that duloxetine (Cymbalta[®]) provides efficacy over other established treatment options.

Safety/Harms

- Discontinuation rates due to adverse drug reactions after 9-12 weeks were statistically significant for duloxetine (Cymbalta[®]) 60mg/day compared to placebo:
 - Number Needed to Harm (NNH) = 12- 13
 - Absolute Risk Increase (ARI) = 7.7 - 8%.
- There is no evidence that duloxetine (Cymbalta[®]) offers a more favorable safety profile than other existing options for depression (such as SSRIs or SNRIs), diabetic neuropathic pain, or fibromyalgia.
- There is currently no evidence that duloxetine (Cymbalta[®]) doses greater than 60mg/day provides any additional clinical benefit that would outweigh any potential harms.

Conclusion

Duloxetine (Cymbalta[®]) is non-preferred/non-formulary because this product provides no additional clinical value relative to other established medication options for depression, diabetic neuropathic pain, or fibromyalgia.

Products

Drug Products	FDA approval ^a	FDA approved indications	Usual Dose/Route	Cost ^b	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	\$114 \$114 - \$228	Pain management Stress urinary incontinance Fibromyalgia
venlafaxine (Effexor [®]) (Effexor XR [®])	12/2003 10/1997	Major depressive disorder, Generalized Anxiety disorder, Social Anxiety disorder	150mg po daily	\$124 \$117	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	\$18 (MAC)	Headache Panic disorder
escitalopram (Lexapro [®])	8/2002	Depression, Generalized anxiety disorders	10mg po daily	\$80	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	\$2 (MAC)	Body dysphoric disorder, fibromyalgia, post-traumatic stress disorder, Raynaud's phenomenon
fluvoxamine	12/1994	Obsessive-compulsive disorder	200mg po daily	\$49 (MAC)	Depression, Autism, Panic disorder, Social anxiety disorder
paroxetine	12/1992	Same as sertraline (Zoloft) and generalized anxiety disorder	20mg po daily	\$54 (MAC)	Pathological gambling
sertraline (Zoloft [®])	12/1991	Depression, obsessive-compulsive disorder, panic disorder, posttraumatic stress disorder, premenstrual dysphoric disorder, social anxiety disorder	100mg po daily	\$91	dysthymia
Tricyclic Antidepressants (TCAs)					
amitriptyline	4/1961	Depression w/ anxiety	25mg po TID	\$3 (MAC)	polyneuropathy, diabetic neuropathic pain, fibromyalgia
desipramine	10/1964	Depression	150mg po daily	\$34 (MAC)	Attention deficit disorder, Diabetic neuropathic pain
imipramine	5/1984	Depression Enuresis (children)	100mg po daily	\$22 (MAC)	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	\$27 (MAC) \$63 (MAC) \$136	
Antiepileptics					
carbamazepine	3/1968	Bipolar disorder, epilepsy, trigeminal neuralgia,	200mg po BID	\$5 (MAC)	Antidiuretic (diabetes insipidus), psychotic disorders
gabapentin	10/1998	Epilepsy, post herpetic neuralgia	900mg/day – 3600mg/day (divided doses TID)	\$83 - \$294 (MAC)	diabetic neuropathic pain, migraine prophylaxis, social phobia
phenytoin	8/1976	Generalized tonic-clonic/complex partial seizures, seizures s/p neurosurgery	100mg po TID	\$14 (MAC)	Antiarrhythmic, antineuralgic, seizures from eclampsia or preeclampsia , skeletal muscle relaxant
topiramate (Topamax [®])	12/1996	Epilepsy, migraine	200mg po BID	\$328	Diabetic neuropathic pain ³⁷⁻³⁸
Opioids					
tramadol	3/1995	Moderate-severe pain	50mg po Q6hrs	\$17 (MAC)	Diabetic neuropathic pain ⁴²⁻⁴³
oxycodone	10/1998	Moderate-severe pain	5mg po Q4-6 hrs	\$22 (MAC)	Diabetic neuropathic pain ⁴⁴⁻⁴⁵
Others					
levocarnitine	12/1985	Carnitine deficiency	330mg po	\$20 (MAC)	Diabetic neuropathic pain ⁴⁷⁻⁴⁸
capsaicin	OTC	Arthritis pain, diabetic peripheral neuropathy, postherpetic neuralgia,	Apply thin layer 3-5x/day	\$10/ 60gms	psoriasis
cyclobenzaprine	8/1977	Muscle spasms	10mg pot id	\$10 (MAC)	Fibromyalgia

^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 or MAC (maximum allowable cost) as of July 2005 for 1 month of therapy.

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

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