



## Therapeutic Class Review<sup>SM</sup>

### Mental Health – Desvenlafaxine (Pristiq<sup>TM</sup>)

June 2008

**New Product for Review:**

Desvenlafaxine (Pristiq<sup>TM</sup>)[Wyeth]

**Dossier Provided by Manufacturer: Yes**

**Dossier Evaluation: 1**

- 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**

*Depression*

- Depression refers to a wide range of mental health problems characterized by:
  - a loss of interest and enjoyment in ordinary things and experiences.
  - low mood.
- The lifetime risk of major depressive disorder (as defined in the DSM-IV) varies from 10% to 25% for women and from 5% to 12% for men. The prevalence rates appear to be unrelated to ethnicity, education, income or marital status.
- Treatment of depression is highly individualized.
- No one antidepressant medication has clearly demonstrated an advantage in terms of efficacy or safety over other agents in this class.
- Regence currently has many generic and preferred/formulary brand alternatives available for the management of patients with major depressive disorder.
- To be useful, new agents in this class must demonstrate a substantial improvement in safety and/or efficacy to provide value to Regence members.

*Desvenlafaxine*

- Desvenlafaxine (Pristiq) is a new selective serotonin and norepinephrine reuptake inhibitor (SNRI) indicated for the management of major depressive disorder.
  - Desvenlafaxine is the major active metabolite of the antidepressant venlafaxine (Effexor<sup>®</sup> and Effexor XR<sup>®</sup>).
  - Desvenlafaxine (Pristiq) is an extended-release tablet for oral administration.
- The efficacy of desvenlafaxine (Pristiq) appears to plateau at 50 mg per day. Early trials of doses up to 400 mg daily failed to demonstrate any efficacy advantage to 50 mg daily, but did demonstrate more adverse events.

## Evidence

- There is no useful evidence that desvenlafaxine (Pristiq) provides greater clinical value than other formulary alternatives in major depressive disorder.
- Though the studies are unreliable, the overall efficacy of desvenlafaxine (Pristiq) appears modest and roughly the same as venlafaxine (Effexor) and duloxetine (Cymbalta).
- There is no useful evidence that desvenlafaxine (Pristiq) is safer in the treatment of major depressive disorder than preferred/formulary alternatives.
  - The clinical relevance of differences in metabolic pathway are uncertain.
  - The overall adverse event profile appears similar to venlafaxine (Effexor).
- Considerations in Subpopulations:
  - **Pediatrics:** Safety and effectiveness in the pediatric population have not been established
  - **Geriatrics:**
    - No overall differences in safety or efficacy were observed between patients 65 years of age or older and younger patients, but greater sensitivity of some older individuals cannot be ruled out.
    - Elderly patients may be at greater risk for hyponatremia.
  - **Race, ethnicity and/or Gender:** Current clinical experience with desvenlafaxine (Pristiq) has not identified differences in safety or efficacy based on race, ethnicity or gender.

## Decision

Desvenlafaxine (Pristiq) is non-preferred/non-formulary because there is no useful evidence that it provides improved safety or efficacy over existing generic and preferred brand treatment options for major depressive disorder.

## Products <sup>[1]</sup>

Drug Products	FDA approval <sup>a</sup>	Patent Expiration(s) <sup>c</sup>	FDA approved indications	Usual Dose/Route	Potential Off-label Uses <sup>c</sup>
<b>Serotonin/Norepinephrine Reuptake Inhibitors (SNRIs)</b>					
duloxetine (Cymbalta <sup>®</sup> )	8/2004	6/2013	Major depressive disorder, Pain associated with diabetic peripheral neuropathy	60mg PO QD 60mg PO QD/BID	Pain management Stress urinary incontinence Fibromyalgia
venlafaxine immediate release (Effexor XR <sup>®</sup> )	12/2003 10/1997	N/A 2010-2013	Major depressive disorder, Generalized Anxiety disorder, Social Anxiety disorder	75 mg PO twice daily 150mg PO daily	Atypical facial pain, Post-mastectomy pain syndrome, Colonic sensorimotor functions, Obsessive-compulsive disorder, Diabetic peripheral neuropathy Painful polyneuropathy <sup>1</sup> , Bipolar depression, Premenstrual dysphoric disorder, Management of hot flushes, diabetic neuropathic pain, <sup>41</sup> Fibromyalgia <sup>49</sup>
desvenlafaxine (Pristiq <sup>TM</sup> )	02/2008	02/2022	Major depressive disorder,	50 mg PO daily	Post-menopausal flushing
<b>Selective Serotonin Reuptake Inhibitors (SSRIs)</b>					
citalopram	7/1998	N/A	Depression	40 mg PO daily	Headache Panic disorder
escitalopram (Lexapro <sup>®</sup> )	8/2002	03/2012	Depression, Generalized anxiety disorders	20 mg PO daily	Anxiety with depression
fluoxetine Prozac Weekly <sup>®</sup>	12/1987 02/2001	N/A 05/2017	Depression, Bulimia nervosa, Obsessive-compulsive disorder, Panic disorder, Premenstrual dysphoric disorder	20mg PO daily 90mg PO Wk	Body dysphoric disorder, fibromyalgia, post-traumatic stress disorder, Raynaud's phenomenon
fluvoxamine	12/1994	N/A	Obsessive-compulsive disorder	100 mg PO twice daily	Depression, Autism, Panic disorder, Social anxiety disorder

Drug Products	FDA approval <sup>a</sup>	Patent Expiration(s) <sup>c</sup>	FDA approved indications	Usual Dose/Route	Potential Off-label Uses <sup>c</sup>
fluvoxamine XR (Luvox CR <sup>®</sup> )		02/2011		150 mg PO daily	
paroxetine	12/1992	N/A	Same as sertraline (Zoloft) and generalized anxiety disorder	20 mg PO daily	Pathological gambling
sertraline	12/1991	N/A	Depression, obsessive-compulsive disorder, panic disorder, posttraumatic stress disorder, premenstrual dysphoric disorder, social anxiety disorder	100 mg PO daily	dysthymia
<b>Tricyclic Antidepressants (TCAs)</b>					
amitriptyline	4/1961	N/A	Depression w/ anxiety	150 mg PO daily	polyneuropathy, diabetic neuropathic pain, fibromyalgia
desipramine	10/1964	N/A	Depression	150mg PO daily	Attention deficit disorder, Diabetic neuropathic pain
imipramine	5/1984	N/A	Depression Enuresis (children)	100mg PO daily	Panic disorder, diabetic neuropathic pain, urinary incontinence
<b>Dopamine reuptake inhibitors</b>					
bupropion bupropion SR bupropion XL	12/1985 10/1996 8/2003	N/A N/A N/A	Depression, smoking cessation	100mg PO TID 150mg PO BID 300mg PO QD	
<b>Monoamine Oxidase Inhibitors (MAOIs)</b>					
isocarboxazid (Marplan)	7/1959	N/A	Depression	20mg PO BID	Dyskinesia, eating disorder, exogenous obesity, orthostatic hypotension, trichotillomania
phenelzine sulfate (Nardil)	6/1961	N/A	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	N/A	Depression	10mg PO TID	Panic disorder, Dymorphophobia, Obsessive-compulsive disorder, Seasonal affective disorder, Social phobia, Subcortical leukoencephalopathy
Selegiline transdermal system (Emsam)	02/2006	06/2018	Depression	6mg to 12mg applied topically each day.	Smoking cessation, HIV-associated cognitive impairment, cocaine addiction, ADHD

<sup>a</sup> Date applies to approval date for the original brand name medication where there are now generics available.

<sup>c</sup> Based on patents listed in Orange Book as of 05/2/2008.

<sup>d</sup> As listed in © 1974 - 2008 Thomson MICROMEDEX database or as referenced.

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