

Medical Policy



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Title: Cymbalta[®], Effexor[®] /venlafaxine and Effexor XR[®] Prior Authorization Criteria

Professional

Original Effective Date: January 1, 2008

Revision Date(s):

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Institutional

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Prior Authorization Form:

http://www.bcbsks.com/CustomService/Forms/pdf/PriorAuth_ACEI-ARB-SSRI-SNRI.pdf

DESCRIPTION

Brand	generic	Dosage Form
Cymbalta [®]	duloxetine	delayed-release capsule
Effexor [®]	venlafaxine*	oral tablet
Effexor XR [®]	venlafaxine	extended-release capsule

*available as a generic, included in the electronic claims edit program

FDA APPROVED INDICATIONS¹⁻³

Cymbalta^{®1}

Major Depressive Disorder

Cymbalta (duloxetine) is indicated for the treatment of major depressive disorder (MDD). The efficacy of Cymbalta has been established in eight and nine week placebo-controlled trials of outpatients who met DSM-IV diagnostic criteria for MDD. The effectiveness of Cymbalta in hospitalized patients with MDD has not been studied.

The effectiveness of Cymbalta in long-term use for major depressive disorder, that is, for more than nine weeks, has not been systematically evaluated in controlled trials.

Diabetic Peripheral Neuropathic Pain

Cymbalta is indicated for the management of neuropathic pain associated with diabetic peripheral neuropathy.

Generalized Anxiety Disorder

Cymbalta is indicated for the treatment of generalized anxiety disorder (GAD). The efficacy of Cymbalta has been established in three 9- or 10-week placebo-controlled trials of outpatients who met DSM-IV diagnostic criteria for generalized anxiety disorder.

The effectiveness of Cymbalta in long-term use for GAD, that is, for more than 10 weeks, has not been systematically evaluated in controlled trials. The physician who elects to

use Cymbalta for extended periods should periodically evaluate the long-term usefulness of the drug for the individual patient.

Effexor^{®2}

Effexor (venlafaxine) is indicated for the treatment of major depressive disorder (MDD). The efficacy of Effexor in the treatment of MDD was established in 6-week controlled trials of adult outpatients whose diagnoses corresponded most closely to the DSM-III or DSM-III-R category of major depression and in a 4-week controlled trial of inpatients meeting diagnostic criteria for major depression with melancholia.

The efficacy of Effexor in maintaining an antidepressant response in patients with recurrent depression who had responded and continued to be improved during an initial 26 weeks of treatment and were then followed for a period of up to 52 weeks was demonstrated in a placebo-controlled trial.

Effexor XR^{®3}

Major Depressive Disorder

Effexor XR (venlafaxine extended-release) is indicated for the treatment of major depressive disorder. The efficacy of Effexor XR in the treatment of MDD was established in 8- and 12- week controlled trials of adult outpatients whose diagnoses corresponded most closely to the DSM-III-R or DSM-IV category of major depressive disorder. The safety and efficacy of Effexor XR in hospitalized depressed patients have not been adequately studied. The efficacy of Effexor XR in maintaining a response in MDD for up to 26 weeks following 8 weeks of acute treatment was demonstrated in a placebo-controlled trial.

Generalized Anxiety Disorder

Effexor XR is indicated for the treatment of Generalized Anxiety Disorder (GAD) as defined in DSM-IV. The efficacy of Effexor XR in the treatment of GAD was established in 8-week and 6-month placebo-controlled trials in adult outpatients diagnosed with GAD according to DSM-IV criteria.

Social Anxiety Disorder

Effexor XR is indicated for the treatment of Social Anxiety Disorder, also known as Social Phobia, as defined in DSM-IV (300.23). The efficacy of Effexor XR in the treatment of Social Anxiety Disorder was established in two 12-week placebo-controlled trials in adult outpatients with Social Anxiety Disorder (DSM-IV). The effectiveness of Effexor XR in the long-term treatment of Social Anxiety Disorder, i.e., for more than 12 weeks, has not been systematically evaluated in adequate and well-controlled trials.

Panic Disorder

Effexor XR is indicated for the treatment of Panic Disorder, with or without agoraphobia, as defined in DSM-IV. The efficacy of Effexor XR in the treatment of Panic Disorder was established in two 12-week placebo-controlled trials in adult outpatients with Panic Disorder (DSM-IV). The efficacy of Effexor XR in prolonging time to relapse in Panic

Disorder among responders following 12 weeks of open-label acute treatment was demonstrated in a placebo-controlled study.

POLICY

RATIONALE FOR SELECTING CYMBALTA, VENLAFAXINE, AND EFFEXOR XR FOR PRIOR AUTHORIZATION

The intent of the prior authorization criteria for Cymbalta (duloxetine), Effexor/venlafaxine and Effexor XR is to encourage the use of generic selective serotonin reuptake inhibiting agents (SSRIs) prior to duloxetine or venlafaxine. Both efficacy and safety issues have been considered. In addition, the intent of the prior authorization is to encourage the use of first-line generic agents before duloxetine when prescribed for neuropathic pain.

Major Depressive Disorder

The American Psychiatric Association (APA) practice guidelines for the treatment of patients with major depressive disorder report comparable efficacy between classes and also within classes.⁴ Selection of an antidepressant agent may be based on anticipated side effects, tolerability, safety, patient preference, quantity and quality of clinical trial data regarding the agent, and its cost.⁴ The APA guidelines recommend selective serotonin reuptake inhibitors (SSRIs), bupropion, venlafaxine, desipramine, and nortriptyline as likely treatment choices for optimal therapy for most patients.⁴ The U.S. Veteran's Administration (VA) treatment guidelines for depression suggests SSRIs as first-line treatment for most patients in the primary care setting.⁵ The United Kingdom Prodigy Treatment Guidelines for adult depression consider tricyclic antidepressants (TCAs) and SSRIs as first-line treatments.⁶

In the review of second generation antidepressants from the Oregon Evidence-based Practice Center of the Oregon Health & Science University⁷, it was found that for the SSRIs and other newer antidepressants (mirtazapine, duloxetine, venlafaxine, bupropion, and nefazodone) overall effectiveness and efficacy were similar and the majority of trials did not identify substantial differences among drugs. Discontinuation rates and response and remission rates assessed on multiple diagnostic scales did not differ substantially when taking all the evidence into consideration.⁷

The guidelines for management of depression from the National Institute for Clinical Excellence (NICE)⁸ state that when an antidepressant is prescribed in routine care, it should be an SSRI, because SSRIs are as effective as TCAs and less likely to be discontinued due to side effects. If the first antidepressant has not been effective or is poorly tolerated, another single drug should be tried. Reasonable choices include a different SSRI or mirtazapine. Venlafaxine should be considered for patients failing to respond to two adequate trials of other antidepressants.⁸

Safety and side effects of therapy should be considered before venlafaxine is prescribed. The NICE guidelines⁸ state that the following issues should be evaluated: increased

likelihood of patients discontinuing treatment due to side effects (compared with the equally effective SSRIs), increased risk for discontinuation/withdrawal symptoms if abruptly stopped, and toxicity in overdose. Before initiation, an ECG and blood pressure measurement should be taken. Consideration should be given to monitoring of cardiac function. Regular monitoring of blood pressure is suggested, especially for patients on high doses.⁸

A 2005 systematic review⁹ includes 46 randomized controlled trials, and 24 observational studies for safety/tolerability, comparing second generation antidepressants (e.g., SSRIs, bupropion, duloxetine, mirtazapine, venlafaxine) with each other. Results suggest that second generation antidepressants do not differ substantially overall for treatment of depression. Differences in efficacy appeared minimal between drugs. Overall incidence of adverse effects appears similar across drugs, although types of adverse events vary between drugs. Degree and quality of adverse event assessment also vary between studies.⁹

Duloxetine was not marketed at the time these guidelines were published. Currently, there are no well-designed published studies directly comparing duloxetine with another antidepressant for the treatment of depression.¹⁰ The mechanism of the antidepressant action of venlafaxine is thought to be associated with potentiation of neurotransmitter activity in the central nervous system.² Venlafaxine and its active metabolite, O-desmethylvenlafaxine, are potent inhibitors of neuronal serotonin and norepinephrine reuptake and weak inhibitors of dopamine reuptake.² Duloxetine is also a serotonin and norepinephrine reuptake inhibitor and its mechanism of action is similar to the TCAs and venlafaxine.³ Until guidelines and/or clinical trials exist that define the place of duloxetine in the treatment of depression, duloxetine will be managed similar to venlafaxine.

Anxiety Disorders – Generalized Anxiety Disorder, Social Anxiety Disorder, Panic Disorder

Generalized Anxiety Disorder (GAD)

The Cochrane review on antidepressants for generalized anxiety disorder¹¹ states that available evidence suggests imipramine, venlafaxine and paroxetine are superior to placebo in GAD in adults, and also that sertraline is superior to placebo in treating GAD in children and adolescents.¹¹ The review of second generation antidepressants from the Oregon Evidence-based Practice Center of the Oregon Health & Science University⁷ found that evidence supports the efficacy of escitalopram, paroxetine, venlafaxine, and sertraline in treatment of generalized anxiety disorder. The review by Goodman (2004)¹² found that paroxetine, escitalopram, and venlafaxine are considered first-line therapy for GAD. The current NICE guideline on anxiety¹³ finds that antidepressants should be the only pharmacological intervention for longer-term management of GAD. There is an evidence base for the effectiveness of the SSRIs.¹³ Recent Canadian and British guidelines recommend use of an SSRI such as paroxetine, sertraline, citalopram, or escitalopram, or venlafaxine extended-release as first-line therapy for GAD; the best evidence supports paroxetine and escitalopram.^{14,15}

Social Anxiety Disorder (SAD)

The consensus statement on Social Anxiety Disorder from the International Consensus Group on Depression and Anxiety (1998)¹⁶ recommends SSRIs as the first-line treatment for social anxiety disorder. At that time, most of the evidence was from well-controlled clinical data on paroxetine. Studies and reports with sertraline, fluvoxamine, fluoxetine, and citalopram reported at that time had positive results but with smaller study groups.¹⁶

The review of second generation antidepressants from the Oregon Evidence-based Practice Center of the Oregon Health & Science University⁷ found similar efficacy of venlafaxine ER with paroxetine and also escitalopram with paroxetine for treatment of SAD. Indirect evidence from a meta-analysis of placebo-controlled trials provides evidence that there is no difference in efficacy between fluvoxamine, paroxetine, and sertraline.⁷

The Cochrane review of pharmacotherapy for SAD¹⁷ does not discuss venlafaxine, but states that the following SSRIs are all effective in social anxiety disorder: paroxetine, sertraline, fluoxetine, fluvoxamine, escitalopram. Expert consensus is that the SSRIs are the first-line medication of choice in this disorder.¹⁷ Recent Canadian and British guidelines recommend paroxetine, sertraline, escitalopram, fluoxetine, fluvoxamine, or venlafaxine extended-release for SAD; best evidence is for the SSRIs.^{14,15}

Panic Disorder (PD)

The APA guidelines for treatment of patients with panic disorder from 1998¹⁸ state that SSRIs, TCAs, benzodiazepines, and monoamine oxidase inhibitors (MAOIs) are all effective. Medications from all four classes were found to have roughly comparable efficacy. SSRIs available at that time included fluoxetine, sertraline, paroxetine, and fluvoxamine. Clinical trials indicating that each of them is effective for panic had been completed.¹⁸ Additional information is published in the APA Guideline Watch of April 2006. The efficacy of SSRIs supported in randomized controlled trials includes additional evidence for fluoxetine, paroxetine (including CR) and sertraline. In addition, there are studies suggesting that both citalopram and escitalopram are effective. Venlafaxine ER was found to be effective in treating PD. Literature since 1998 suggests that the large number of SSRIs, TCAs, and benzodiazepines used to treat PD are equivalent in their efficacy.¹⁹

A recent review by Pollack²⁰ finds that randomized studies support efficacy of fluoxetine, paroxetine, sertraline, escitalopram, citalopram, and venlafaxine for the treatment of PD.²⁰ In the review of second generation antidepressants from the Oregon Evidence-based Practice Center of the Oregon Health & Science University⁷ evidence was found to support the use of fluoxetine, paroxetine, sertraline, citalopram, escitalopram, and fluvoxamine in treatment of PD.⁷ The NICE guidelines for anxiety¹³ state that antidepressants should be the only pharmacological intervention used in longer term management of PD. The two classes that have an evidence base for effectiveness are SSRIs and TCAs.¹³ Recent Canadian and British guidelines recommend paroxetine,

sertraline, citalopram, escitalopram, fluoxetine, fluvoxamine, or venlafaxine extended-release for PD; best evidence is for the SSRIs.^{14,15}

Of the SSRI agents, Celexa (citalopram), Paxil immediate-release (paroxetine hydrochloride), Prozac (fluoxetine), and Zoloft (sertraline) are available as AB-rated generics in the oral solid dosage forms. Exceptions are Prozac Weekly (90 mg fluoxetine extended-release capsules) and Sarafem[®] (20 mg fluoxetine capsules). Fluvoxamine is available as a generic only; brand Luvox[®] is no longer being marketed. The oral solutions of Prozac and Celexa are available as AA-rated generics; the generic sertraline oral concentrate is AB-rated to Zoloft oral concentrate; the generic paroxetine hydrochloride oral suspension is AB-rated to Paxil. Lexapro (escitalopram), Paxil CR (paroxetine hydrochloride controlled-release), and Pexeva (paroxetine mesylate) are not available in generic formulations.

Duloxetine and venlafaxine are not FDA-labeled for psychiatric indications other than those listed above under Food and Drug Administration (FDA) Approved Indications. For psychiatric indications, the following table summarizes the FDA-approved uses for AB-rated generic SSRIs and the SSRIs that have accepted unlabeled uses documented in the pharmaceutical compendia, USP/DI (accepted indications) and Micromedex DrugDex (treatment considered useful in some or most cases), and also systematic reviews such as Clinical Evidence Concise 2005 (beneficial or likely to be beneficial), or practice guidelines.^{14,15,29-36} SSRIs are considered accepted treatment for all of these indications.

Table 1. Generically-available SSRIs, FDA Approved Indications and Unlabeled Uses

Indication	FDA-approved agents ²¹⁻²⁹	Accepted Unlabeled agents ^{14,15,29-36}
Depression	citalopram, fluoxetine, paroxetine, sertraline	
OCD	fluvoxamine, fluoxetine, paroxetine, sertraline	citalopram ³¹
PD	fluoxetine, paroxetine, sertraline	citalopram ^{14,30,32} , fluvoxamine ^{14,30,32}
GAD	paroxetine	sertraline ^{14,15,33}
SAD	paroxetine, sertraline	fluvoxamine ^{14,15,30}
PMDD	sertraline	citalopram ^{0,34} , fluvoxamine ³⁴ , paroxetine ³⁴
PTSD	paroxetine, sertraline	fluoxetine ^{14,15,30,35,36}
Bulimia	fluoxetine	fluvoxamine ³⁰

*OCD= obsessive compulsive disorder; PD= panic disorder; GAD= generalized anxiety disorder; SAD= social anxiety disorder or social phobia; PMDD= premenstrual dysphoric disorder; PTSD= post traumatic stress disorder.

Neuropathic Pain

Duloxetine is also approved for treatment of pain associated with diabetic peripheral neuropathy (DPNP). Current guidelines on the treatment of DPNP from the American Diabetes Association^{37,38} recommend TCAs (especially amitriptyline and imipramine) as

first-line agents, anticonvulsants such as gabapentin, pregabalin, lamotrigine, or topiramate as second-line, and opioid pain medications (tramadol, oxycodone) as the third step.^{37,38} At the time of the preparation of this statement the evidence of efficacy of duloxetine was published only in abstract form and not discussed in the guidelines.^{37,38}

Mayo Clinic guidelines for DPNP³⁹ recommend TCAs (specifically amitriptyline and desipramine), pregabalin, duloxetine, and oxycodone CR in first tier, with carbamazepine, gabapentin, lamotrigine, tramadol, and venlafaxine ER in second tier. Topical capsaicin cream and lidocaine patches may also be used.³⁹ The 2004 review article by Duby, Campbell, et al.,⁴⁰ finds that evidence from clinical trials supports the use of desipramine, amitriptyline, capsaicin, tramadol, gabapentin, bupropion, and venlafaxine as preferred medications for the treatment of DPNP. Opioids and nonsteroidal anti-inflammatory drugs (NSAIDs) may be used as adjuvant agents. Alternate consideration is given to some SSRIs (citalopram, paroxetine) and other anticonvulsants (lamotrigine, oxcarbazepine).⁴⁰

There are no trials comparing duloxetine with other agents used to treat peripheral neuropathy. The Veteran's Administration review of duloxetine use in painful diabetic neuropathy and fibromyalgia⁴¹ states that: "Given (1) the lack of direct evidence of the relative treatment benefits of duloxetine in patients with diabetic peripheral neuropathy and fibromyalgia, (2) the indirect evidence suggesting that duloxetine is not better than alternative formulary agents, as well as, (3) the lack of long-term (>1 year) safety trials, duloxetine should generally be used as a second-line agent after adequate trials of alternative oral, non-opioid formulary agents."⁴¹ The 2005 review by the Medical Letter on Drugs and Therapeutics⁴² concludes that duloxetine has efficacy in treatment of pain, but that there are no studies comparing duloxetine with other drugs used for pain due to diabetic neuropathy. Duloxetine was more effective than placebo in clinical trials, but the duration of trials was relatively short; and long-term effectiveness remains unclear.⁴²

A 2005 review⁴³ on treatment of non-cancer pain suggests that TCAs are the preferred initial therapy for neuropathic pain, although the authors acknowledge that duloxetine has also been found effective. Meta-analyses have confirmed TCA efficacy; noncyclic antidepressants are suggested to have shown variable degrees of benefit. Gabapentin was recommended for patients intolerant of TCA side effects or having contraindications.⁴³ The Cochrane Collaboration has reviewed the use of anticonvulsants for acute and chronic pain.⁴⁴⁻⁴⁶ These published reviews have concluded that TCAs should be used before anticonvulsants for chronic pain; that none of the anticonvulsants is beneficial for acute pain; and that gabapentin has been shown to be effective for a variety of types of neuropathic pain.^{44,45}

Other reviews with treatment recommendations for treatment of neuropathic pain^{43,47-49} include the following agents as first-line for neuropathic pain: TCAs (amitriptyline, nortriptyline, desipramine), gabapentin, pregabalin, lidocaine patch, tramadol, Second-line agents include other anticonvulsants (lamotrigine, carbamazepine) and other antidepressants (paroxetine, citalopram, venlafaxine, bupropion).^{43,47-49} A recent review of clinical trials by Irving⁵⁰ found the following to be effective agents, based on published

studies: lidocaine patch, gabapentin, carbamazepine, lamotrigine, oxcarbazepine, topiramate, valproate, TCAs (amitriptyline, nortriptyline, imipramine, desipramine), venlafaxine, duloxetine, bupropion, tramadol, and other opioids such as oxycodone. Only gabapentin was specifically listed as a first-line agent.⁵⁰ The 2006 European Federation of Neurological Societies (EFNS) guidelines⁵¹ recommended TCAs or gabapentin or pregabalin as first choice agents with highest efficacy for painful polyneuropathies (e.g. DPNP) and PHN. Duloxetine or venlafaxine are considered second line due to more moderate efficacy, although they may have fewer adverse effects.⁵¹

Although carbamazepine is considered by some to have “stood the test of time” as far as effectiveness in neuropathic pain,⁴⁶ recent evaluations consider carbamazepine to be highly effective for trigeminal neuralgia but not always beneficial for other types of neuropathic pain.^{44,46,51-54}

Specific guidelines from American Academy of Neurology on treatment of PHN recommend the following as effective first-line therapies: amitriptyline, nortriptyline, desipramine, and maprotiline, gabapentin, pregabalin, topical lidocaine, and opioids.⁵⁵ A Clinical Evidence review from 2005 supports the use of TCAs and gabapentin for treatment of PHN.⁵⁶ Topical counterirritants, topical anesthetics, and oral opioids are considered of unknown effectiveness.⁵⁶

Dworkin et al.⁴⁷ state that most randomized controlled trials of chronic neuropathic pain have examined only 2 pain syndromes, DPNP and PHN. These authors suggest that while the applicability of the results of clinical trials for one chronic neuropathic pain syndrome to others cannot be determined, most of the first-line therapies have been tested with multiple types of neuropathic pain and have shown similar results.⁴⁷ Because of this, the PA Criteria for Approval for use of duloxetine for neuropathic pain will include as possible pre-requisites the generic agents included as first-line therapy in the guidelines and reviews listed above—amitriptyline, nortriptyline, imipramine, desipramine, and gabapentin. Oxycodone ER and tramadol will not be included due to their higher potential for overuse, abuse, and dependence.

Electronic Claims Edit

The overall process for meeting the electronic claims edit requires that another drug or drugs be tried for a specific quantity of drug in the previous time period before the claim drug. If the patient has met any of the requirements outlined below, the requested prior authorization medication will be paid under the patient’s current prescription benefit. If the patient does not meet the electronic claims criteria, then the system will reject with the message indicating that prior authorization is necessary or that higher co-pay(s) will be applicable. The PA criteria for approval would then be applied to requests submitted by the patient’s practitioner for evaluation.

The initial electronic claims edit will identify patients who are taking or have taken a generic SSRI in the 365 days prior to the duloxetine or venlafaxine claim. The initial electronic claims edit will also look for the identical GPI to the claim drug within the

previous 90 days. The 365-day timeframe was selected because therapy for all of the above-listed diagnoses may be long-term and may require numerous changes in agents and dose adjustments. The 90-day parameter identifies previous therapy with a brand agent and assures continuation of therapy.

The initial electronic claims edit for duloxetine will also identify patients that have already used or are currently using first-line generic gabapentin or TCAs for neuropathic pain. First-line TCAs include amitriptyline, nortriptyline, imipramine, and desipramine. The system references previous history to 90 days prior to the claim in order to verify previous or concurrent gabapentin or tricyclic antidepressant therapy.

Prior Authorization (PA) Criteria for Approval

The intent of the prior authorization criteria for approval is to ensure that patients who require duloxetine or venlafaxine and who have not met the electronic claims edit criteria will be evaluated for use of the target drug. The PA criteria for duloxetine or venlafaxine will approve the requested agent for the patient who has tried and failed a generic SSRI. The target drug will also be approved when the patient is allergic to or intolerant of generic agents; if the patient has contraindications to the SSRIs that are available as generics; if the patient has responded to the target drug in the past; or if the patient is currently on duloxetine or venlafaxine has had an adequate response, and switching may cause harm or health risk. Initiation of duloxetine or venlafaxine prescribed for other indications will be evaluated through the prior authorization process if the prescriber submits information documenting the use of the target drug to treat the patient's condition.

In addition, the PA criteria will allow for evaluation of duloxetine for the treatment of neuropathic pain. Duloxetine will also be approved if the patient has tried and failed a first-line agent for neuropathic pain (amitriptyline, nortriptyline, imipramine, desipramine, gabapentin), and also when the patient is allergic to, intolerant of, or has contraindications to these first-line agents; if the patient has been initiated on duloxetine, has had an adequate response, and switching may cause harm or health risk; or if the prescriber has considered all first-line agents for neuropathic pain and determined that duloxetine will best treat the patient.

Duloxetine or venlafaxine will be approved indefinitely in patients with a documented diagnosis of Major Depressive Disorder, Recurrent, due to their high risk for significant disease morbidity. Indefinite approvals granted through the Clinical Review PA process may be re-evaluated at some future time if new information changes selection criteria or safety issues develop that may place these patients at higher risk from drug therapy.

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL***Effexor (venlafaxine), Effexor XR (venlafaxine extended-release)*****Initial and Renewal Evaluation**

1. Is the patient's diagnosis Major Depressive Disorder, Recurrent (ICD-9 296.3X)?
If yes, approve indefinitely. If no, continue to 2.
2. Has the patient previously responded to the requested drug or is the patient currently receiving and responding to the requested drug and switching could potentially cause harm or a health risk?
If yes, approve indefinitely. If no, continue to 3.
3. Does the patient's past prescription history include the use of a generic SSRI for treatment in this patient?
If yes, approve indefinitely. If no, continue to 4.
4. Is the patient allergic to, intolerant of, or have a contraindication to generic SSRIs?
If yes, approve indefinitely. If no, continue to 5.
5. Has the prescriber submitted documentation in support of the requested therapeutic use for Effexor (venlafaxine) or Effexor XR (venlafaxine extended-release) in this patient?
If yes, pharmacist may approve indefinitely based on review of information provided. If no, deny.

Cymbalta (duloxetine)**Initial and Renewal Evaluation**

1. Is the patient's diagnosis Major Depressive Disorder, Recurrent (ICD-9 296.3X)?
If yes, approve indefinitely. If no, continue to 2.
2. Has the patient previously responded to Cymbalta (duloxetine) or is the patient currently receiving and responding to Cymbalta (duloxetine) and switching could potentially cause harm or a health risk?
If yes, approve indefinitely. If no, continue to 3.
3. Is the patient's diagnosis neuropathic pain?
If yes, continue to 6. If no, continue to 4.
4. Does the patient's past prescription history include the use of a generic SSRI for treatment in this patient?
If yes, approve indefinitely. If no, continue to 5.
5. Is the patient allergic to, intolerant of, or have a contraindication to generic SSRIs?
If yes, approve indefinitely. If no, continue to 8.
6. Has the patient tried and failed one of the following agents; 1) a tricyclic antidepressant - amitriptyline, nortriptyline, desipramine or imipramine, 2) gabapentin?
If yes, approve indefinitely. If no, continue to question 7.

7. Does the patient have an allergy, intolerance, or contraindication to one of the agents listed above in 6?
If yes, approve indefinitely. If no, continue to 8.
8. Has the prescriber submitted documentation in support of the requested therapeutic use for Cymbalta (duloxetine) in this patient?
If yes, pharmacist may approve indefinitely based on review of information provided. If no, deny.

CONCLUSION

Electronic claims edit electronic edits are designed to identify patients electronically by their medication history. The duloxetine and venlafaxine edit allows for automatic payment of claims when the patient's medication history indicates prior use of a generic SSRI bypassing the manual PA process. The edit also allows for automatic payment if a medical diagnosis of Major Depressive Disorder, Recurrent is documented. The PA process provides a member-specific review process where practitioner provided patient-specific parameters are taken into consideration when reviewed. The electronic claims edit protocol for duloxetine and venlafaxine optimizes the utilization of generic SSRIs or generic alternatives for neuropathic pain for the individual benefit plan.

REFERENCES

1. Cymbalta® prescribing information. Eli Lilly and Company. February 2007.
2. Effexor® prescribing information. Wyeth Pharmaceuticals Inc. August 2006.
3. Effexor XR® prescribing information. Wyeth Pharmaceuticals Inc. August 2006.
4. American Psychiatric Association. Practice guideline for the treatment of patients with major depression. April 2000. Available at: http://www.psych.org/psych_pract/treatg/pg/Practice%20Guidelines8904/MajorDepressiveDisorder_2e.pdf . Accessed on June 12, 2006.
5. Veteran's Administration Medical Advisory Panel for the Pharmacy Benefits Management Strategic Health Group. The pharmacologic management of major depression in the primary care setting. Dept of Veteran's Affairs. Veteran's Health Administration. May 2000. Publication. 00-0016 Available at: http://www.vapbm.org/guidelines/depressionguidelines_1.pdf. Accessed June 12, 2006.
6. Department of Health, United Kingdom. Prodigy Guidance-Depression. July 2004. Available at: <http://www.prodigy.nhs.uk/guidance.asp?gt=depression> Accessed June 12, 2006.
7. Gartlehner G, Hansen RA, Kahwati L, et al. Drug class review on second generation antidepressants. Final Report March 2006. Oregon Health & Science University. Available at <http://www.ohsu.edu/drugeffectiveness/reports/final.cfm>. Accessed June 12, 2006.
8. National Institute for Clinical Excellence (NICE). Management of depression in primary and secondary care. December 2004. Clinical Guideline 23. United Kingdom. Available at: <http://www.nice.org.uk/pdf/word/CG023NICEguideline.doc>. Accessed June 15, 2006.
9. Hansen R, Gartlehner G, Lohr K, et al. Efficacy and safety of second-generation antidepressants in treatment of major depressive disorder. *Ann Intern Med.* 2005;143:415-426.
10. Leshner B. Comparison of commonly used antidepressants. *Pharmacist's Letter/Prescriber's Letter.* September 2004;20: #200901.
11. Kapczinski F, Lima M, Souza J, Schmitt R. Antidepressants for generalized anxiety disorder. *Cochrane Database Syst Rev.* 2003(2):CD003592.
12. Goodman WR. Selecting pharmacotherapy for generalized anxiety disorder. *J Clin Psychiatry.* 2004;65(suppl 13):8-13.
13. National Institute for Clinical Excellence (NICE). Anxiety: Management of anxiety (panic disorder, with or without agoraphobia, and generalized anxiety disorder) in adults in primary, secondary and

- community care. December 2004. Clinical Guideline 22. United Kingdom. Available at: <http://www.nice.org.uk/pdf/word/CG0223NICEguideline.doc>. Accessed June 15, 2006.
14. Swinson R, Working Group Members, et al. Clinical Practice Guidelines: Management of anxiety disorders. *Can J Psychiatry*. 2006;51(suppl 2):1s-93s.
 15. Baldwin D, Anderson I, Nutt D, et al. Evidence based guidelines for the pharmacological treatment of anxiety disorders: Recommendations from the British Association for Psychopharmacology. *J Psychopharmacology*. 2005;19(6):567-596.
 16. Ballenger JC. Consensus Statement on Social Anxiety Disorder from the International Consensus Group on Depression and Anxiety. *J Clin Psychiatry*. 1998;59(suppl17):54-60.
 17. Stein DJ, Ipser JC, van Balkom AJ. Pharmacotherapy for social anxiety disorder. *Cochrane Database Syst Rev*. 2000(4): CD001206.
 18. Gorman J, Shear K, Cowley D, et al. for the American Psychiatric Association Work Group on Panic Disorder. Practice Guideline for the Treatment of Patients with Panic Disorder. May 1998. Available at: <http://www.psych.org>. Accessed June 15, 2006.
 19. Campbell-Sills L, Stein MB. Guideline Watch: Practice guideline for the treatment of patients with panic disorder. American Psychiatric Association, 2006. Available at http://www.psych.org/psych_pract/treatg/pg/prac_guide.cfm. Accessed on June 15, 2006.
 20. Pollack MH. The pharmacotherapy of panic disorder. *J Clin Psychiatry*. 2005;66(suppl 4): 23-27.
 21. Celexa® prescribing information. Forest Pharmaceuticals, Inc. February 2005.
 22. Lexapro® prescribing information. Forest Pharmaceuticals, Inc. February 2005.
 23. Paxil® prescribing information. GlaxoSmithKline. December 2005.
 24. Paxil CR® prescribing information. GlaxoSmithKline. December 2005.
 25. Pexeva® prescribing information. JDS Pharmaceuticals, LLC. December 2005.
 26. Prozac® prescribing information. Eli Lilly and Company. December 2005.
 27. Zoloft® prescribing information. Roerig/Pfizer Inc. July 2004.
 28. Fluvoxamine prescribing information. Apotex Corporation. May 2004.
 29. Klasco RK (Ed): *USP DI® Drug Information for the Health Care Professional*. Thomson Micromedex, Greenwood Village, Colorado (Edition expires 2006).
 30. Klasco RK (Ed): DRUGDEX® System. Drug Evaluations for Citalopram, Escitalopram, Fluoxetine, Fluvoxamine, Paroxetine, Sertraline. Thomson Micromedex, Greenwood Village, Colorado (Vol. 128 expires 6/2006).
 31. Soomro GM. Obsessive compulsive disorder. *Clin Evid Concise*. 2005;14:337-9.
 32. Kumar S, Oakley-Browne M. Panic disorder. *Clin Evid Concise*. 2005;14:340-1.
 33. Gale C, Oakley-Browne M. Generalised anxiety disorder. *Clin Evid*. 2005;14:334-6.
 34. Wyatt K. Premenstrual syndrome. October 2002. *Clin Evid*. 2003;9:2125-44.
 35. Bisson J. Post-traumatic stress disorder. *Clin Evid Concise*. 2005;14:342-5.
 36. Ballenger J. Consensus statement on posttraumatic stress disorder from the international consensus group on depression and anxiety. *J Clin Psychiatry*. 2000;61(suppl 5):60-6.
 37. Boulton AJM, Vinik AI, Arezzo JC, et al. Diabetic neuropathies: a statement by the American Diabetes Association. *Diabetes Care*. 2005;28:956-62.
 38. Boulton AJM, Malik RA, Arezzo JC, Sosenko JM. Diabetic somatic neuropathies. *Diabetes Care*. 2004;27:1458-86.
 39. Argoff CE, Backonia MM, Belgrade MJ, et al. Consensus guidelines: treatment planning and options. *Mayo Clin Proc*. 2006;81(4 suppl):S12-S25.
 40. Duby JJ, Campbell RK, et al. Diabetic neuropathy: an intensive review. *Am J Health-Syst Pharm*. 2004;61:160-76.
 41. Veteran's Administration. Abbreviated National PBM Drug Monograph: Duloxetine (duloxetine) in painful diabetic neuropathy and fibromyalgia. January 2005. Accessed March 2005 at: <http://www.vapbm.org/monograph/6upaeDuloxetine.pdf>.
 42. Anon. Duloxetine for diabetic neuropathic pain. *Med Lett Drugs Ther* 2005;47(1215-1216):67-8.
 43. Maizels M, McCarberg B. Antidepressants and antiepileptic drugs for chronic non-cancer pain. *Am Fam Physician*. 2005;71:483-490.

44. Wiffen P, Collins S, McQuay H, et al. Anticonvulsant drugs for acute and chronic pain. *Cochrane Database of Systematic Reviews*. 2005, Issue 3. Art. No.: CD001133. DOI: 10.1002/14651858.CD001133.pub2
45. Wiffen PJ, McQuay HJ, Edwards JE, Moore RA. Gabapentin for acute and chronic pain. *Cochrane Database of Systematic Reviews*. 2005, Issue 3. Art. No.: CD005452. DOI: 10.1002/14651858.CD005452.pub2
46. Wiffen PJ, McQuay HJ, Moore RA. Carbamazepine for acute and chronic pain. *Cochrane Database of Systematic Reviews*. 2004, Issue 3. Art. No.: CD005451. DOI: 10.1002/14651858.CD005451.pub2.
47. Dworkin RH, Backonja M, Rowbotham MC, et al. Advances in neuropathic pain: diagnosis, mechanisms, and treatment recommendations. *Arch Neurol*. 2003;60:1524-34.
48. Finnerup NB, Otto M, McQuay HJ, et al. Algorithm for neuropathic pain treatment: an evidence based proposal. *Pain*. 2005;118:289-305.
49. Hansson PT, Dickenson AH. Pharmacological treatment of peripheral neuropathic pain conditions based on shared commonalities despite multiple etiologies. *Pain*. 2005;113:251-54.
50. Irving GA. Contemporary assessment and management of neuropathic pain. *Neurology*. 2005;64(suppl 3):S21-S27.
51. Attal N, Cruccu G, Haanpaa M, Hansson P, et al. EFNS guidelines on pharmacological treatment of neuropathic pain. *European Journal of Neurology*. 2006;13:1153-69.
52. ICSI Health Care Guideline: Assessment and Management of Chronic Pain. November 2005. Available at: http://www.icsi.org/pain_chronic/assessment_and_management_of_chronic_pain_2.html Accessed on February 15, 2007.
53. Gilron I, Watson PN, Cahill CM, Moulin DE. Neuropathic pain: a practical guide for the clinician. *CMAJ*. 2006;175:265-75.
54. Zakrzewska JM, Lopez BC. Trigeminal neuralgia (August 2005). *Clinical Evidence*. 2006;15. Available at: <http://www.clinicalevidence.com/ceweb/conditions/nud/1207/1207.pdf> Accessed February 22, 2007.
55. Dubinsky RM, Kabbani H, El-Chami Z et al. Practice Parameter: Treatment of postherpetic neuralgia. An evidence-based report of the quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 2004;63:959-65.
56. Wareham D. Postherpetic neuralgia. (December 2005) *Clinical Evidence*. 2006;15. Available at: <http://www.clinicalevidence.com/ceweb/conditions/ind/0905/0905.pdf>. Accessed February 22, 2007.
57. Karasu TB, Gelenberg A, Merriam A, Wang P. Practice guideline for the treatment of patients with major depressive disorder, second edition. American Psychiatric Association, 2000. Available at http://www.psych.org/psych_pract/treatg/pg/prac_guide.cfm. Accessed on July 3, 2006.
58. Fochtmann LJ, Gelenberg AJ. Guideline Watch: Practice guideline for the treatment of patients with major depressive disorder. American Psychiatric Association, 2005. Available at http://www.psych.org/psych_pract/treatg/pg/prac_guide.cfm. Accessed on June 15, 2006.
59. Williams MG, Crane C, Barnhofer T, Vander Does AJW, Segal ZV. Recurrence of suicidal ideation across depressive episodes. *J Affect Disord*. 2006;91:189-94.
60. Vos T, Haby MM, Barendregt JJ, et al. The burden of major depression avoidable by longer-term treatment strategies. *Arch Gen Psychiatry*. 2004;61:1097-103.
61. Montgomery SA. The need for long term treatment of depression. *Eur Neuropsychopharmacol*. 1997;7:S309-S313.
62. Keller MB, Boland RJ. Implications of failing to achieve successful long-term maintenance treatment of recurrent unipolar major depression. *Biol Psychiatry*. 1998;44:348-60.
63. Thase ME. Long-term nature of depression. *J Clin Psychiatry*. 1999;60(suppl 14):3-9.
64. Thase ME. Achieving remission and managing relapse in depression. *J Clin Psychiatry*. 2003;64(suppl 18):3-7.
65. Kennedy N, Abbott R, Paykel ES. Remission and recurrence of depression in the maintenance era: long-term outcome in a Cambridge cohort. *Psychological Medicine*. 2003;33:827-38.
66. Lee AS. Better outcomes for depressive disorders? *Psychological Medicine*. 2003;33:769-74.