Medical Policy

BlueCross BlueShield of Kansas
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Title: Antidepressant Agents

- **Prime Therapeutics will review Prior Authorization requests.**

  Prior Authorization Form:
  http://www.bcbsks.com/CustomerService/Forms/pdf/PriorAuth-6082KS-STQL.pdf

  Link to Drug List (Formulary):
  https://www.bcbsks.com/drugs/

Professional
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Institutional
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Current Effective Date: June 15, 2018

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DESCRIPTION

The intent of the Antidepressant Agents Prior Authorization program is to encourage the use of generic antidepressant agents - selective serotonin reuptake inhibiting agents (SSRIs), serotonin norepinephrine reuptake inhibiting agents (SNRIs), bupropion/bupropion extended-release, or mirtazapine [or generic trazodone extended-release if it becomes available] - prior to brand antidepressant agents and to accommodate for use of brand antidepressant agents when generic prerequisite agents cannot be used due to previous trial, documented intolerance, FDA labeled contraindication, or hypersensitivity. The criteria for Cymbalta also encourage its use for neuropathic pain after trial of amitriptyline, nortriptyline, imipramine, desipramine, or gabapentin, for fibromyalgia (FM) after a trial of amitriptyline, nortriptyline, imipramine, desipramine, cyclobenzaprine, tramadol, or gabapentin, and for chronic musculoskeletal pain (CMP; for example, osteoarthritis or chronic low back pain) after a trial of acetaminophen, oral NSAID, topical NSAID, or any other prerequisite for FM or neuropathic pain already listed. The criteria for duloxetine (delayed release capsule, brand product) and Irenka also encourage its use for neuropathic pain after trial of amitriptyline, nortriptyline, imipramine, desipramine, or gabapentin; and for chronic musculoskeletal pain (CMP; for example, osteoarthritis or chronic low back pain) after a trial of acetaminophen, oral NSAID, topical NSAID, amitriptyline, nortriptyline, imipramine, desipramine, cyclobenzaprine, tramadol, or gabapentin. Requests for brand antidepressant agents will be reviewed when patient-specific documentation has been provided.

Target Agents

Aplenzin™ (bupropion)	**Oleptro™** (trazodone extended-release) [b]
Celexa® (citalopram) [a]	**Paxil®** (paroxetine hydrochloride) [a]
Cymbalta® (duloxetine) [a]	**Paxil CR®** (paroxetine extended-release) [a]
Desvenlafaxine (ER tablets, brand product)	**Pexeva®** (paroxetine mesylate)
Desvenlafaxine fumarate (ER tablets, brand product)	**Pristiq®** (desvenlafaxine succinate) [a]
Duloxetine (delayed release capsule, brand product)	**Prozac®** (fluoxetine) [a]
Effexor® (venlafaxine) [a]	**Prozac® Weekly™** (fluoxetine delayed-release)[a]
Effexor XR® (venlafaxine extended-release) [a]	**Remeron®** (mirtazapine) [a]
Fetzima® (levomilnacipran extended-release)	**Remeron SolTab®** (mirtazapine) [a]
Fluvoxamine extended release [a]	**Trintellix™** (vortioxetine)
Fluoxetine 60 mg (tablets, brand product) [a]	**Venlafaxine ER** (tablets, brand product) [a]
Forfivo XL® (bupropion extended–release)	**Viibryd™** (vilazodone)
Irenka™ (duloxetine delayed release)	**Wellbutrin®** (bupropion)[a]
Khedezla™ (desvenlafaxine extended release)	**Wellbutrin SR®** (bupropion extended-release) [a]
Lexapro® (escitalopram) [a]	**Wellbutrin XL®** (bupropion extended-release) [a]
Maprotiline (tablets, brand product)	**Zoloft®** (sertraline) [a]

a-available as a generic; generic included as a *prerequisite* in prior authorization program
b-generic product anticipated

FDA Approved Indications and Dosage [1-20,26,27,30,32-35,37-39,40,41,43]

Agents	MDD	OCD	PD	GAD	SAD	PDD	PTSD	Bulimia	Other Diagnoses	Dosing (adults)
Selective Serotonin Reuptake Inhibitors (SSRIs)										
Celexa (citalopram) tablets, oral solution	✓									MDD: 20 mg/day up to 40 mg/day; doses above 40 mg/day are not recommended due to the risk of QT prolongation. 20 mg/day is maximum recommended dose for CYP2C19 poor metabolizers, patients taking cimetadine or another CYP2C19 inhibitor, with hepatic impairment, or age >60
Fluoxetine 60 mg tablets	✓	✓	✓					✓		MDD, OCD, PD, Bulimia: 60 mg/day
Fluvoxamine ER capsules		✓			✓					OCD: 100-300 mg/day
Fluvoxamine tablets		✓								OCD: 50 mg/day as a single dose titrated up to 100-300 mg/day (divided twice daily)
Lexapro (escitalopram) tablets, oral solution	✓			✓						MDD: 10-20 mg/day GAD: 10 mg/day
Paxil (paroxetine) tablets, oral suspension	✓	✓	✓	✓	✓		✓			MDD: 20-50 mg/day OCD: 20-60 mg/day (target 40 mg/day) PD: 10-60 mg/day (target 40 mg/day) GAD: 20-50 mg/day (target 20 mg/day) SAD: 20-60 mg/day (target 20 mg/day) PTSD: 20-50 mg/day (target 20 mg/day)
Paxil CR (paroxetine CR) tablets	✓		✓		✓	✓				MDD: 25-62.5 mg/day PD: 12.5-75 mg/day SAD: 12.5-37.5 mg/day PDD: 12.5-25 mg/day (daily throughout cycle or limited to luteal phase)
Pexeva (paroxetine mesylate) tablets	✓	✓	✓	✓						MDD: 20-50 mg/day OCD: 20-60 mg/day (target 40 mg/day) PD: 10-60 mg/day (target 40 mg/day) GAD: 20-50 mg/day (target 20 mg/day)
Prozac Weekly (fluoxetine DR) capsules	✓									MDD: 90 mg once weekly
Prozac (fluoxetine) tablets, capsules, oral solution	✓	✓	✓					✓		MDD, OCD: 20-80 mg/day Bulimia: 60 mg/day PD: Initially 10 mg/day; titrated to 20 mg/day; up to 60 mg/day
Zoloft (sertraline) tablets, oral concentrate	✓	✓	✓		✓	✓	✓			MDD, OCD: Initially 50 mg/day PD, PTSD, SAD: Initial titration 25 to 50 mg/day; Range: 50-200 mg/day PDD: Initially 50 mg/day (daily throughout cycle or luteal phase only); Range: 50-100 mg/day for luteal phase only; up to 150 mg/day if taken throughout cycle

Agents	MDD	OCD	PD	GAD	SAD	PDD	PTSD	Bulimia	Other Diagnoses	Dosing (adults)
Serotonin Norepinephrine Reuptake Inhibitors (SNRIs)										
Cymbalta (duloxetine DR) capsules	✓			✓					✓ DPNP, FM, CMP	MDD: 20 mg twice daily to 60 mg/day (once or divided twice daily); may titrate from 30 to 60 mg once daily GAD: 60 mg/day (titrate from 30 mg/day) MDD, GAD: 120 mg/day shown effective but no evidence of added benefit and more adverse effects from doses >60 mg/day DPNP: 60 mg/day FM, CMP: 30 mg/day x one week; then 60 mg/day no evidence of added benefit and more adverse effects from doses >60 mg/day
Desvenlafaxine ER tablets	✓									MDD: 50 mg/day (range 50-400 mg/day); no evidence of additional benefit and more adverse effects from doses >50 mg/day
Duloxetine DR capsules	✓			✓					✓ DPNP CMP	MDD: 40 mg/day – 120 mg/day; no evidence of additional benefit for doses >60 mg/day GAD: 30 mg/day – 120 mg /day; no evidence of additional benefit for doses >60 mg/day DPNP: 60 mg/day; no evidence of additional benefit for doses >60 mg/day CMP: 30 mg/day – 60 mg/day; no evidence of additional benefit for doses >60 mg/day
Effexor (venlafaxine) tablets	✓									MDD: In 2-3 divided doses, 75-225 mg/day (moderately depressed outpatients); up to 350 mg/day (severely depressed inpatients) Maximum 375 mg/day in divided doses
Effexor XR (venlafaxine ER) capsules	✓		✓	✓	✓					MDD, GAD, PD: Initially 37.5 mg/day for 7 days; then range of 75-225 mg/day SAD: 75 mg/day
Fetzima (levomilnacipran ER} capsules	✓									MDD: Initial 20 mg once daily, then 40 mg once daily. Based on efficacy/tolerability, increase in increments of 40 mg at intervals of >2 days. Range 40 mg to 120 mg once daily. Maximum recommended dose is 120 mg once daily.
Khedezla (desvenlafaxine ER tablets	✓									MDD: 50 mg/day (range 50-400 mg/day); no evidence of additional benefit and more adverse effects from doses >50 mg/day
Irenka (duloxetine DR) capsules	✓			✓					✓ DPNP CMP	MDD: 40 mg/day – 120 mg/day; no evidence of additional benefit for doses >60 mg/day GAD: 30 mg/day – 120 mg /day; no evidence of additional benefit for doses >60 mg/day DPNP: 60 mg/day; no evidence of additional benefit for doses >60 mg/day CMP: 30 mg/day – 60 mg/day; no evidence of additional benefit for doses >60 mg/day
Pristiq (desvenlafaxine succinate) Tablets	✓									MDD: 50 mg/day (range 50-400 mg/day); no evidence of additional benefit and more adverse effects from doses >50 mg/day

Agents	MDD	OCD	PD	GAD	SAD	PDD	PTSD	Bulimia	Other Diagnoses	Dosing (adults)
Venlafaxine ER Tablets	✓				✓					MDD: Initially 37.5 to 75 mg/day; range of 75-225 mg/day SAD: 75 mg/day
Other Antidepressants										
Aplenzin (bupropion ER) tablets	✓									MDD: Initially, 174 mg/day; usual target dose is 348 mg/day; consider maximum dose 522 mg/day if no response to 348 mg
Forfivo XL (bupropion ER) Tablets	✓									MDD: Initially start with another formulation of bupropion until a patient has been on 300mg of bupropion per day for at least 2 weeks, and requires a dosage of 450mg per day
Maprotiline tablets	✓									MDD: 25 mg three times daily; may increase by 25-50 mg/day at weekly intervals depending on response. Usual dose: 75-150 mg/day (single dose at bedtime or divided). Maximum of 150-220 mg/day (1-3 doses)
Oleptro (trazodone ER) tablets	✓									MDD: Initially 150 mg once daily; increase by 75 mg/day; maximum 375 mg/day
Remeron, Remeron SolTab (mirtazapine) tablets, ODT tablets	✓									MDD: Initially 15 mg/day; range 15-45 mg/day
Trintellix (vortioxetine) tablets	✓									MDD: Initially, 10 mg once daily; increase to 20 mg/day as tolerated. Efficacy and safety of doses above 20 mg/day have not been evaluated
Viibryd (vilazodone) tablets	✓									MDD: Initially, 10 mg/day for 7 days; then 20 mg/day for 7 days; then 40 mg/day (recommended dose).
Wellbutrin, (bupropion) **Wellbutrin SR** (bupropion SR) tablets	✓									MDD: Wellbutrin: Initially 100 mg twice daily; may increase to 100 mg three times daily; Maximum of 450 mg/day (divided doses <150 mg each) MDD: Wellbutrin SR: Initially 150 mg once daily; then 150 mg twice daily as early as day 4; Maximum of 200 mg twice daily.
Wellbutrin XL (bupropion ER) tablets	✓								✓ SAFD	MDD: 150 mg/day titrated to 300 mg/day as early as day 4; Maximum 450 mg/day. SAFD: 150 mg/day for one week; then 300 mg/day (target dose).

MDD=major depressive disorder; OCD= obsessive compulsive disorder; PD= panic disorder; GAD= generalized anxiety disorder; SAD= social anxiety disorder or social phobia; PDD= premenstrual dysphoric disorder; PTSD= post traumatic stress disorder; DPNP=diabetic peripheral neuropathic pain; FM=fibromyalgia; CMP=chronic musculoskeletal pain; CR = controlled release; DR= delayed release; ER=extended release, ODT=orally disintegrating; SR= sustained release

POLICY

Prior Authorization Criteria for Approval

A. **Brand Antidepressant Agents** (except Cymbalta, Duloxetine (delayed release capsule, brand product), and Irenka, see below) will be approved when BOTH of the following are met:
   1. The patient has not filled a prescription for a monoamine oxidase (MAO) inhibitor in the past 30 days
      AND
   2. ONE of the following:
      a. The patient's medication history includes use of a generic antidepressant agent - SSRI, SNRI, bupropion, or mirtazapine [or generic trazodone extended-release if it becomes available] in the past 365 days
         OR
      b. There is documentation that the patient is currently being treated with the requested agent
         OR
      c. The prescriber states that the patient is currently being treated with the requested agent AND is at risk if therapy is changed
         OR
      d. The patient has a documented intolerance, FDA-labeled contraindication, or hypersensitivity to ONE generic antidepressant agent - SSRI, SNRI, bupropion, or mirtazapine, [or generic trazodone extended-release if it becomes available]

B. **Cymbalta, Duloxetine (delayed release capsule, brand product), and Irenka** will be approved when BOTH of the following are met:
   1. The patient has NOT filled a prescription for a monoamine oxidase (MAO) inhibitor in the past 30 days
      AND
   2. ONE of the following:
      a. The patient's medication history includes use of a generic antidepressant agent - SSRI, SNRI, bupropion, or mirtazapine, [or generic trazodone extended-release if it becomes available] in the past 365 days
         OR
      b. The patient has a diagnosis of neuropathic pain and has a medication history that includes use of amitriptyline, nortriptyline, desipramine, imipramine, or gabapentin in the past 90 days
         OR

c. For Cymbalta only, the patient has a diagnosis of fibromyalgia and has a medication history that includes use of amitriptyline, nortriptyline, desipramine, imipramine, cyclobenzaprine, gabapentin, or tramadol in the past 90 days
OR
d. The patient has a diagnosis of chronic musculoskeletal pain and has a medication history that includes use of acetaminophen, oral NSAID, topical NSAID, tramadol, amitriptyline, nortriptyline, desipramine, imipramine, cyclobenzaprine, or gabapentin in the past 90 days
OR
e. There is documentation that the patient is currently being treated with the requested agent
OR
f. The prescriber states that the patient is currently being treated with the requested agent AND is at risk if therapy is changed
OR
g. The patient has a documented intolerance, FDA-labeled contraindication, or hypersensitivity to ONE prerequisite for the requested diagnosis

Length of approval: 12 months

RATIONALE

Depression
Selective serotonin reuptake inhibitors (SSRIs) along with serotonin norepinephrine reuptake inhibitors (SNRIs), bupropion, and mirtazapine are considered first line treatment options for adults with major depressive disorder (MDD). The choice of medication is based on side effect profiles, history of prior response, family history of response, type of depression, concurrent medical illnesses, concurrently prescribed medications, and cost of medication. Although all these drugs may have similar efficacy, they differ significantly in their side effect profiles. Patients who cannot tolerate one agent may do well with another.[43-46]

Anxiety Disorders
Guidelines for treatment of anxiety include several anxiety-related conditions: obsessive compulsive disorder (OCD), panic disorder (PD), social anxiety disorder (SAD), post-traumatic stress disorder (PTSD), and generalized anxiety disorder (GAD). SSRIs or SNRIs (e.g. venlafaxine) are efficacious for the treatment of GAD. Although all these drugs may have similar efficacy, they differ significantly in their side effect profiles. Treatment choice is typically based on several factors including patient preference and medical history, side effect profile, and drug interactions. If effective, antidepressant treatment for GAD should be continued for at least 12 months. [47]

Neuropathic Pain
Treatment for neuropathic pain include TCAs, gabapentin, pregabalin, and SNRI antidepressants (duloxetine [most studied], venlafaxine) as first-line therapies. [21,22] For patients with diabetic

neuropathy, an antidepressant (e.g., amitriptyline, duloxetine, venlafaxine) or anticonvulsant (e.g., pregabalin) is recommend as initial therapy. Available evidence suggests these agents have similar modest benefit, though few high-quality comparative trials have been done. Among these options, the preference is to start with amitriptyline, particularly in younger healthier patients. Patients who fail to improve with a reasonable trial of one of these agents can be switched to monotherapy with another agent. For patients who do not improve on one drug, suggest combination therapy employing two drugs from different medication classes as the next step in the treatment paradigm. For patients who are unable to tolerate any of these drugs, alternative treatments include capsaicin cream, lidocaine patch, alpha-lipoic acid, isosorbide dinitrate topical spray, and transcutaneous electrical nerve stimulation.[48] Due to risk of addiction, abuse, sedation, and other complications associated with opioid use, opioids are not recommended for treatment of neuropathic pain.[22,48]

Fibromyalgia

Nonpharmacological therapy should be first-line therapy and then if there is a lack of effect, therapy should be individualized according to patient need, which may include pharmacological therapy. Pharmacologic therapies include: duloxetine, milnacipran, tramadol, pregabalin, cyclobenzaprine. Strength of recommendation for all these options is weak.[23,49] A review (2015) suggests pharmaceuticals (e.g., pregabalin, duloxetine, milnacipran) will provide clinically meaningful improvement without any major adverse events for a relatively small subset of patients only. In many other patients, the benefits do not outweigh the adverse effects, while the remainder do not experience any symptom improvement or even get worse.[23,50]

Pharmacological therapy should be guided by predominant symptoms that accompany pain. All patients should have a good therapeutic trial of a low-dose tricyclic compound (e.g., cyclobenzaprine, amitriptyline, or nortriptyline). Patients with comorbid depression or fatigue should next try a serotonin norepinephrine reuptake inhibitor (SNRI). Patients with comorbid anxiety or sleep issues should next try a gabapentinoid. It is often necessary to use several classes of drugs together. Use of opioids is discouraged. Nonsteroidal antiinflammatory drugs (NSAIDs) and acetaminophen can be used to treat comorbid peripheral pain generators.[-25]

Tramadol may be used in patients who require additional pain relief on a temporary basis for exacerbations or for patients who have inadequate pain control with other therapies.[51]

Chronic Musculoskeletal Pain

The American Psychiatric Association recommends the use of TCAs and SNRIs for treating chronic pain and comorbid depression.[28,41] SNRIs, which target both serotonin and norepinephrine, have a greater analgesic effect than antidepressants targeting either neurotransmitter alone. Duloxetine and venlafaxine have effectively reduced symptoms in patients with pain disorders and comorbid depression.[57]

Duloxetine is indicated for the management of chronic musculoskeletal pain, which was established in studies of patients with chronic low back pain and chronic pain due to osteoarthritis (OA).[13] A guideline on treatment of chronic noncancer pain including neuropathic, somatic, myofascial and visceral types of pain (American Society of Anesthesiologists, 2010) includes anticonvulsants, antidepressants (TCAs and SNRIs), benzodiazepines, NMDA receptor antagonists, NSAIDs, opioids, skeletal muscle relaxants, and topical agents as part of a multimodal strategy for a variety of patients with chronic pain. [31]

Adverse Effects

SSRIs

SSRIs commonly cause nausea, vomiting, diarrhea, nervous activation (e.g., insomnia, restlessness, anxiety), and headaches and these may dissipate over time. Although sexual dysfunction (e.g., loss of libido, erectile/ejaculatory problems) can occur with any antidepressant, this appears to be more common with SSRIs, and may also disappear with time. Paroxetine is associated with a higher incidence of weight gain than other SSRIs. Serotonin syndrome is associated with simultaneous use of SSRIs plus other serotonergic agents (e.g., monoamine oxidase inhibitors [MAOIs]) and should be avoided. SSRIs should not be abruptly discontinued to avoid discontinuation syndrome; most likely with paroxetine, least likely with fluoxetine. [28]

Citalopram doses above 40 mg/day are not recommended due to the risk of QT prolongation; 20 mg/day is the maximum recommended dose for CYP2C19 poor metabolizers or those patients taking a CYP2C19 inhibitor.[4] Citalopram should not be used in patients with QT syndrome, bradycardia, hypokalemia, hypomagnesemia, recent acute myocardial infarction, uncompensated heart failure, or with other drugs that prolong the QTc interval. Patients at risk for electrolyte disturbances should have baseline serum potassium and magnesium checked with periodic monitoring.[4,24]

SNRIs

SNRI side effects are similar with those of SSRIs (nausea, vomiting, nervous activation, sexual dysfunction) and may attenuate with continued use. SNRI effects are also more likely to reflect noradrenergic activity (increased pulse, dilated pupils, dry mouth, excess sweating, and constipation). All three SNRIs have a risk of increased blood pressure, especially at higher doses. As with SSRIs, serotonin syndrome is associated with simultaneous use of SNRIs plus other serotonergic agents (e.g., MAOIs) and should be avoided. Like SSRIs, SNRIs should not be abruptly discontinued to avoid discontinuation syndrome; more likely with venlafaxine and desvenlafaxine than duloxetine.[28]

Vortioxetine

Most common adverse reactions in patients on vortioxetine were nausea, constipation and vomiting. [38]

Vilazodone

Most common adverse effects of vilazodone in clinical trials were diarrhea, nausea, vomiting, and insomnia. Vilazodone is an SSRI and partial serotonergic 5-HT_{1a} agonist. Like SSRIs and SNRIs, the drug is associated with serotonin and discontinuation syndromes, and should not be given with other serotonergic agents or discontinued abruptly. [30]

Bupropion

Bupropion has fewer sexual side effects than other antidepressants. Neurologic adverse effects include headache, tremors, and seizures. Risk of seizures is minimized by avoiding high doses, avoiding rapid titration, using divided dosing schedules, avoiding use in patients at risk of seizures. Other side effects may include agitation/nervousness, mild cognitive dysfunction, insomnia, gastrointestinal upset. [28]

Mirtazapine
Most common side effects of mirtazapine include dry mouth, sedation, and weight gain (greater risk than other antidepressants). Mirtazapine is often given at bedtime and may be chosen for depressed patients with initial insomnia and weight loss. Mirtazapine increases serum cholesterol levels in some patients. [28]

Trazodone
The most common side effect with trazodone is sedation; this may be an advantage in patients with initial insomnias. Trazodone can also cause cardiovascular side effects, including orthostasis, particularly among elderly patients or those with preexisting heart disease. Use of trazodone has also been associated with life-threatening ventricular arrhythmias in several case reports. Trazodone also can cause sexual side effects, including erectile dysfunction in men; in rare instances, priapism occurs, which might require surgical correction. [28]

Maprotiline
Side effects with maprotiline may be similar to those seen with tricyclic antidepressants (TCAs), and can include cardiovascular effects including arrhythmias, anticholinergic effects, sedation, orthostatic hypotension, weight gain and seizures at therapeutic doses. Potentially dangerous interactions, including hypertensive crises and serotonin syndrome, can develop when TCAs are administered with MAOIs. [28]

Serotonin Syndrome
Serotonin syndrome is presumed to result from high levels of serotonin in the brain. Features of serotonin syndrome include abdominal pain, diarrhea, flushing, sweating, hyperthermia, lethargy, mental status changes, tremor and myoclonus, rhabdomyolysis, renal failure, cardiovascular shock, and possibly death. Although it can occur with administration of one or more serotonergic medications, it is most severe when an MAOI is coadministered with another serotonergic medication (such as an antidepressant). [28]

Other antidepressants should not be used in patients concomitantly taking an MAOI. [29]

REVISIONS	
04-01-2014	Policy posted July 15, 2014.
	Administrative Update
	In Description section: ▪ Added to Target Drugs: Brintellix™ (vortioxetine), Khedezla (Desvenlafaxine ER tablets), and Fetzima™ (levomilnacipran extended-release) ▪ Updated FDA Approved Indications and Dosage
	References updated
07-01-2014	Administrative Update In Description section: ▪ Added target drugs: Desvenlafaxine (ER tablets, brand product) and Desvenlafaxine fumarate (ER tablets, brand product) ▪ FDA Approved Indications and Dosage chart updated
	References updated
09-17-2014	Description section updated ▪ Target Drugs chart revised.

REVISIONS	
	▪ FDA Approved Indications and Dosage chart updated to add Fluoxetine and correct dosage for Brintellix
	In Policy section: ▪ In Items A 2 a, A 2 d, and B 2 a added "antidepressant agent" "generic", and "if it becomes available" to read, "... antidepressant agent - SSRI, SNRI, bupropion, or mirtazapine [or generic trazodone extended-release if it becomes available]" ▪ In Items A 2 c and B 2 f removed "prescribing physician" and added "provider" to read, "The prescriber states the patient..."
	Rationale section updated
	In Coding section ▪ HCPCS Codes confirmed
	In Revision section ▪ Removed update details for 12-31-2009, 05-20-2011.
	References updated
06-10-2015	Description section updated FDA Approved Indications and Dosage chart updated
	In Policy section: ▪ In Items A 2 c and B 2 f, grammar corrections made.
	Rationale section updated
	Coding section removed
	References updated
10-01-2015	Policy published 11-10-2015, Administrative Update retro-effective to 10-01-2015.
	Description section updated to include addition of "Duloxetine 40 mg (brand)" and "Irenka (duloxetine delayed release)" drug to Target Drugs chart and "Irenka (duloxetine delayed release)" to the FDA Approved Indications and Dosage chart.
	In Policy section: ▪ In Item A added “and Irenka” to read, “Brand Antidepressant Agents (except Cymbalta and Irenka, see below) will be approved when BOTH of the following are met:...” ▪ In Item B added “and Irenka” to read, “Cymbalta and Irenka will be approved when BOTH of the following are met:...” ▪ In Item B 2 c added “For Cymbalta only,” to read, “For Cymbalta only, the patient has a diagnosis of fibromyalgia and...” ▪ In Item B 2 e added “the requested agent” and removed “Cymbalta (duloxetine)” to read, “There is documentation that the patient is currently using the requested agent” ▪ In Item B 2 f added “the requested agent” and removed “Cymbalta (duloxetine)” to read, “The prescriber states that the patient is using the requested agent AND...”
	Rationale section updated
	References updated
06-01-2016	Published 05-25-2016. Effective 06-01-2016.
	Description section updates to Target Drugs and FDA Approved Indications and Dosage charts.
	In Policy section: ▪ In Item A added "Duloxetine (delayed release capsule, brand product)," to read "Brand Antidepressant Agents (except Cymbalta, Duloxetine (delayed release capsule, brand product), and Irenka, see below) will be approved when BOTH of the following are met:" ▪ In Item A 2 a, B 2 a, B 2 b, and B 2 c added "in the past 365 days" ▪ In Item B added "Duloxetine (delayed release capsule, brand product)," to read "Cymbalta, Duloxetine (delayed release capsule, brand product), and Irenka will be approved when BOTH of the following are met:"
	Rationale section updated
	References updated

REVISIONS	
07-01-2016	Published 07-20-2016. Retro-effective to 07-01-2016.
	The Brand drug name Brintellex was changed to Trintellix to avoid confusion with the antiplatelet drug Brilinta (ticagrelor).
	In Description section: ▪ Trintellix added to Target Drugs; FDA Approved Indications and Dosage charts.
	In Revision section: ▪ Removed Revision narratives for the following revision dates: 02-01-2012, 08-30-2012, 10-01-2013
	References updated
04-01-2017	In Description section: ▪ Noted availability of first generic drug for Pristiq in Target Drugs chart.
07-01-2017	In Description section: ▪ Target Drugs updated to remove Brintellix and Luvox CR and add fluvoxamine extended release FDA Approved Indications and Dosage updated to reflect Target Drugs updates
	In Policy section: ▪ In Item A 2 b and A 2 c removed "brand antidepressant" and added "agent" to read "...the patient is currently using the requested agent..." ▪ In Item B 2 b, B 2 c, and B 2 d revised "365 days" to "90 days".
	Rationale section updated
	References updated
12-11-2017	Policy published 01-05-2018. Policy retro-effective to 12-11-2017.
	In Description section: ▪ Updated Target Drugs list to note generic availability of Prozac 60 mg.
06-15-2018	Description section updated with updates to the FDA Approved Indications and Dosage chart.
	In Policy section ▪ In Item A 2 d removed "history of a" and added "ONE" to read "The patient has documented intolerance, FDA-labeled contraindication, or hypersensitivity to ONE generic antidepressant agent - SSRI, SNRI, bupropion, or mirtazapine, [or generic trazodone extended-release if it becomes available]" ▪ In Item B 2 g removed "history of a" and added "ONE" to read "The patient has a documented intolerance, FDA-labeled contraindication, or hypersensitivity to ONE prerequisite for the requested diagnosis"
	Rationale section updated
	References updated

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