Clinical Policy: Antidepressant Step Therapy

Reference Number: CP.CPA.219
Effective Date: 11.16.16
Last Review Date: 11.17
Line of Business: Commercial

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

The following are antidepressants requiring prior authorization: Bupropion ER (Aplenzin®), bupropion hydrochloride extended-release tablets (Forfivo XL®), desvenlafaxine fumarate extended release tablets, desvenlafaxine succinate (Pristiq®, Khedezla®), levomilnacipran (Fetzima®), vilazodone (Viibryd™), vortioxetine (Trintellix).

FDA approved indication

Aplenzin, Forfivo XL, Pristiq, Khedezla, Fetzima, Viibryd, and Trintellix are indicated:

- For the treatment of major depressive disorder (MDD)
- For Aplenzin only for the treatment of seasonal affective disorder (SAD)

Policy/Criteria

Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of health plans affiliated with Centene Corporation® that Aplenzin, desvenlafaxine fumarate extended release tablets, Fetzima, Forfivo XL, Khedezla, Pristiq, Trintellix, and Viibryd are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Major Depressive Disorder (must meet all)**:**

1. Diagnosis of depression;
2. One of the following (a or b):
   a. Failure of TWO of the following generic antidepressants: budeprion SR, bupropion, bupropion SR, bupropion XL, citalopram, desvenlafaxine succinate, duloxetine, escitalopram, fluoxetine, fluvoxamine, mirtazapine, paroxetine, sertraline, venlafaxine, venlafaxine XR unless contraindicated or clinically significant adverse effects are experienced;
   b. Member or a first degree relative has been successfully treated in the past with the requested agent;
3. Dose does not exceed: Aplenzin – 522 mg/day; Forfivo XL – 450 mg/day, desvenlafaxine fumarate extended release tablets – 400 mg/day, Pristiq – 400 mg/day, Khedezla - 400 mg/day, Fetzima - 120 mg/day, Viibryd - 40 mg/day, Trintellix - 20 mg/day.

Approval duration: Length of Benefit

B. Seasonal Affective Disorder (must meet all)**:**
1. Diagnosis of season affective disorder;
2. Request is for Aplenzin;
3. Failure or clinically adverse effects to generic bupropion extended release (generic Wellbutrin XL);
4. Dose does not exceed 522 mg/day.

Approval duration: Length of Benefit

C. Other diagnoses/indications
1. Refer to CP.CPA.09 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indication in Section I (must meet all)**:**
1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed : Aplenzin – 522 mg/day; Forfivo XL – 450 mg/day, desvenlafaxine fumarate extended release tablets – 400 mg/day, Pristiq – 400 mg/day, Khedezla - 400 mg/day, Fetzima - 120 mg/day, Viibryd - 40 mg/day, Trintellix - 20 mg/day.

Approval duration: Length of Benefit

B. Other diagnoses/indications(must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to CP.CPA.09 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – CP.CPA.09 or evidence of coverage documents;

B. Use of monamine oxidase inhibitors.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
MDD: Major Depressive Disorder
SAD: Seasonal Affective Disorder

Appendix B: General Information

- Desvenlafaxine fumarate extended release tablets is not a generic equivalent of Pristiq® (desvenlafaxine succinate extended release) or Khedezla™ (desvenlafaxine extended release) but is a new dosage form of existing agents for the same indication.

- Failure of antidepressant therapy for major depressive disorder is defined as the inability toachieve minimal or partial response after 4 weeks of therapy at maximum tolerated doses.
- Nefazodone requires prior authorization and is not included as a required agent; however, a prior trial of nefazodone will be sufficient for approval of a step therapy agent.
- A first-degree relative is defined as a parent, sibling, or offspring.
- In clinical trials, doses of Pristiq 50-400 mg/day were shown to be effective, although no additional benefit was demonstrated at doses greater than 50 mg/day and adverse events and discontinuations were more frequent at higher doses
- Aplenzin and Forfivo are not FDA-approved for smoking cessation treatment.
- Black box warning for Aplenzin, Forfivo, Pristiq, Khedezla and Viibryd includes that these agents are not approved for use in pediatric patients. Pooled analyses of short-term placebo-controlled studies of antidepressant drugs (SSRIs and others) showed that these drugs increase the risk of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults (ages 18-24) with MDD and other psychiatric disorders.
- Use of monoamine oxidase inhibitors (MAOI) with Aplenzin, Pristiq, Forfivo, Khedezla or Viibryd concomitantly is contraindicated due to the risk of serious, sometimes, fatal, drug interactions with serotonergic drugs. These interactions have been associated with symptoms that include tremor, myoclonus, diaphoresis, nausea, vomiting, flushing, dizziness, hyperthermia with features resembling neuroleptic malignant syndrome, seizures, rigidity, autonomic instability with possible rapid fluctuations of vital signs, and mental status changes that include extreme agitation progressing to delirium and coma. Allow at least 14 days after stopping Aplenzin, Forfivo, Pristiq, Khedezla or Viibryd before starting an MAOI.

Appendix C: Therapeutic Alternatives

Drug	Dosing Regimen	Dose Limit/ Maximum Dose
Selective Serotonin Reuptake Inhibitors		
citalopram (Celexa®)	20 mg PO QD	40 mg/day
escitalopram (Lexapro®)	10-20 mg PO QD	20 mg/day
fluvoxamine (Luvox CR®)	50-300 mg PO QD	300 mg/day
fluoxetine (Prozac®)	20 mg PO QD	80 mg/day
paroxetine (Paxil®)	20 mg PO QD	50 mg/day
paroxetine controlled release (Paxil CR®)	25 mg PO QD	62.5 mg/day
sertraline (Zoloft®)	50 mg PO QD	200 mg/day
Dual-acting Antidepressants		
mirtazapine (Remeron® or Remeron® SolTab)	15 mg PO QD	45 mg/day
venlafaxine (Effexor®)	75 mg/day PO in divided BID-TID	375 mg/day

Drug	Dosing Regimen	Dose Limit/ Maximum Dose
venlafaxine extended release (Effexor XR®)	37.5-75 mg PO QD	225 mg/day
duloxetine (Cymbalta®)	40-60 mg PO QD	60 mg/day
Dopaminergic Agents		
bupropion (Wellbutrin®, Budeprion®)	100 mg PO TID	450 mg/day
bupropion sustained release (Wellbutrin SR®, Budeprion SR®)	150 mg PO BID	400 mg/day
bupropion sustained release 24 hour (Wellbutrin XL®)	150-450 mg PO QD	450 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
bupropion ER (Aplenzin),	Major Depressive Disorder	Starting dose: 174 mg PO QD. After 4 days, may increase to 348 mg PO QD	522 mg/day
	Seasonal Affective Disorder	Initiate treatment in the autumn prior to onset of seasonal depressive symptoms. Starting dose: 174 mg PO QD (equivalent to 150 mg bupropion HCl). Usual target dose: 348 mg PO QD (equivalent to 300 mg bupropion HCl). After one week, may increase the dose to 348 mg PO QD. Continue treatment through the winter season.	

bupropion hydrochloride extended-release tablets (Forfivo XL)	Major Depressive Disorder	450 mg PO QD Do not initiate treatment with Forfivo XL, use another bupropion formulation for initial dose titration. Patients currently treated with other bupropion products at 450 mg/day can be switched to equivalent dose of Forfivo XL.	450 mg/day
desvenlafaxine fumarate extended release tablets	Major Depressive Disorder	50 mg PO QD	400 mg/day
desvenlafaxine succinate (Pristiq)	Major Depressive Disorder	50 mg PO QD	400 mg/day
desvenlafaxine succinate (Khedezla),	Major Depressive Disorder	50 mg PO QD	400 mg/day
levomilnacipran (Fetzima)	Major Depressive Disorder	40 mg PO QD for 2 days then increase to 40 mg QD Increase dose in increments of 40 mg at intervals of 2 or more days up to a maximum of 120 mg QD.	120 mg/day
vilazodone (Viibryd)	Major Depressive Disorder	20-40 mg PO QD	40 mg/day
vortioxetine (Trintellix)	Major Depressive Disorder	10 mg PO QD Increase to 20 mg/day as tolerated.	20 mg/day

VI. Product Availability

Drug	Availability
bupropion ER (Aplenzin)	Tablets: 174 mg, 348 mg, 522 mg
bupropion hydrochloride extended-release (Forfivo XL),	Tablets: 450 mg
desvenlafaxine fumarate extended release	Tablets: 50 mg, 100 mg
desvenlafaxine succinate (Pristiq)	Tablets: 25 mg, 50 mg, 100 mg
desvenlafaxine succinate (Khedezla)	Tablets: 50 mg, 100 mg
levomilnacipran (Fetzima)	Capsules: 20 mg, 40 mg, 80 mg, 120 mg
vilazodone (Viibryd)	Tablets: 10 mg, 20 mg, 40 mg

vortioxetine (Trintellix)	Tablets: 5 mg, 10 mg, 20 mg

VII. References

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Converted to new template. Minor changes to verbiage and grammar. References updated.	06.21.17	11.17

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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