INITIAL APPROVAL: JULY 11, 2018
REVISED DATES: SEPTEMBER 10, 2020
JULY 8, 2020; OCTOBER 9, 2019;
JULY 10, 2019; OCTOBER 10, 2018

CRITERIA FOR PRIOR AUTHORIZATION

Antidepressant Medications – Safe Use for All Ages

BILLING CODE TYPE For drug coverage and provider type information, see the KMAP Reference Codes webpage.

MANUAL GUIDELINES Prior authorization will be required for all current and future dose forms available of the medications below:

Amitriptyline (Elavil®)
Amoxapine
Bupropion (Aplenzin®, Forfivo® XL, Wellbutrin®, Wellbutrin® SR, Wellbutrin® XL)
Citalopram (Celexa®)
Clomipramine (Anafranil®)
Desipramine (Norpramin®)
Desvenlafaxine (Khedezla®, Pristiq®)
Doxepin (Sinequan®)
Duloxetine (Cymbalta®, Drizalma Sprinkle™)
Escitalopram (Lexapro®)
Esketamine (Spravato®)
Fluoxetine (Prozac®, Prozac Weekly®)
Fluvoxamine (Luvox®, Luvox CR®)
Imipramine (Tofranil®, Tofranil® PM)
Isocarboxazid (Marplan®)
Levomilnacipran (Fetzima®)
Maprotiline
Milnacipran (Savella®)
Nefazodone
Nortriptyline (Pamelor®)
Olanzapine/Fluoxetine (Symbyax®)
Paroxetine (Paxil®, Paxil CR®, Pexeva®)
Phenelzine (Nardil®)
Protriptyline (Vivactil®)
Selegiline (Emsam®)
Sertraline (Zoloft®)
Tranylcypromine (Parnate®)
Trimipramine (Surmontil®)
Venlafaxine (Effexor®, Effexor XR®)
Vilazodone (Viibryd®)
Vortioxetine (Trintellix®)

CRITERIA FOR PRIOR AUTHORIZATION FOR ANTIDEPRESSANTS MEDICATIONS:

- For all agents listed, the preferred PDL drug, if applicable, which covers this indication, is required unless the patient meets the non-preferred PDL PA criteria.

- MULTIPLE CONCURRENT USE:
  - Each of the following criteria for multiple concurrent use will require prior authorization:
    - For patients **< 13 years of age**, two or more different antidepressants used concurrently for greater than 60 days
    - For patients **≥ 13 years of age**, three or more different antidepressants used concurrently for greater than 60 days
    - Two or more different selective serotonin reuptake inhibitors (SSRIs) used concurrently for greater than 60 days (defined in table 1)
    - Two or more different serotonin norepinephrine reuptake inhibitors (SNRIs) used concurrently for greater than 60 days (defined in table 2)
    - Two or more different tricyclic antidepressants (TCAs) used concurrently for greater than 60 days (defined in table 3)

APPROVED PA Criteria

- Prior authorization will require written peer-to-peer consult with health plan psychiatrist, medical director, or pharmacy director for approval, followed by a verbal peer-to-peer if unable to approve written request.

- DOSING LIMITS:
  - The antidepressant dose must not exceed the dosing limit listed in Table 7. If the dosing limit is exceeded, prior authorization will be required.
    - Prior authorization will require a written peer-to-peer consult with health plan psychiatrist, medical director, or pharmacy director for approval, followed by a verbal peer-to-peer, if unable to approve written request.

LENGTH OF APPROVAL: 12 months

RENEWAL CRITERIA: Patient is stable and has been seen in the past year.

STEP THERAPY

CRITERIA FOR PRIOR AUTHORIZATION FOR APLENZIN®, FORFIVO® XL, VIIBRYD®, FETZIMA®, OR TRINTELLIX:

- Patient must have an adequate trial (at least 4 weeks) of at least 2 preferred agents from any of the following Preferred Drug list classes or individual drugs listed below:
  - Antidepressants – SNRIs
  - Antidepressants – SSRIs
  - Antidepressants – Tricyclics
  - Antidepressants – Other mechanisms, including:
    - Nefazodone
    - Mirtazapine
    - Buproprion
  - Monoamine Oxidase Inhibitors

CRITERIA FOR PRIOR AUTHORIZATION FOR ESKETAMINE (SPRAVATO™) NASAL SPRAY:

- Age ≥ 18 years of age.[7]
- Patient must have a diagnosis of treatment-resistant depression, including ALL of the following:
  - DSM-5 criteria for major depressive disorder.
  - Inadequate response (in the current episode) to at least 3 different antidepressants (listed in Tables 1-4) despite therapeutic dose and 6 weeks[1] duration of each medication.
- Patient must be maintained on antidepressant(s) while on therapy with Spravato.
- Patient must have an adequate trial (at least 4 weeks) of at least ONE of the following augmentation therapies, or a contraindication to all therapies listed in Table 5:[1]
  - Addition of a second-generation antipsychotic listed in Table 5 to the current regimen.
  - Addition or change in medication therapy to a fixed-dose combination product of olanzapine/fluoxetine.
- Prescriber must provide baseline Montgomery-Asberg Depression Rating Scale (MADRS) or Hamilton Depression scale (HAM-D) or Patient Health Questionnaire (PHQ-9) before initial treatment with intranasal esketamine.
  - Patient must have severe depression as defined by MADRS or HAM-D or the PHQ-9. See Table 6 below.
- Patient, provider, and provider's staff must be registered, educated, and be in good standing with the associated REMS program.
- Dose does not exceed 168mg (6 nasal spray devices) per week for induction (initial 4 weeks).[7]
- Dose does not exceed 84mg (3 nasal spray devices) per week for maintenance (beyond initial 4 weeks).[7]
- Patient must be screened for active/risk for substance use disorder.
- Prescriber has addressed the appropriateness of psychotherapy with the patient.

APPROVED PA Criteria

LENGTH OF INITIAL APPROVAL: 6 months

RENEWAL CRITERIA:

- Prescriber must provide the following response measure(s).
  - Stable response was maintained, defined as MADRS or HAM-D or PHQ-9 average decrease ≥50% from baseline, with a minimum of 3 assessments with the same tool.
- Patient has < 2 relapses since the most recent approval. A relapse is defined as hospitalization or overnight observation for worsening depression.
- Patient must be screened for active/risk for substance use disorder.
- Dose does not exceed 84mg (3 nasal spray devices) per week for maintenance.[7]

LENGTH OF APPROVAL FOR RENEWAL: 12 months

TABLE 1. SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIS)

SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIS)
Citalopram (Celexa®)
Escitalopram (Lexapro®)
Fluoxetine (Prozac®, Prozac Weekly®)
Fluvoxamine (Luvox®, Luvox CR®)
Paroxetine (Paxil®, Paxil CR®, Pexeva®)
Sertraline (Zoloft®)
Vilazodone (Viibryd®)*
Vortioxetine (Trintellix®)**

*Vilazodone also has partial agonistic 5-HT_{1A} activity

**Vortioxetine also has agonistic 5-HT_{1A} and antagonistic 5-HT_3 activity

TABLE 2. SEROTONIN-NOREPINEPHRINE REUPTAKE INHIBITORS (SNRIS)

SEROTONIN-NOREPINEPHRINE REUPTAKE INHIBITORS (SNRIS)
Desvenlafaxine (Khedezla®, Pristiq®)
Duloxetine (Cymbalta®, Drizalma Sprinkle™)
Levomilnacipran (Fetzima®)
Milnacipran (Savella®)
Venlafaxine (Effexor®, Effexor XR®)

TABLE 3. TRICYCLIC ANTIDEPRESSANTS (TCAS)

TRICYCLIC ANTIDEPRESSANTS (TCAS)
Amitriptyline (Elavil®)
Amoxapine
Clomipramine (Anafranil®)
Desipramine (Norpramin®)
Doxepin (Sinequan®)
Imipramine (Tofranil®)
Imipramine Pamoate (Tofranil® PM)
Nortriptyline (Pamelor®)
Protriptyline (Vivactil®)
Trimipramine (Surmontil®)
TETRACYCLIC ANTIDEPRESSANTS
Maprotiline

APPROVED PA Criteria

TABLE 4. OTHER ANTIDEPRESSANTS

DOPAMINE NOREPINEPHRINE REUPTAKE INHIBITORS
Bupropion (Aplenzin®, Forfivo® XL, Wellbutrin®, Wellbutrin® SR, Wellbutrin® XL)
SEROTONIN MODULATORS
Nefazodone (Serzone)
Monoamine Oxidase Inhibitors (MAOIs)
Phenelzine (Nardil®)
Tranylcypromine (Parnate®)
Isocarboxazid (Marplan)
Selegiline transdermal system (Emsam®)

TABLE 5. AUGMENTATION THERAPIES[1,8-11]

SECOND-GENERATION ANTI-PSYCHOTICS (SGAS)
Aripiprazole (Abilify®)
Brexpiprazole (Rexulti®)
Olanzapine/fluoxetine (Symbyax®) (fixed combination product)
Quetiapine Extended Release (Seroquel XR®)

TABLE 6. CUTOFFS FOR SEVERE DEPRESSION[3-4]

RATING SCALE	CUTOFF SCORE FOR SEVERE DEPRESSION
MADRS	≥ 35
HAM-D	≥ 19
PHQ-9	≥ 20

TABLE 7. ANTIDEPRESSANT MEDICATION DOSING LIMITS

MEDICATION	PEDIATRIC* MINIMUM AGE (YEARS) (LITERATURE-BASED)**	PEDIATRIC* MAX DOSE/DAY (LITERATURE-BASED)**	ADULT MAX DOSE/DAY (FDA-APPROVED)
Amitriptyline (Elavil®)	Not Approved	Not Approved	300mg
Amoxapine	Not Approved	Not Approved	400mg
Bupropion (Aplenzin®)	Not Approved	Not Approved	522mg
Bupropion (Forfivo® XL)	Not Approved	Not Approved	450mg
Bupropion (Wellbutrin®)	≥6	≤6mg/kg or 300mg	450mg
Bupropion (Wellbutrin® SR)		400mg	400mg
Bupropion (Wellbutrin® XL)		450mg	450mg
Citalopram (Celexa®)	≥6	40mg	40mg
Clomipramine (Anafranil®)	≥10	≤3mg/kg or 200mg	200mg (OCD)
Desipramine (Norpramin®)	Not Approved	Not Approved	150mg
Desvenlafaxine (Khedezla®, Pristiq®)	≥7	50mg	100mg
Doxepin (Sinequan®)	Not Approved	Not Approved	300mg
Duloxetine (Cymbalta®, Drizalma Sprinkle™)	≥7	120mg	120mg
Escitalopram (Lexapro®)	≥6	20mg	20mg
	≥12	30mg	20mg
Esketamine (Spravato®)	Not Approved	Not Approved	Induction (initial 4 weeks): 168mg/week,

APPROVED PA Criteria

			Maintenance: 84mg/week
Fluoxetine (Prozac®, Prozac Weekly®)	≥6	60mg	80mg
Fluvoxamine (Luvox®)	≥8	200mg	200mg (OCD)
	≥12	300mg	300mg (OCD)
Fluvoxamine (Luvox CR®)	Not Approved	Not Approved	300mg (OCD)
Imipramine HCl (Tofranil®)	≥6	2.5mg/kg/day	200mg
Imipramine pamoate (Tofranil PM®)	Not Approved	Not Approved	300mg
Isocarboxazid (Marplan)	Not Approved	Not Approved	60mg
Levomilnacipran (Fetzima®)	Not Approved	Not Approved	120mg
Maprotiline	Not Approved	Not Approved	150mg
Milnacipran (Savella®)	Not Approved	Not Approved	200mg (fibromyalgia)
Nefazodone	Not Approved	Not Approved	200mg
Nortriptyline (Pamelor®)	≥6	≤2mg/kg or 100mg	150mg
Paroxetine (Paxil®, Pexeva®)	Not Approved	Not Approved	50mg
Paroxetine (Paxil CR®)	Not Approved	Not Approved	62.5mg
Phenelzine (Nardil®)	Not Approved	Not Approved	90mg
Protriptyline (Vivactil®)	Not Approved	Not Approved	60mg
Selegiline transdermal system (Emsam®)	≥12	12mg per 24 hours	12mg
Sertraline (Zoloft®)	≥6	200mg	200mg
Tranylcypromine (Parnate®)	Not Approved	Not Approved	60mg
Trimipramine (Surmontil®)	Not Approved	Not Approved	200mg
Venlafaxine (Effexor®, Effexor XR®)	Not Approved	Not Approved	225mg (IR), 375mg (ER)
	Not Approved	Not Approved	
Vilazodone (Viibryd®)	≥12	30mg	40mg
Vortioxetine (Trintellix®)	Not Approved	Not Approved	20mg

"Not Approved" means insufficient evidence available or pediatric dosing was reviewed, but not recommended.
*"Pediatric" means age < 18 years.
**Adapted from the Texas Department of Family and protective Services. See reference #2 below.

Notes:

- Mirtazapine, and trazodone are FDA-indicated for depression, but are not listed because they are primarily used for other indications.

References:

1. Practice Guideline for the Treatment of Patients with Major Depressive Disorder, Third Edition. American Psychiatric Association, October 2010. Available at https://psychiatryonline.org/guidelines. Accessed 7/24/19.
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3. Grade Scores of the Montgomery-Asberg Depression and the Clinical Anxiety Scales. Br J Psychiatry 1986; 148:599-601. Available at https://www.cambridge.org/core/journals/the-british-journal-of-psychiatry/article/grade-scores-of-the-montgomeryasberg-depression-and-the-clinical-anxiety-scales/E03CC2A39EEE29F47DAAE56A48B4EA60. Accessed 9/17/19.
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5. Patient Health Questionnaire (PHQ9). Available at https://www.integration.samhsa.gov/clinical-practice/screening-tools. Accessed 10/21/19.

6. Zimmerman, M. Using the 9-item Patient Health Questionnaire to Screen for and Monitor Depression. JAMA October 2019. [Epub ahead of print]. Available at https://jamanetwork.com/journals/jama/article-abstract/2753532. Accessed on 10/22/19.
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8. Abilify (aripiprazole) [package insert]. Rockville, MD: Otsuka America Pharmaceutical, Inc.; February 2017.
9. Rexulti (brexipiprazole) [package insert]. Otsuka America Pharmaceutical, Inc.; February 2018.
10. Symbyax (olanzapine/fluoxetine) [package insert]. Indianapolis, IN: Lilly USA, LLC; March 2018.
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DRUG UTILIZATION REVIEW COMMITTEE CHAIR

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DATE

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PHARMACY PROGRAM MANAGER
DIVISION OF HEALTH CARE FINANCE
KANSAS DEPARTMENT OF HEALTH AND ENVIRONMENT

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DATE