# Pharmacy Management Drug Policy

**SUBJECT: Spravato® (esketamine) Nasal Spray**
**POLICY NUMBER: PHARMACY-144**
**EFFECTIVE DATE: 05/2026**
**LAST REVIEW DATE: 05/29/2026**

*If the member's subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. This drug policy applies to the following line/s of business:*

**Policy Application**

| | | |
|---|---|---|
| **Category**: | ☒ Commercial Group (e.g., EPO, HMO, POS, PPO) | ☒ Medicare Advantage |
| | ☒ On Exchange Qualified Health Plans (QHP) | ☐ Medicare Part D |
| | ☒ Off Exchange Direct Pay | ☒ Essential Plan (EP) |
| | ☒ Medicaid & Health and Recovery Plans (MMC/HARP) | ☒ Child Health Plus (CHP) |
| | ☐ Federal Employee Program (FEP) | ☐ Ancillary Services |
| | ☒ Dual Eligible Special Needs Plan (D-SNP) | |

## DESCRIPTION:

### Major Depressive Disorder

Major Depressive Disorder (MDD) is a common, serious, and recurrent psychiatric condition characterized by persistent depressive symptoms associated with clinically significant functional impairment. MDD is defined and diagnosed according to the diagnostic criteria outlined in the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR).*

A diagnosis of MDD requires the presence of five or more depressive symptoms occurring during the same two-week period, representing a change from prior functioning, with at least one symptom being depressed mood or markedly diminished interest or pleasure (anhedonia). Associated symptoms may include disturbances in sleep, appetite, energy, psychomotor activity, cognition, self-worth, or recurrent thoughts of death or suicide. Symptoms must result in clinically significant distress or impairment in social, occupational, or other important areas of functioning and must not be attributable to substance use, medication effects, or another medical condition.

MDD affects a substantial portion of the adult population and is a leading cause of disability worldwide. The disorder frequently follows a chronic or recurrent course, with many patients experiencing multiple depressive episodes over their lifetime. MDD is associated with increased healthcare utilization, reduced workplace productivity, medical comorbidity, and elevated suicide risk. Severity is commonly categorized as mild, moderate, or severe, based on symptom burden and degree of functional impairment, and severity guides treatment selection and intensity.

Standard treatment of MDD is evidence-based and stepwise, with therapeutic interventions selected according to episode severity, patient history, and clinical presentation. First-line treatments include psychotherapy, pharmacologic antidepressant therapy such as SSRIs or SNRIS, or a combination of both. Psychotherapy alone may be sufficient for mild episodes, while moderate to severe depression frequently requires pharmacologic intervention, often in combination with psychotherapy. The goal of treatment is remission of symptoms, restoration of function, and prevention of relapse or recurrence.

Although many patients respond to initial treatment, up to one-third of individuals with major depressive disorder (MDD) experience an inadequate response to currently available medications; these patients are considered to have treatment-resistant depression.

**Treatment-Resistant Depression**

Treatment-Resistant Depression (TRD) is generally defined as Major Depressive Disorder that does not achieve an adequate clinical response despite multiple trials of evidence-based antidepressant treatment, administered at appropriate doses and durations with documented adherence. Although there is no single universally accepted definition, TRD is commonly defined as failure to respond to at least two antidepressant therapies from different pharmacologic classes, given at therapeutic doses for an adequate period of time.

TRD represents a distinct and clinically significant subgroup of patients with MDD. Individuals with TRD experience greater symptom severity, longer episode duration, higher relapse rates, increased functional impairment, and greater healthcare utilization compared with patients whose depression responds to first-line therapy. TRD is also associated with higher rates of psychiatric comorbidity, medical comorbidity, disability claims, and suicide attempts.

Management of TRD typically involves escalation beyond first-line interventions and may include antidepressant switching, pharmacologic augmentation strategies, structured psychotherapy in combination with medication, or neuromodulation and novel therapeutics for appropriately selected patients. TRD is recognized as a condition with higher unmet clinical need, warranting consideration of additional or specialized treatment options when standard therapies have been insufficient.

**Spravato (esketamine) nasal spray**

Spravato (esketamine) is the S-enantiomer of racemic ketamine, and is a non-selective, non-competitive antagonist of the N-methyl-D-aspartate (NMDA) receptor, an ionotropic glutamate receptor. The precise mechanism by which esketamine produces antidepressant effects is not fully understood. Esketamine is indicated for the treatment of treatment-resistant depression (TRD) in adults as monotherapy or in conjunction with an oral antidepressant. Esketamine is also indicated for depressive symptoms in adults with major depressive disorder (MDD) with acute suicidal ideation or behavior.

*Clinical Efficacy*

The efficacy of esketamine in TRD was evaluated in the TRANSFORM trials, multiple short-term randomized, double-blind clinical trials in which esketamine plus a newly initiated oral antidepressant was compared with placebo nasal spray plus antidepressant over a 4-week treatment period. Eligible participants had a diagnosis of moderate to severe depression and were required to meet the study definition of treatment-resistant depression, which was nonresponse to an adequate trial (dosage, duration, and adherence) of at least two antidepressants in the current episode. The primary endpoint was the change in the Montgomery-Åsberg Depression Rating Scale (MADRS) from baseline to day 28. Across these studies, esketamine demonstrated rapid antidepressant effects, with statistically significant improvement observed in one pivotal short-term trial and supportive efficacy trends observed in additional studies, including in older adult populations. The TRANSFORM-2 trial was the pivotal positive short-term study supporting FDA approval, demonstrating the change in MADRS score with esketamine plus antidepressant was significantly greater than with antidepressant plus placebo at day 28 (difference of least square means = -4.0, SE = 1.69, 95% CI = -7.31, -0.64; p=0.020).[11,12,13,14]

The clinical development program also included the SUSTAIN-1 study, a randomized maintenance-of-effect trial evaluating relapse prevention. Patients were enrolled directly or were transferred into this study following participation in the TRANSFORM-1 or TRANSFORM-2 trials. All subjects who experienced ≥ 50% reduction from baseline in MADRS total score by the end of the 4-week induction phase were eligible to enter the 12-week optimization phase during which study drug dosages remained fixed but the frequency of intranasal dosing was reduced to once weekly for 4 weeks then individualized to weekly or every 2 weeks based on the severity of depressive symptoms. At week 16 of the optimization phase, patients who achieved stable remission (defined as MADRS score ≤ 12 for ≥ 3 of the last 4 weeks) and those who achieved stable response (defined as ≥50% reduction in MADRS score from baseline in the last 2 weeks of the optimization phase but without achieving remission) entered the maintenance phase. Patients were separately randomized 1:1 according to a computer-generated schedule to continue esketamine treatment or discontinue esketamine treatment and switch to placebo nasal spray, each in addition to oral antidepressant treatment. In this study, continued treatment with esketamine plus an oral antidepressant significantly delayed time to relapse compared with antidepressant plus placebo among patients who achieved stable remission or stable response. The risk of relapse was reduced by approximately 50% among patients in stable remission and by approximately 70% among patients in stable response, with clinically meaningful numbers needed to treat (patients who achieved stable remission: HR, 0.49; 95% CI, 0.29-0.84; P = .003, number needed to treat [NNT], 6; patients who achieved stable response: HR, 0.30; 95% CI, 0.16-0.55: P < .001, NNT, 4).[11,16]

The efficacy of esketamine nasal spray for use as monotherapy for treatment-resistant depression was evaluated in a Phase 4 trial. In this randomized, double-blind, placebo-controlled short-term trial, adults with TRD were randomized (1:1:2) to receive fixed-dose esketamine nasal spray (56 mg or 84mg) or placebo without concomitant oral antidepressant therapy. The primary efficacy endpoint was the change in the MADRS score from baseline to day 28. A key secondary endpoint was the change in MADRS 24-hour post-first dose (Day 2). Esketamine monotherapy demonstrated statistically significant and clinically meaningful reductions in depressive symptoms compared with placebo, with improvements observed as early as 24 hours after the first dose and sustained through the 4-week treatment period. On day 28, the least-square (LS) mean difference (SE) between esketamine and placebo was −5.1 (1.42) (95%CI, −7.91 to −2.33) for the 56-mg dose and −6.8 (1.38) (95%CI, −9.48 to −4.07) for the 84-mg dose (for each, 2-sided P < .001). Observed effect sizes were 0.48 and 0.63 for the 56-mg and 84-mg dose groups, respectively. At day 2 (approximately 24 hours post–first dose), the between-group difference was significant for both esketamine doses: −3.8 (1.29) (95%CI,−6.29 to −1.22; 2-sided P = .004) for 56mg and −3.4 (1.24) (95%CI, −5.89 to −1.00; 2-sided P = .006) for 84mg.[11,17]

Esketamine was studied for use in major depressive disorder with acute suicidal ideation or behavior (MDD-SI) in the ASPIRE clinical trial program. The ASPIRE I and ASPIRE II trials were two identical Phase 3 short-term (4-week) randomized, double-blind, placebo-controlled studies in which hospitalized patients with MDD and acute suicidal ideation received esketamine nasal spray or placebo, each in combination with comprehensive standard of care, including hospitalization and initiation or optimization of oral antidepressant therapy. In both trials, esketamine produced a rapid reduction in depressive symptoms compared with placebo at 24 hours. However, although severity of suicidality improved in both treatment groups, the between-group difference in suicidality measures did not achieve statistical significance. These data supported approval for use of esketamine, in conjunction with an oral antidepressant, for depressive symptoms in patients with MDD and acute suicidal ideation or behavior, while underscoring that esketamine is

not indicated for the prevention of suicide or for use without ongoing standard psychiatric care.[11,18,19,20]

*Limitations of Evidence*
The available clinical evidence for esketamine is subject to several limitations. Short-term efficacy trials were generally limited to approximately four weeks in duration. Most pivotal trials evaluated esketamine in combination with a newly initiated oral antidepressant, limiting conclusions regarding long-term comparative effectiveness versus other treatment strategies. In studies of patients with MDD and acute suicidal ideation or behavior, improvements in depressive symptoms were observed; however, between-group differences in measures of suicidality were not statistically significant, and esketamine has not been demonstrated to reduce suicide risk or prevent suicidal behavior.

*Safety*
Esketamine is associated with clinically significant safety risks, including but not limited to sedation, dissociation, and respiratory depression. Due to these risks, esketamine is subject to a Risk Evaluation and Mitigation Strategy (REMS).

Under the REMS program:
- Esketamine must be administered in a certified healthcare setting.
- Patients are required to be monitored for a minimum of two hours following each administration.
- Patients must be assessed for clinical stability prior to discharge from the healthcare setting.
- Esketamine is not dispensed directly to patients for at-home use.

**POLICY:**

**Universal Criteria:**
1. Spravato will not be covered in patients with:
    a. A current or prior diagnosis of primary psychotic disorder (schizophrenia, schizoaffective disorder, delusional disorder, brief psychotic disorder, schizophreniform disorder)
    b. Current psychotic features (delusions, hallucinations, disorganized thinking) regardless of underlying diagnosis
    c. Major Depressive Disorder (MDD) with psychotic features (per DSM-5 criteria)
2. The prescriber must attest that Spravato will be administered at a treatment facility that is certified through the REMS program and that the patient has been enrolled in the REMS program

**For moderate-to-severe Major Depressive Disorder (MDD) with acute suicidal ideation or behavior:**
1. The patient must be 18 years of age or older **AND**
2. The patient must have moderate-to-severe Major Depressive Disorder (MDD) with recent suicidal behavior **OR** imminent high risk of suicide, defined as:
    a. Suicide attempt within the past 3 months
    b. Active suicidal ideation with intent to act (with or without a specific plan)
    c. Preparatory actions toward suicide (e.g., acquiring means, putting affairs in order) **AND**
3. Documentation must include:
    a. Validated suicide risk assessment (e.g., C-SSRS showing high risk) **AND**
    b. Clinical documentation of moderate-to-severe depression with functional impairment (e.g., MADRS score >28, PHQ-9 score ≥15, or equivalent)

4. The diagnosis must be confirmed by a mental health provider (e.g., psychiatrist, psychiatric nurse practitioner) **AND**
5. The mental health provider must perform and document an evaluation of suicide risk and determine the appropriate level of care. Documentation must confirm one of the following:
    a. The patient required inpatient psychiatric hospitalization **OR**
    b. The patient was evaluated and determined appropriate for a structured outpatient level of care with active monitoring and follow-up plan **AND**
6. The provider must attest that the patient is on concurrent oral antidepressant therapy (either continuing current therapy, optimizing current therapy, or initiating new therapy as clinically appropriate).
7. Recertification for moderate-to-severe major depressive disorder (MDD) with acute suicidal ideation or behavior will not be approved.
    a. According to the prescribing information: "The use of Spravato, in conjunction with an oral antidepressant, beyond 4 weeks has not been systematically evaluated in the treatment of depressive symptoms in patients with MDD with acute suicidal ideation or behavior."
    b. For consideration of continued treatment, refer to the medical necessity criteria for treatment-resistant single episode or treatment-resistant recurrent major depressive disorder (MDD) without psychotic features.
8. Approval timeframe:
    a. Approval will be granted for 1 month to allow a maximum of 4 weeks of treatment for this diagnosis.

**For treatment-resistant Single Episode or treatment-resistant Recurrent Major Depressive Disorder (MDD) without psychotic features:**

1. The patient must be 18 years of age or older **AND**
2. The patient must have a diagnosis of Recurrent Major Depressive Disorder **OR** Single-Episode Major Depressive Disorder of ≥2 years duration, without psychotic features, confirmed by DSM-5 criteria **AND**
3. The diagnosis must be confirmed by a mental health provider (e.g., psychiatrist, psychiatric nurse practitioner) **AND**
4. The patient must have a confirmed diagnosis of Treatment-Resistant Depression, defined as Major Depressive Disorder (single episode ≥2 years duration or recurrent), without psychotic features, that has not responded adequately to treatment in the current depressive episode.
    a. Treatment-Resistant Depression is defined as an inadequate response to ≥2 oral antidepressants of adequate dose and duration (minimum 6 weeks each) in the current episode
        i. Inadequate response is defined as ≤ 25% improvement in depressive symptoms **OR** failure to achieve remission despite adequate dose and duration **AND**
5. There must be documentation of at least one of the following:
    a. Failure of an evidence-based augmentation strategy (e.g., atypical antipsychotic, lithium, thyroid hormone, or combination antidepressant therapy) **OR**
    b. Prolonged episode duration (≥12 months) or recurrent episodes with insufficient inter-episode recovery **OR**
    c. Persistent moderate-to-severe symptoms (e.g., MADRS ≥28, PHQ-9 ≥15, or equivalent) despite treatment **OR**
    d. Significant functional impairment (occupational, social, or ADLs) attributable to depression **OR**
    e. Clinician determination that further standard antidepressant sequencing is unlikely to provide meaningful benefit (with documented rationale) **AND**

6. For patients naive to treatment with Spravato (this criterion does not apply to Medicare Advantage or Medicaid/HARP):
    a. Spravato is FDA-approved as monotherapy or in combination with an oral antidepressant for TRD. Combination therapy is preferred based on higher remission rates in clinical trials. Therefore, Spravato will only be covered in combination with an oral antidepressant (e.g., SSRI, SNRI) for patients with treatment-resistant depression. For patients unable to tolerate oral antidepressants due to serious side effects or contraindication, Spravato may be approved for use as monotherapy with appropriate documentation on a case-by-case basis **AND**
7. The patient's baseline depression symptoms must be measured and documented with an appropriate rating scale (such as PHQ-9, Clinically Useful Depression Outcome Scale, Quick Inventory of Depressive Symptomatology-Self Report 16 Item, MADRS, or HAM-D) as a tool for monitoring response to therapy
8. Recertification
    a. Initial recertification will require documentation of clinically meaningful improvement in depression symptoms (e.g.,> 25% reduction from baseline, or meeting established minimal clinically important difference thresholds for the scale used) measured after 4-8 weeks of therapy with Spravato by the same rating scale used at baseline.
        i. For patients using Spravato in combination with an oral antidepressant (as necessitated on initial review), documentation is required that confirms the patient will continue to use an oral antidepressant in combination with Spravato for at least 6- months post-remission as combination therapy has demonstrated lower relapse rates compared to monotherapy. Recertification will be approved for 6 months if improvement in symptoms is demonstrated, and the REMS protocol continues to be followed.
    b. Ongoing recertification requires documentation that the member has maintained improvement in symptoms and the REMS protocol continues to be followed
9. Approval timeframe:
    a. Initial: 2 months
    b. Recertification:
        i. Initial: 6 months
        ii. Ongoing: 1 year

**POLICY GUIDELINES:**

1. Utilization management are contract dependent. Refer to specific contract/benefit language for exclusions.
    a. Coverage criteria may be dependent on the contract renewal date.
    b. Coverage of drugs listed in this policy are contract dependent.
    c. Not all contracts/benefits allow coverage of healthcare professional administered drugs as part of their pharmacy benefit
    d. Not all contracts/benefits cover all medical infusible drugs.
2. All utilization management requirements outlined in this policy are compliant with applicable New York State insurance laws and regulations. Policies will be reviewed and updated as necessary to ensure ongoing compliance with all state and federally mandated coverage requirements.
3. Unless otherwise indicated within drug specific criteria, the drugs listed in this policy are administered by a healthcare professional and therefore are covered under the medical benefit.
4. Clinical documentation must be submitted for each request (initial and recertification) unless otherwise specified (e.g., provider attestation required). Supporting documentation includes,

but is not limited to, progress notes documenting previous treatments and treatment history, diagnostic testing, laboratory test results, genetic testing or biomarker results, imaging and other objective or subjective measures of clinical benefit.
For recertification, continued approval requires documentation continued approval requires documentation demonstrating that the requested product is providing ongoing benefit to the patient, evidenced by improvement or stability in the disease state or condition, and that continued use remains medically necessary. Ongoing use of the requested product must continue to align with the current policy's preferred formulary. Recertification reviews may result in a requirement to trial more cost-effective treatment alternatives as they become available (e.g., generics, biosimilars, or other guideline-supported treatment options). Requested dosing must remain consistent with FDA-approved or off-label/guideline-supported dosing recommendations.

5. All requests will be reviewed to ensure they are being used for an appropriate indication and may be subject to an off-label review in accordance with our Off-Label Use of FDA Approved Drugs Policy (Pharmacy-32).
6. Dose and frequency should be in accordance with the FDA label or recognized compendia (for off-label uses). When services are performed in excess of established parameters, they may be subject to review for medical necessity.
7. This policy does not apply to Medicare Part D and D-SNP pharmacy benefits. The drugs in this policy may apply to all other lines of business including Medicare Advantage.
8. For members with Medicare Advantage, medications with a National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) will be covered pursuant to the criteria outlined by the NCD and/or LCD. NCDs/LCDs for applicable medications can be found on the CMS website at https://www.cms.gov/medicare-coverage-database/search.aspx. Indications that have not been addressed by the applicable medication's LCD/NCD will be covered in accordance with criteria determined by the Health Plan (which may include review per the Health Plan's Off-Label Use of FDA Approved Drugs policy). Step therapy requirements may be imposed in addition to LCD/NCD requirements.
9. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS permits a Medicare Advantage Organization (MAO) to establish its own coverage determinations in accordance with 42 CFR § 422.101(b)(6).
10. For contracts where Insurance Law § 4903(c-1), and Public Health Law § 4903(3-a) are applicable, if trial of preferred drug(s) is the only criterion that is not met for a given condition, and one of the following circumstances can be substantiated by the requesting provider, then trial of the preferred drug(s) will not be required.
    - The required prescription drug(s) is (are) contraindicated or will likely cause an adverse reaction or physical or mental harm to the member;
    - The required prescription drug is expected to be ineffective based on the known clinical history and conditions and concurrent drug regimen;
    - The required prescription drug(s) was (were) previously tried while under the current or a previous health plan, or another prescription drug or drugs in the same pharmacologic class or with the same mechanism of action was (were) previously tried and such prescription drug(s) was (were) discontinued due to lack of efficacy or effectiveness, diminished effect, or an adverse event;
    - The required prescription drug(s) is (are) not in the patient's best interest because it will likely cause a significant barrier to adherence to or compliance with the plan of care, will likely worsen a comorbid condition, or will likely decrease the ability to achieve or maintain reasonable functional ability in performing daily activities;

- The individual is stable on the requested prescription drug. The medical profile of the individual (age, disease state, comorbidities), along with the rational for deeming stability as it relates to standard medical practice and evidence-based practice protocols for the disease state will be taken into consideration;
- The above criteria are not applicable to requests for brand name medications that have an AB rated generic. We can require a trial of an AB-rated generic equivalent prior to providing coverage for the equivalent brand name prescription drug.

11. This policy is based on available evidence as of the last review date. Coverage determinations are subject to applicable plan documents, state and federal regulations, and individual patient circumstances. This policy does not constitute medical advice.
12. For commercial contracts, medical necessity determinations align with the Certificate of Coverage issued by the Health Plan, which states that covered services must be clinically appropriate and not primarily for the convenience of the member, the member's family, or the provider.
13. Manufacturers may either discontinue participation in, or may not participate in, the Medicaid Drug Rebate Program (MDRP). Under New York State Medicaid requirements, physician-administered drugs must be produced by manufacturers that participate in the MDRP. Products made by manufacturers that do not participate in the MDRP will not be covered under Medicaid Managed Care/HARP lines of business. Drug coverage will not be available for any product from a non-participating manufacturer. For a complete list of New/Reinstated & Terminated Labelers please visit: https://www.medicaid.gov/medicaid/prescriptiondrugs/medicaid-drug-rebate-program/newreinstated-terminated-labeler-information/index.html

**CODES:**

Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.
CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.
Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.

Code Key:
Experimental/Investigational = (E/I),
Not medically necessary/ appropriate = (NMN).


**HCPCS**:

| HCPCS Codes | Description |
|---|---|
| G2082 | Office or other outpatient visit for the evaluation and management of an established patient that requires the supervision of a physician or other qualified health care professional and provision of up to 56 mg of esketamine nasal self-administration, includes 2 hours post administration observation |
| G2083 | Office or other outpatient visit for the evaluation and management of an established patient that requires the supervision of a physician or other qualified health care professional and provision of greater than 56 mg esketamine nasal self-administration, includes 2 hours post administration observation |
| J0013 | Esketamine, nasal spray, 1 mg |

**UPDATES:**

| Date | Revision |
|---|---|
| 05/29/2026 | Revised |
| 05/22/2026 | Created and Implemented |
| 05/14/2026 | P&T Committee Approval |

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**Appendix:**

**Validated Assessment Tools:**

- Columbia-Suicide Severity Rating Scale (C-CCRS): A standardized tool used to assess the severity and immediacy of suicide risk through structured questions about suicidal thoughts and behaviors. C-SSRS Screen Version

- Montgomery-Asberg Depression Rating Scale (MADRS): A clinician-administered scale developed to monitor treatment response to antidepressant medication, consisting of ten items that assess various depressive symptoms rated on a seven-point scale, yielding a total score between 0 and 60**.** https://www.psychdb.com/_media/mood/madrs.pdf

- Patient Health Questionnaire (PHQ-9): A 9-item self-report questionnaire that assesses the severity of depression based on DSM-IV criteria. https://www.apa.org/depression-guideline/patient-health-questionnaire.pdf

- Clinically Useful Depression Outcome Scale (CUDOS): A brief, quickly scored, self-report scale used to assess depressive symptoms over the past 1 week. The CUDOS consists of 18 questions. The first 16 are scored from 0 to 4 for frequency of symptoms over the past week. The final 2 questions cover the impact of these symptoms on the respondent's life and their overall quality of life in the past week. https://www.mcgill.ca/psy/files/psy/cudos.pdf

- Quick Inventory of Depressive Symptomatology-Self-Report (QIDS-SR): A 16-item, self-administered questionnaire to assess the severity of depressive symptoms in adults. https://www.mdcalc.com/calc/1845/quick-inventory-depressive-symptomatology-qids

- Hamilton Depression Rating Scale (HAM-D): A clinician-administered tool consisting of 17 core items (some versions include up to 21 items) used to assess the severity of depressive symptoms in patients with major depressive disorder. https://www.apa.org/depression-guideline/hamilton-rating-scale.pdf