OVERVIEW
Spravato™ (esketamine) is indicated, in conjunction with an oral antidepressant, for the treatment of treatment-resistant depression (TRD) in adults.

This policy is applicable to BlueCHiP for Medicare products only. For Commercial Products, see related policy section.

MEDICAL CRITERIA
Initial Evaluation
Spravato™ (esketamine) will be approved when ALL of the following are met:
1) The patient is 18 years of age or older
   AND
2) Both of the following:
   a) The patient has a diagnosis of Treatment-Resistant Depression
   AND
   b) ONE of the following:
      i) The patient has tried and had an inadequate response to medication augmentation (i.e. dual combination treatment- with a second drug or psychotherapy
      OR
      ii) The patient has tried and had an inadequate response to electroconvulsive therapy (ECT)
   AND
3) The prescriber is a specialist (e.g. psychiatrist) or the prescriber has consulted with a specialist
   AND
4) The patient is currently being treated and will continue treatment with an oral antidepressant
   AND
5) ONE of the following:
   a) The patient does not have a substance use disorder
   OR
   b) The patient is being treated for substance use disorder and is NOT at risk for relapse
   AND
6) The baseline depression rating scale results are provided (e.g. MADRS)
   AND
7) Medication will be administered in a setting equipped to monitor patient vital signs and provide supportive care as needed
   AND
8) The patient does NOT have any FDA labeled contraindications to the requested agent
   AND
9) The requested dose is within FDA labeled dosing for the requested indication

Length of Approval: 6 months
Renewal Evaluation
Spravato™ (esketamine) will be approved when ALL of the following are met:
1) The patient has been previously approved for the requested agent through the Prime Therapeutics Medical Drug Review process
2) The patient has had clinical benefit with the requested agent as demonstrated by 50% improvement from baseline in depression rating scale (e.g. MADRS) (submit documentation)
3) The prescriber is a specialist (e.g. psychiatrist) or the prescriber has consulted with a specialist
4) The patient is currently being treated with an oral antidepressant
5) The patient does NOT have any FDA labeled contraindications to the requested agent
6) The requested dose within FDA labeled dosing for the requested indication

Length of Approval: 12 months

PRIOR AUTHORIZATION
Prior authorization is required for BlueCHiP for Medicare.

POLICY STATEMENT
BlueCHiP for Medicare
Spravato™ (esketamine) is medically necessary when the criteria above have been met.

COVERAGE
Benefits may vary between groups and contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage or Subscriber Agreement for applicable physician administered drug benefits/coverage.

BACKGROUND
Clinical Rationale
Treatment-resistant depression (TRD) refers to a major depressive episode with an inadequate response to therapy of adequate dosing and duration. The failure of two or more trials of antidepressant monotherapies are commonly considered TRD, but the number of trials has not been standardized. Some TRD drug trials include patients with failure of only one or more trials. Overall, approximately one in three patients with depression are considered ‘treatment resistant’.

Spravato™ was approved on a short-term and a long-term study. The short-term study was a randomized, placebo-controlled, double-blind, multicenter, 4-week study in patients aged 18 to <65 years old. Patients met the DSM-5 criteria for major depressive order, and in the current depressive episode, had not responded adequately to at least two different antidepressants of adequate dose and duration. Patients were randomized to either twice weekly doses of Spravato™ (flexible at 56 or 84 mg) or placebo. Both groups were given concomitant treatment with a newly-initiated oral antidepressant. The primary efficacy measure was the change in baseline in the Montgomery-Asberg Depression Rating Scale (MADRS). The MADRS is scored from 0 to 60, with the higher MADRS scores indicating more severe depression. Scoring is usually broken down with 0 and 6 indicating no depression, 7-19 mild depression, 20-34 moderate depression, and over 34 severe depression.3 The Spravato™ arm had a mean baseline score of 37.0, while the control arm had a score of 37.3. The Spravato™ plus antidepressant arm demonstrated statistically superiority in the primary efficacy measure over the placebo plus antidepressant arm. Spravato caused a decrease in score of 19.8, versus a decrease of 15.8 for placebo.

The long-term study was a randomized, double-blind, parallel group, multicenter maintenance of effect study in adults 18 to <65 years of age who were known responders to Spravato™. After at least 16 weeks of
treatment with Spravato™ and an oral antidepressant, stable patients were randomized to continue the Spravato™ and antidepressant or to be switched to a placebo spray and antidepressant. The primary endpoint was time to relapse, where relapse was defined as a MADRS score of ≥ 22 for 2 consecutive weeks or hospitalization for depression. Patients who continued Spravato with an antidepressant experienced a statistically significantly longer time of relapse than did placebo patients.

Safety
Spravato™ is available only through a restricted program under a REMS because of the risks of serious adverse outcomes from sedation, dissociation, and abuse and misuse. Spravato™ is contraindicated in aneurysmal vascular disease (including thoracic and abdominal aorta, intracranial and peripheral arterial vessels) or arteriovenous malformation, intracerebral hemorrhage, and hypersensitivity to esketamine, ketamine, or any of the excipients.

CODING
BlueCHiP for Medicare
There is no specific HCPCS code. Claims must be filed with an unlisted code such as J3490 and the NDC number.

RELATED POLICIES
Prior Authorization of Drugs

PUBLISHED
Provider Update, October 2019

REFERENCES

This medical policy is made available to you for informational purposes only. It is not a guarantee of payment or a substitute for your medical judgment in the treatment of your patients. Benefits and eligibility are determined by the member’s subscriber agreement or member certificate and/or the employer agreement, and those documents will supersede the provisions of this medical policy. For information on member-specific benefits, call the provider call center. If you provide services to a member which are determined to not be medically necessary (or in some cases medically necessary services which are non-covered benefits), you may not charge the member for the services unless you have informed the member and they have agreed in writing in advance to continue with the treatment at their own expense. Please refer to your participation agreement(s) for the applicable provisions. This policy is current at the time of publication; however, medical practices, technology, and knowledge are constantly changing. BCBSRI reserves the right to review and revise this policy for any reason and at any time, with or without notice. Blue Cross & Blue Shield of Rhode Island is an independent licensee of the Blue Cross and Blue Shield Association.