Effective Date: 4/1/2020
Last P&T Approval: 4/2022
Next Review Due By: 4/2023
Policy Number: C18438-A

Invega Sustenna Illinois Medicaid Only

PRODUCTS AFFECTED

INVEGA SUSTENNA (paliperidone palmitate) extended-release injectable suspension

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive

DIAGNOSIS:
Schizophrenia and Schizoaffective disorder

REQUIRED MEDICAL INFORMATION:
A. SCHIZOPHRENIA OR SCHIZOAFFECTIVE DISORDER:
1. The member is using the requested drug for an FDA-Approved indication
AND
2. The member is currently prescribed and tolerating oral paliperidone OR oral or injectable risperidone

CONTINUATION OF THERAPY:
A. FOR ALL INDICATIONS:
1. Prescriber attestation of target symptom improvement
OR
2. Prescriber provides clinical rationale for continued use

DURATION OF APPROVAL:
Initial authorization: 12 months or duration of prescription (whichever is shorter)
Continuation of Therapy: 12 months or duration of prescription (whichever is shorter)

PRESCRIBER REQUIREMENTS:
None

AGE RESTRICTIONS:
18 years of age or older

QUANTITY:
Initial Dosing: One injection (one package) on day 1 and day 8
Maintenance: One injection (one package) every 28 days
Note: Maintenance dosing administration 5 weeks after the first injection; missed maintenance dosing may require an additional dose if the member's previous injection was more than 6 weeks since last injection.

Maximum Quantity Limits – 234 mg Maximum Monthly Dose per FDA approved package labeling

PLACE OF ADMINISTRATION:
The recommendation is that injectable medications in this policy will be for pharmacy or medical benefit coverage and the intramuscular injectable products be administered in a place of service that is a non-hospital facility-based location.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Intramuscular injection

DRUG CLASS:
Benzisoxazoles

FDA-APPROVED USES:
Indicated for the treatment of schizophrenia in adults and treatment of schizoaffective disorder in adults as monotherapy and as an adjunct to mood stabilizers or antidepressants.

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

DOSAGE:

Indication	Initiation Dosing (deltoid)		Monthly Maintenance Dose[a] (deltoid or gluteal)	Maximum Monthly Dose
	Day 1	Day 8		
Schizophrenia (2.2)	234 mg	156 mg	39-234 mg[b]	234 mg
Schizoaffective disorder (2.2)	234 mg	156 mg	78-234 mg[c]	234 mg

[a] Administered 5 weeks after the first injection.
[b] The recommended maintenance dose for treatment of schizophrenia is 117 mg. Some patients may benefit from lower or higher maintenance doses within the additional available strengths (39 mg, 78 mg, 156 mg, and 234 mg).
[c] Adjust dose based on tolerability and/or efficacy using available strengths. The 39 mg strength was not studied in the long-term schizoaffective disorder study.

Renal Impairment
For patients with mild renal impairment (creatinine clearance ≥ 50 mL/min to < 80 MI/MIN [Cockcroft-Gault Formula]), initiate Invega Sustenna with a dose of 156 mg on treatment day 1 and 117 mg one week later. Administer both doses in the deltoid muscle. Thereafter, follow with monthly injections of 78 mg in either the deltoid or gluteal muscle

Switching from Other Antipsychotics
There are no systematically collected data to specifically address switching patients with schizophrenia or schizoaffective disorder from other antipsychotics to Invega Sustenna or concerning concomitant administration with other antipsychotics.

Switching from Oral Antipsychotics
For patients who have never taken oral paliperidone or oral or injectable risperidone, tolerability should be established with oral paliperidone or oral risperidone prior to initiating treatment with Invega Sustenna. Previous oral antipsychotics can be gradually discontinued at the time of initiation of treatment with Invega Sustenna. Recommended initiation of Invega Sustenna is with a dose of 234 mg on treatment day 1 and 156 mg one week later, both administered in the deltoid muscle. Patients previously stabilized on different doses of Invega Extended-Release tablets can attain similar paliperidone steady-state exposure during maintenance treatment with Invega Sustenna monthly doses as depicted below:

Doses of Invega and Invega Sustenna Needed to Attain Similar Steady-State Paliperidone Exposure During Maintenance Treatment

Formulation	INVEGA® Extended-Release Tablet	INVEGA SUSTENNA® Injection
Dosing Frequency	Once Daily	Once every 4 weeks
Dose (mg)	12	234
	9	156
	6	117
	3	39-78

Switching from Long-Acting Injectable Antipsychotics
For patients who have never taken oral paliperidone or oral or injectable risperidone, tolerability should be established with oral paliperidone or oral risperidone prior to initiating treatment with

Invega Sustenna. When switching patients currently at steady-state on a long-acting injectable antipsychotic, initiate Invega Sustenna therapy in place of the next scheduled injection. Invega Sustenna should then be continued at monthly intervals. The one-week initiation dosing regimen is not required. Based on previous clinical history of tolerability and/or efficacy, some patients may benefit from lower or higher maintenance doses within the available strengths (39 mg, 78 mg, 117 mg, 156 mg, and 234 mg). The 39 mg strength was not studied in the long-term schizoaffective disorder study. Monthly maintenance doses can be administered in either the deltoid or gluteal muscle. If Invega Sustenna is discontinued, its prolonged-release characteristics must be considered. As recommended with other antipsychotic medications, the need for continuing existing extrapyramidal symptoms (EPS) medication should be re-evaluated periodically.

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

After an intramuscular (IM) injection, paliperidone palmitate dissolves slowly due to its extremely low water solubility. Paliperidone palmitate is hydrolyzed to paliperidone and then absorbed into the systemic circulation. Release of the IM formulation begins as early as day 1 and continues for as long as 126 days. After a single IM dose, the median time to maximum plasma concentration (Tmax) is 13 days. Results from single dose studies with therapeutic IM doses have shown that the average maximal concentration (Cmax) is 28% higher after a deltoid muscle injection than after a gluteal injection. The recommended regimen of administering the first two doses by deltoid injection was designed to quickly attain steady-state concentrations without using oral supplementation. The volume of distribution of paliperidone is 391 Liters. The median elimination half-life after single dose administration of 39 to 234 mg intramuscularly ranges from 25 days to 49 days.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Invega Sustenna are considered experimental/investigational and therefore, will follow Molina's Off- Label policy.

Known hypersensitivity to paliperidone, risperidone, or to any excipients in Invega Sustenna. Invega Sustenna is not recommended in patients with moderate or severe renal impairment (creatinine clearance < 50 mL/min).

OTHER SPECIAL CONSIDERATIONS:

WARNINGS AND PRECAUTIONS

1. Black Box Warning: Increased mortality in elderly patients with dementia-related psychosis: Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Paliperidone is not approved for use in patients with dementia-related psychosis.
2. Cerebrovascular Adverse Reactions, Including Stroke, in Elderly Patients with Dementia-Related Psychosis: Increased incidence of cerebrovascular adverse reactions (e.g. stroke, transient ischemic attack, including fatalities). INVEGA SUSTENNA® is not approved for use in patients with dementia-related psychosis
3. Neuroleptic Malignant Syndrome: Manage with immediate discontinuation of drug and close monitoring
4. QT Prolongation: Avoid use with drugs that also increase QT interval and in patients with risk factors for prolonged QT interval
5. Tardive Dyskinesia: Discontinue drug if clinically appropriate
6. Metabolic Changes: Atypical antipsychotic drugs have been associated with metabolic changes that may increase cardiovascular/cerebrovascular risk. These metabolic changes include:

a. Hyperglycemia and Diabetes Mellitus: Monitor for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Monitor glucose regularly in patients with diabetes or at risk for diabetes.
b. Dyslipidemia: Undesirable alterations have been observed.
c. Weight Gain: Significant weight gain has been reported. Monitor weight gain.

7. Orthostatic Hypotension and Syncope: Use with caution in patients with known cardiovascular or cerebrovascular disease and patients predisposed to hypotension
8. Leukopenia, Neutropenia, and Agranulocytosis: Monitor complete blood count in patients with a history of a clinically significant low white blood cell count (WBC) or a drug-induced leukopenia/neutropenia. Consider discontinuation if clinically significant decline in WBC in the absence of other causative factors
9. Hyperprolactinemia: Prolactin elevations occur and persist during chronic administration
10. Potential for Cognitive and Motor Impairment: Use caution when operating machinery
11. Seizures: Use cautiously in patients with a history of seizures or with conditions that lower the seizure threshold

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
J2426	Injection, paliperidone palmitate extended release, 1 mg

AVAILABLE DOSAGE FORMS:
Invega Sustenna Extended-release injectable suspension: 39 mg/0.25 mL, 78 mg/0.5 mL, 117 mg/0.75 mL, 156 mg/mL, or 234 mg/1.5 mL

REFERENCES

1. Invega Sustenna (paliperidone palmitate) [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; August 2021.
2. Paliperidone. Clinical Pharmacology [Internet]. Elsevier. c2020- [cited March 2020]. Available from: http://www.clinicalpharmacology.com
3. Illinois HFS Drugs with Stipulated PA Language per Contract for MCOs 4.1.22, revised
4. Illinois Medicaid Preferred Drug List, Effective April 1, 2022

SUMMARY OF REVIEW/REVISIONS	DATE
ANNUAL REVIEW COMPLETED- No coverage criteria changes with this annual review.	Q2/2022