Effective Date: 04/2020
Last P&T Approval/Version: 04/2022
Next Review Due By: 04/2023
Policy Number: C21110-C

Invega Trinza (paliperidone palmitate) extended-release injectable suspension, for intramuscular use IL Medicaid Only

PRODUCTS AFFECTED

Invega Trinza (paliperidone palmitate)

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 [per package label]

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review

A. FOR ALL INDICATIONS:
   1. Pharmacy claims or medical records documenting the use of Invega Sustenna (1-month paliperidone palmitate extended-release injectable suspension) once monthly for at least 4 months.

CONTINUATION OF THERAPY:
A. FOR ALL INDICATIONS:
   1. Documentation that member meets initial criteria.

NOTE: If 4 months to 9 months have elapsed since the last injection of Invega Trinza, two doses of Invega Sustenna should be administered on days 1 and 8, then Invega Trinza can be administered 1 month later. If more than 9 months have elapsed since the last injection of INVEGA TRINZA®, re-initiate treatment with the 1-month paliperidone palmitate extended-release injectable suspension as described in the prescribing information for that product.

DURATION OF APPROVAL:
Initial authorization: 6 months. Continuation of Therapy: 6 months

PRESCRIBER REQUIREMENTS:
None

AGE RESTRICTIONS:
18 years of age and older

QUANTITY:
Quantity limit of one injection (one package) every 84 days.

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

DRUG CLASS:
Antipsychotics/Antimanic Agents, benzisoxazole

FDA-APPROVED USES:
Indicated for the treatment of schizophrenia in patients after they have been adequately treated with INVEGA SUSTENNA® (1-month paliperidone palmitate extended-release injectable suspension) for at least four months.

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
After an intramuscular (IM) injection, paliperidone palmitate dissolves slowly due to its extremely low water solubility. Paliperidone palmitate is then hydrolyzed to paliperidone and absorbed into the systemic circulation. The release of the drug starts as early as 1 day and lasts for as long as 18 months. After a single IM dose, the plasma concentrations gradually reach maximum levels at a median Tmax of 30 to 33 days. Following IM deltoid injections at doses of 273 mg to 819 mg, the Cmax is an average of 11% to 12% higher than with the gluteal injection. The apparent volume of distribution is 1960 Liters. The mean steady-state peak:trough ratios are similar between gluteal and deltoid injections. The median half-life over the therapeutic dose range is 84 to 95 days following deltoid injections, and the median half-life is 118 to 139 days following gluteal injections. The

concentration of paliperidone remaining in the circulation 18 months after discontinuation of the 819 mg dose at steady-state is estimated to be 3% with deltoid injection and 7% with gluteal injection. When Invega Trinza is administered at doses that are 3.5-fold higher than the corresponding dose of the 1-month injection (Invega Sustenna), paliperidone exposures are similar to those obtained with corresponding monthly doses of Invega Sustenna and corresponding once daily doses of the extended-release tablets. The pharmacokinetic between-subject variability for Invega Trinza was similar to the variability for paliperidone extended-release tablets. Because of the difference in median pharmacokinetic profiles among the three formulations, caution is recommended when making a direct comparison of their pharmacokinetic properties.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
Known hypersensitivity to paliperidone, risperidone, or to any excipients in Invega Sustenna.

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

DOSAGE:
Use Invega Trinza only after the patient has been adequately treated with the 1-month paliperidone palmitate extended-release injectable suspension for at least four months. Invega Trinza should be

administered once every 3 months. In order to establish a consistent maintenance dose, it is recommended that the last two doses of Invega Sustenna be the same dosage strength before starting Invega Trinza. Initiate Invega Trinza when the next 1-month paliperidone palmitate dose is scheduled with an Invega Trinza dose based on the previous 1-month injection dose as shown below:

If the Last Dose of Invega Sustenna is:	Initiate Invega Trinza at the Following Dose:
78 mg	273 mg
117 mg	410 mg
156 mg	546 mg
234 mg	819 mg

Renal Impairment
Mild renal impairment (creatinine clearance ≥50 mL/min to < 80 mL/min): Adjust dosage and stabilize the patient using Invega Sustenna, then transition to Invega Trinza. Invega Trinza is not recommended in patients with moderate or severe renal impairment (creatinine clearance < 50 mL/min)

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
NA	

AVAILABLE DOSAGE FORMS:

PRODUCT NAME
Invega Trinza SUSY 273MG/0.88ML
Invega Trinza SUSY 410MG/1.32ML
Invega Trinza SUSY 546MG/1.75ML

PRODUCT NAME
Invega Trinza SUSY 819MG/2.63ML

REFERENCES

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

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