Original Effective Date: 10/01/2018
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Policy Number: C15214-A

Iron Chelating Agents (Desferal, Exjade, Ferriprox, Jadenu)

PRODUCTS AFFECTED

Desferal (deferoxamine), Exjade (deferasirox), Jadenu (deferasirox), Ferriprox (deferiprone)

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:
Acute iron intoxication, Chronic iron overload due to blood transfusions (transfusional iron overload), Chronic iron overload in non-transfusion dependent thalassemia syndromes, Transfusional iron overload due to thalassemia syndromes

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. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review.

A. FOR EXJADE/JADENU (DEFERASIROX):
1. Documentation of either of the following diagnosis:
   (a) i. Chronic transfusional iron overload due to blood transfusions

AND

ii. Transfusion history of ≥ 100 mL/kg of packed red blood cells (e.g., ≥ 20units of packed red blood cells for a 40 kg person) AND a serum ferritin level > 1,000 mcg/L [DOCUMENTATION REQUIRED]

OR

(b) i. Chronic iron overload resulting from non-transfusion dependent thalassemia (NTDT)
AND
ii. Documentation of a liver iron concentration (LIC) greater than or equal to 5 milligrams of iron per gram of liver dry weight (mg Fe/g dw) and a serum ferritin greater than 300 mcg/L. [DOCUMENTATION REQUIRED]

AND

2. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to deferasirox include: estimated GFR less than 40 mL/min/1.73 m^2, poor performance status, high-risk myelodysplastic syndrome (MDS), advanced malignancies, platelet count less than 50 x 10^9/L, known hypersensitivity to deferasirox or any component of the requested product, severe (Child-Pugh C) hepatic impairment, use with nephrotoxic drugs]
AND
3. Prescriber attests to member appropriate monitoring as recommended within drug label including, but not limited to ophthalmologic exams, kidney function testing, liver transaminases and bilirubin, and auditory testing
AND
4. IF THE REQUEST NON-FORMULARY/ NON-PREFERRED PRODUCT: Documentation of trial/failure of or intolerance to a majority (not more than 3) of the preferred formulary/PDL alternatives for the given diagnosis. Submit documentation including medication(s) tried, dates of trial(s)and reason for treatment failure(s).

B. FOR FERRIPROX (DEFERIPRONE):
1. Documented diagnosis of transfusional iron overload due to thalassemia syndrome, sickle cell disease or other anemias
AND
2. Documentation of an inadequate response (as defined by serum ferritin >2,500mcg/L), serious side effects, or a labeled contraindication to Desferal (deferoxamine) AND Exjade (deferasirox) or Jadenu (deferasirox)
AND
3. Documentation serum ferritin levels are consistently > 2500 mcg/L demonstrated by at least 2 lab values in the previous 3 months [DOCUMENTATION REQUIRED]
AND
4. Documentation of member's absolute neutrophil count (ANC) >1.5 x10^9/L [DOCUMENTATION REQUIRED]
AND
5. Prescriber attests to appropriate monitoring as recommended within drug label including, but not limited to, ANC (weekly for the first 6 months of therapy, then once every two week for the next 6 months of therapy, then every two to four weeks after one year of therapy), ALT (before and monthly during therapy), Zinc levels (before and regularly during therapy)
AND
6. For women of child-bearing potential: Provider attests that member is NOT pregnant or planning on becoming pregnant
AND
7. For women of child-bearing potential or males with female partners of child-bearing potential: Prescriber attests that member has been counseled to use an effective method of contraception during treatment and for at least six months (females) or 3 months (males) after the last dose

C. FOR DESFERAL (DEFEROXAMINE):
1. Documentation of either of the following diagnosis:
   (a) Acute iron intoxication
   OR
   (b) i. Chronic iron overload due to transfusion-dependent anemia (e.g., congenital/acquired anemias including thalassemia, sickle cell anemia, aplastic anemia, myelodysplasia)
   AND
   ii. Member has a Transfusion history of ≥ 100 mL/kg of packed red blood cells (e.g., ≥ 20 units of packed red blood cells for a 40 kg person) AND a serum ferritin level >1,000 mcg/L [DOCUMENTATION REQUIRED]
   AND
2. Prescriber attests to member appropriate monitoring as recommended within drug label (visual acuity tests, slit-lamp examinations, fundoscopy and audiometry are recommended periodically in patients treated for prolonged periods of time; monitor renal function).
   AND
3. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to deferoxamine include: known hypersensitivity to the active substance, patients with severe renal disease or anuria.]

CONTINUATION OF THERAPY:

A. FOR EXJADE/JADENU (DEFERASIROX): CHRONIC IRON OVERLOAD DUE TO BLOOD TRANSFUSIONS:
1. Documentation showing member's current (within last 30 days) serum ferritin level ≥ 500 mcg/L [DOCUMENTATION REQUIRED]
   AND
2. Prescriber attests to continued serum ferritin level monitoring and adjusting member's dose, if necessary, every 3 to 6 months based on serum ferritin levels
   AND
3. Prescriber attests (or the clinical reviewer has found) that at time of request, member's estimated glomerular filtration rate is NOT less than 40mL/min/1.73m2 or platelet count less than 50 x 109/L
   AND
4. Prescriber attests to continued appropriate monitoring as recommended within drug label including, but not limited to visual acuity tests, kidney function, liver transaminases and bilirubin and auditory testing
   AND
5. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity

B. FOR EXJADE/JADENU (DEFERASIROX): CHRONIC IRON OVERLOAD DUE TO NON-TRANSFUSION DEPENDENT THALASSEMIA SYNDROME:
1. (a) If member has received < 6 months of Exjade/Jadenu, a serum ferritin level ≥ 300 mcg/L or an LIC ≥ 3 mg Fe/g dw [DOCUMENTATION REQUIRED]
   OR
   (b) If member has received ≥ 6 months of Exjade/Jadenu, an LIC is ≥ 3 mg Fe/g dw [DOCUMENTATION REQUIRED]
   AND
2. Prescriber attests (or the clinical reviewer has found) that at time of request, member's estimated glomerular filtration rate is NOT less than 40 mL/min/1.73m2 or platelet count less than 50 x 109/L
   AND
3. Prescriber attests to continued appropriate monitoring as recommended within drug label including, but not limited to visual acuity tests, kidney function, and auditory testing

AND

4. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity

C. FOR FERRIPROX (DEFERIPRONE): TRANSFUSIONAL IRON OVERLOAD DUE TO THALASSEMIA SYNDROME, SICKLE CELL DIASESE OR OTHER ANEMIAS:

1. Documentation of current (within the past 30 days) member's serum ferritin level ≥500 mcg/L [DOCUMENTATION REQUIRED]
   AND
2. Prescriber attests to continued appropriate monitoring as recommended within drug label including but not limited to ANC (weekly for the first 6 months of therapy, then once every two week for the next 6 months of therapy, then every two to four weeks after one year of therapy), ALT (before and monthly during therapy), Zinc levels (before and regularly during therapy)
   AND
3. For women of child-bearing potential or males with female partners of child-bearing potential: Prescriber attests member or their partner is not pregnant, and member has been counseled to use an effective method of contraception during treatment and for at least six months (females) or 3 months (males) after the last dose
   AND
4. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity

D. FOR DESFERAL (DEFEROXAMINE): CHRONIC IRON OVERLOAD DUE TO BLOOD TRANSFUSIONS:

1. Documentation showing member's current (within last 30 days) serum ferritin level ≥ 500 mcg/L [DOCUMENTATION REQUIRED]
   AND
2. Prescriber attests to continued serum ferritin level monitoring and adjusting member's dose if necessary, every 3 to 6 months based on serum ferritin levels
   AND
3. Prescriber attests to member appropriate monitoring as recommended within drug label (visual acuity tests, slit-lamp examinations, fundoscopy and audiometry are recommended periodically in patients treated for prolonged periods of time; monitor renal function).
   AND
4. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity

DURATION OF APPROVAL:

ACUTE IRON TOXICITY: Initial authorization: 3 months, Continuation of therapy: NA
ALL OTHER INDICATIONS: Initial authorization: 3 months, Continuation of Therapy: 6 months

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with a board-certified hematologist or oncologist. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:

Exjade/Jadenu:
Transfusional iron overload: 2 years of age and older
Chronic iron overload in non-transfusion dependent thalassemia (NTDT): 10 years of age and older
Ferriprox: Tablets: 8 years of age and older; Oral Solution: 3 years of age and older
Desferal: 3 years of age and older

QUANTITY:

Desferal (deferoxamine):

Acute Iron Toxicity:
IM: 1000 mg initially. This may be followed by 500 mg every 4 hours for two doses. Depending upon the clinical response, subsequent doses of 500 mg may be administered every 4-12 hours. The total amount administered should not exceed 6000 mg in 24 hours.
IV: An initial dose of 1000 mg should be administered at a rate NOT TO EXCEED 15 mg/kg/hr. This may be followed by 500 mg over 4 hours for two doses. Depending upon the clinical response, subsequent doses of 500 mg may be administered over 4-12 hours. The total amount administered should not exceed 6000 mg in 24 hours.
Chronic Iron Overload:
SC: 1000-2000 mg/day (20-40 mg/kg/day)
IV: Maximum 40 mg/kg/day for children and maximum 60 mg/kg/day in adults
IM: 1000 mg/day

Exjade (deferasirox):
Transfusional Iron Overload: Initial: 20 mg/kg/day. Maximum: 40 mg/kg/day
NTDT Syndromes: Initial: 10 mg/kg/day. Maximum: 20 mg/kg/day

Jadenu (deferasirox):
Transfusional Iron Overload: Initial: 14 mg/kg/day. Maximum: 28mg/kg/day
NTDT Syndromes: Initial: 7 mg/kg/day. Maximum: 14 mg/kg/day

Ferriprox (deferiprone) [tablets and oral solution]:
Initial: 75mg/kg/day. Individualize dose based on response and therapeutic goal. Maximum dose: 99 mg/kg/day.

Maximum Quantity Limits – << based on FDA label>>

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

Exjade (deferasirox), Jadenu (deferasirox) and Ferriprox (deferiprone):
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral, Intramuscular, Intravenous, Subcutaneous

DRUG CLASS:
Antidotes - Chelating Agents

FDA-APPROVED USES:
Desferal (deferoxamine):
Indicated as an adjunct to standard measures for the treatment of acute iron intoxication and for the treatment of transfusional iron overload in patients with chronic anemia.
Limitations of Use: Desferal is not indicated for the treatment of primary hemochromatosis (since phlebotomy is the method of choice for removing excess iron in this disorder).

Exjade/Jadenu (deferasirox):
Indicated for the treatment of chronic iron overload due to blood transfusions in patients 2 years of age and older; for the treatment of chronic iron overload in patients 10 years of age and older with non-

transfusion dependent thalassemia (NTDT) syndromes, and with a liver iron (Fe) concentration (LIC) of at least 5 mg Fe per gram of dry weight and a serum ferritin greater than 300 mcg/L.
Limitations of Use: The safety and efficacy of Exjade and Jadenu when administered with other iron chelation therapy have not been established.

Ferriprox (deferiprone) tablets:
Indicated for the treatment of transfusional iron overload in adult and pediatric patients 8 years of age and older with sickle cell disease or other anemias.
Ferriprox (deferiprone) oral solution:
Indicated for the treatment of transfusional iron overload in adult and pediatric patients 3 years of age and older with thalassemia syndromes, sickle cell disease or other anemias.
Limitations of use: Safety and effectiveness have not been established for the treatment of transfusional iron overload in patients with myelodysplastic syndrome or in patients with Diamond Blackfan anemia.

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
Reserved for State specific information. *Information includes, but is not limited to, State contract language, Medicaid criteria and other mandated criteria.*

State Specific Information
State Marketplace
Kentucky (Source: Kentucky Revised Statutes)
KY304.17A-167 Time span of authorizations
(Subsection 2) “Unless otherwise provided in subsection (3) of this section or prohibited by state or federal law, if a provider receives a prior authorization for a drug prescribed to a covered person with a condition that requires ongoing medication therapy, and the provider continues to prescribe the drug, and the drug is used for a condition that is within the scope of use approved by the United States Food and Drug Administration or has been proven to be a safe and effective form of treatment for the patient's specific underlying condition based on clinical practice guidelines that are developed from peer-reviewed publications, the prior authorization received shall: (a) Be valid for the lesser of: 1. One (1) year from the date the provider receives the prior authorization; or 2. Until the last day of coverage under the covered person's health benefit plan during a single plan year; and (b) Cover any change in dosage prescribed by the provider during the period of authorization.” (Subsection 3) “Except as provided in paragraph (b) of this subsection, the provisions of subsection (2) of this section shall not apply to: 1. Medications that are prescribed for a non-maintenance condition; 2. Medications that have a typical treatment period of less than twelve (12) months; 3. Medications where there is medical or scientific evidence that does not support a twelve (12) month approval; or 4. Medications that are opioid analgesics or benzodiazepines. (b) Paragraph (a) of this subsection shall not apply to any medication that is prescribed to a patient in a community-based palliative care program.”
Re-authorization (approved authorization previously issued by Molina Healthcare) for maintenance medications within this policy shall be approved for a 12 month duration when request meets policy requirements, unless exceptions noted above have been met.

State Medicaid
Kentucky (Source: Kentucky Revised Statutes)
KY304.17A-167 Time span of authorizations
(Subsection 2) “Unless otherwise provided in subsection (3) of this section or prohibited by state or federal law, if a provider receives a prior authorization for a drug prescribed to a covered person with a condition that requires ongoing medication therapy, and the provider continues to prescribe the drug, and the drug is used for a condition that is within the scope of use approved by the United States Food and Drug Administration or has been proven to be a safe and effective form of treatment for the patient's specific underlying condition

based on clinical practice guidelines that are developed from peer-reviewed publications, the prior authorization received shall: (a) Be valid for the lesser of: 1. One (1) year from the date the provider receives the prior authorization; or 2. Until the last day of coverage under the covered person's health benefit plan during a single plan year; and (b) Cover any change in dosage prescribed by the provider during the period of authorization." (Subsection 3) "Except as provided in
paragraph (b) of this subsection, the provisions of subsection (2) of this section shall not apply to: 1. Medications that are prescribed for a non-maintenance condition; 2. Medications that have a typical treatment period of less than twelve (12) months; 3. Medications where there is medical or scientific evidence that does not support a twelve (12) month approval; or 4. Medications that are opioid analgesics or benzodiazepines. (b) Paragraph (a) of this subsection shall not apply to any medication that is prescribed to a patient in a community-based palliative care program."

Re-authorization (approved authorization previously issued by Molina Healthcare) for maintenance medications within this policy shall be approved for a 12 month duration when request meets policy requirements, unless exceptions noted above have been met.

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

None

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Iron chelating Agents (Desferal, Exjade, Ferriprox, Jadenu) are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Contraindications to Desferal (deferoxamine) include: known hypersensitivity to the active substance, patients with severe renal disease or anuria . Contraindications to Ferriprox (deferiprone) include: Hypersensitivity to deferiprone or to any of the excipients in the formulation. Contraindications to Exjade/Jadenu include: an estimated GFR less than 40 mL/min/1.73 m2, patients with poor performance status, patients with high-risk MDS, patients with advanced malignancies, patients with platelet counts less than 50 x 10^9/L, patients with a known hypersensitivity to deferasirox or any component of the requested product, severe (Child-Pugh C) hepatic impairment, use with nephrotoxic drugs.

OTHER SPECIAL CONSIDERATIONS:

Jadenu and Exjade have a Black Box Warning for renal failure, hepatic failure, and gastrointestinal hemorrhage.

Ferriprox has a Black Box Warning for agranulocytosis and neutropenia.

For Exjade and Jadenu: For patients with renal impairment (eGFR 40–60 mL/min/1.73 m^2), reduce the starting dose by 50%. Exercise caution in pediatric patients with eGFR between 40 and 60 mL/min/1.73 m2.

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
J0895	Injection, deferoxamine mesylate, 500mg

AVAILABLE DOSAGE FORMS:
Deferasirox Granules PACK 180MG
Deferasirox Granules PACK 360MG
Deferasirox Granules PACK 90MG
Deferasirox PACK 180MG
Deferasirox PACK 360MG
Deferasirox PACK 90MG
Deferasirox TABS 180MG
Deferasirox TABS 360MG
Deferasirox TABS 90MG
Deferasirox TBSO 125MG
Deferasirox TBSO 250MG
Deferasirox TBSO 500MG
Deferiprone TABS 1000MG
Deferiprone TABS 500MG
Deferoxamine Mesylate SOLR 2GM
Deferoxamine Mesylate SOLR 500MG
Desferal SOLR 500MG
Exjade TBSO 125MG
Exjade TBSO 250MG
Exjade TBSO 500MG
Ferriprox SOLN 100MG/ML
Ferriprox TABS 1000MG
Ferriprox TABS 500MG
Ferriprox Twice-A-Day TABS 1000MG
Jadenu Sprinkle PACK 180MG
Jadenu Sprinkle PACK 360MG
Jadenu Sprinkle PACK 90MG
Jadenu TABS 180MG
Jadenu TABS 360MG
Jadenu TABS 90MG

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SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Diagnosis Required Medical Information Continuation of Therapy Duration of Therapy Age Restrictions Quantity Route of Administration FDA-Approved Uses Contraindications/Exclusions/Discontinuation Other Special Considerations Available Dosage Forms References	Q3 2023
REVISION- Notable revisions: Diagnosis Required Medical Information Continuation of Therapy References	Q3 2022
Q2 2022 Established tracking in new format	Historical changes on file