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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

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Drug and Biologic Coverage Criteria

AND

ii. 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]

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 m², poor performance status, high-risk myelodysplastic syndrome (MDS), advanced malignancies, platelet count less than 50×10^9 /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 $> 2,500$ mcg/L), serious side effects, or a labeled contraindication to Desferal (deferroxamine) 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) $> 1.5 \times 10^9$ /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

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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, funduscopy 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

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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 DISEASE 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 weeks 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, funduscopy 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):

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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-

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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:

None

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 (deferioxamine) 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 10⁹/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 m²), 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

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HCPCS CODE	DESCRIPTION
J0895	Injection, deferoxamine mesylate, 500mg

AVAILABLE DOSAGE FORMS:

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

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Drug and Biologic Coverage Criteria

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