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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; treatment of chronic iron overload due to blood transfusions (transfusional iron overload); treatment of chronic iron overload in non-transfusion dependent thalassemia syndromes ;transfusional iron overload due to thalassemia syndromes when current chelation therapy is inadequate; treatment of transfusional iron overload in adult and pediatric patients 8 years of age and older with sickle cell disease or other anemias.

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

i. 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]
AND
ii. Member is 2 years of age and older
OR

(b) Chronic iron overload resulting from non-transfusion dependent thalassemia (NTDT) AND
i. 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
ii. Member is 10 years of age and older

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, and auditory testing
AND
4. Documentation of member's current weight (within the last 30 days)
AND
5. IF THE REQUEST NON-FORMULARY PRODUCT: Documentation of trial/failure of or intolerance to a majority (not more than 3) of the preferred formulary alternatives for the given diagnosis. If yes, please 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) intolerance or a labeled contraindication to Desferal (deferoxamine) AND Exjade (deferasirox) or Jadenu (deferasirox)
AND
3. Serum ferritin levels that 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 ~~ab~~solute 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
   AND
8. Member is 8 years of age and older
   AND
9. Documentation of member's current weight (within the last 30 days)

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. Member is 3 years of age or older
   AND
4. For IV requests for Chronic Iron Overload: Documentation member's current weight (within the last 30 days)

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, and auditory testing
   AND
5. Documentation member's current weight (within the last 30 days

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. Documentation member's current weight (within the last 30 days

C. FOR FERRIPROX (DEFERIPRONE): TRANSFUSIONAL IRON OVERLOAD DUE TO THALASSEMIA SYNDROME:

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. Documentation member's current weight (within the last 30 days

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

1. 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
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. For IV requests: Documentation member's current weight (within the last 30 days

DURATION OF APPROVAL:
ACUTE IRON TOXICITY: Initial authorization: 3 months, Continuation of therapy: NA
ALL OTHER INDICAITONS: Initial authorization: 3 months, Continuation of Therapy: for up to 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:
See required medical information

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 in24 hours.
Chronic Iron Overload:
SC: 1000-2000 mg/day (20-40 mg/kg/day)
IV: 40 mg/kg/day for children and 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

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

Ferriprox (deferiprone) Initial: 25mg/kg, orally, three times per day, for a total daily dose of 75mg/kg/day. Individualize dose based on response and therapeutic goal. Maximum dose: 33mg/kg, three times per day, for a total of 99mg/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 administered in a place of service that is anon-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

DRUG CLASS:
Antidotes - Chelating Agents

FDA-APPROVED USES:
Desferal (deferoxamine): acute iron intoxication; chronic iron overload

Exjade (deferasirox): treatment of chronic iron overload due to blood transfusions in patients 2 years of age and older; 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.

Jadenu (deferasirox): treatment of chronic iron overload due to blood transfusions (transfusional iron overload); treatment of chronic iron overload in non-transfusion dependent thalassemia syndromes

Ferriprox (deferiprone): transfusional iron overload due to thalassemia syndromes when current chelation therapy is inadequate; treatment of transfusional iron overload in adult and pediatric patients 8 years of age and older with sickle cell disease or other anemias.

Limitations of use (Exjade, Jadenu): The safety and efficacy of Exjade when administered with other iron chelation therapy have not been established.

Limitations of use (Ferriprox): Safety and effectiveness have not been established for the treatment of transfusional iron overload in patients with myelodysplastic syndrome or in patients with Diamond Black fan 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 (deferoxamine) include patients with severe renal disease or anuria since the drug and the iron chelate are excreted primarily by the kidney. 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, members with poor performance status, members with high-risk MDS, members with advanced malignancies, members with platelet counts less than 50 x 10^9/L and members with a known hypersensitivity to deferasirox or any component of Exjade.

OTHER SPECIAL CONSIDERATIONS:
Boxed warnings:
Jadenu/Exjade: renal failure, hepatic failure, and gastrointestinal hemorrhage
Ferriprox: agranulocytosis and neutropenia

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, 500 mg

AVAILABLE DOSAGE FORMS:
Desferal (deferoxamine) 500 mg vials
Desferal (deferoxamine) 2-gram vials
Exjade (deferasirox)125 mg tablet for oral suspension
Exjade (deferasirox) 250 mg tablets for oral suspension
Exjade (deferasirox) 500 mg tablets for oral suspension
Jadenu (deferasirox) 90 mg oral granules and tablets
Jadenu (deferasirox) 180 mg oral granules and tablets
Jadenu (deferasirox) 360 mg oral granules and tablets
Ferriprox (deferiprone) 100mg/ml oral solution
Ferriprox (deferiprone) 500 mg tablet
Ferriprox (deferiprone) 1000 mg tablet

REFERENCES

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2. Ferriprox (deferiprone) [prescribing information]. NC: ChiesiUSA, Inc November 2021
3. Pennell DJ, Udelson JE, Arai AE, et al. Cardiovascular function, and treatment in βthalassemia major.Circulation.2013;128:281-308.
4. Jadenu (deferasirox) [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2020.
5. Exjade [Package Insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2020
6. Desferal [Package Insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; October 2020
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SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Diagnosis Required Medical Information Continuation of Therapy Quantity References	Q3 2022
Q2 2022 Established tracking in new format	Historical changes on file