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PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 7/16/15**
SECTION: DRUGS	**LAST REVIEW DATE: 11/16/17**
	LAST CRITERIA REVISION DATE: 11/16/17
	ARCHIVE DATE:

IRON CHELATING AGENTS:
EXJADE® (deferasirox) tablet for oral suspension
FERRIPROX® (deferiprone) tablet for oral use and oral solution
JADENU® (deferasirox) tablet for oral use
JADENU® Sprinkle (deferasirox) granules for oral use

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy 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 BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602)

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864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

Description:

Exjade (deferasirox) tablet for oral suspension & Jadenu (deferasirox) oral tablets are indicated for the treatment of chronic iron (Fe) overload in patients 2 years of age and older whose iron overload is due to blood transfusions (transfusional hemosiderosis) with at least 100 mL/kg of packed red blood cells and have a serum ferritin that is consistently greater than 1,000 mcg/L. Both are also indicated for the treatment of chronic iron overload in patients 10 years of age and older with non-transfusion-dependent thalassemia (NTDT) syndromes with liver iron concentration (LIC) of at least 5 milligrams of iron per gram of liver dry weight (mg Fe/g dw) and a serum ferritin greater than 300 mcg/L.

Ferriprox (deferiprone), tablet and solution, is another oral iron chelating agent indicated for the treatment of patients with transfusional iron overload due to thalassemia syndromes when current chelation therapy is inadequate. The safety and effectiveness have not been established for the treatment of transfusional iron overload in patients with other chronic anemias.

An injectable iron chelating agent, deferoxamine (Desferal and generics), is available and is administered intramuscularly, subcutaneously, or intravenously. It is indicated for the treatment of acute iron intoxication and of chronic iron overload due to transfusion-dependent anemias.

Iron, iron overload, & iron chelation

- All body cells need iron
  - It is crucial for oxygen transport, energy production, and cellular growth and proliferation
- The human body contains an average of 3.5 g of iron (males 4 g, females 3 g)
- Iron is bound and transported in the body by the glycoprotein carrier protein transferrin and it is stored in ferritin molecules
  - Ferritin is particularly abundant in the liver and heart
- When there is an excess of iron, the body responds by producing more ferritin to facilitate iron storage
  - When iron concentrations exceed the storage capacity of ferritin molecules, unbound iron deposits in many organs and causes free-radical formation in cells, resulting in membrane lipid peroxidation, cellular injury, and organ dysfunction
- Iron overload may result from either inherited or acquired disorders such as transfusion dependent anemia, various liver diseases, hemolytic anemia, thalassemia, sickle cell anemia and excessive iron ingestion

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- Determination of iron status can be accomplished by several methods
    - Serial measurement of serum ferritin is a reliable and the easiest method to evaluate iron overload
        - Elevated serum ferritin is a sensitive test for iron overload, but it is not very specific
        - The normal range for ferritin in plasma or serum is approximately 40-200 mcg/L (40-200 ng/mL; 89.9-449.4 picomoles/L)
        - A ferritin level ≥ 200 to 300 mcg/L in a man (or ≥ 150 to 200 mcg/L in a woman) is consistent with iron overload, and a level below these values is good evidence that the patient does not have iron overload
        - Ferritin levels in iron overload may range of up to 2000 to 3000 mcg/L (ng/mL)
    - Determination of liver iron concentration (LIC) can be done via a liver biopsy but it is an invasive procedure with the possibility of complications
        - Recently, nuclear magnetic resonance imaging techniques for assessing total body iron has become available
        - R2 and T2* parameters have been validated for liver iron concentration

- LIC estimated by MRI > 2-7 mg Fe/g dry weight (equivalent to approximately 53-125 micromol/g dry weight) indicates the presence of hepatic iron overload
    - A cardiac T2* by MRI < 20 milliseconds (normal: > 20) indicates the presence of cardiac iron overload
    - Values < 10 milliseconds have been associated with severe myocardial iron loading and the development of cardiac failure

- Myelodysplastic syndrome (MDS) refers to a heterogeneous group of clonal hematopoietic disorders with the potential to transform into acute myelocytic leukemia (AML)
    - Anemia is often seen and may require red blood cell (RBC) transfusions and subsequent iron overload

- Guidelines suggest the use of iron chelating agents in patients with MDS and iron overload, although the benefit of iron chelation in MDS is unproven and the optimal agent to use is unclear at this time

- Prophylactic or therapeutic iron chelation treatment is suggested for low risk MDS who have had, or are anticipated to have, prolonged red cell transfusion requirements (more than 20-30 transfusions), demonstrate evidence of iron overload (serum ferritin >1000 mcg/L), the LIC is > 3 mg Fe/g dry weight, and/or the cardiac T2* is <20 milliseconds

- The International Prognostic Scoring System (IPSS) and a revised IPSS (IPSS-R) use cytogenetic, morphologic, and clinical data to define MDS risk groups
    - IPSS for MDS stratifies patients into four distinctive risk groups in terms of both survival and AML evolution
    - The IPSS-R defines five risk groups
        - The IPSS-R has been validated in a number of studies

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- The latest National Comprehensive Cancer Network (NCCN) Guidelines Clinical Practice Guidelines in Oncology: Myelodysplastic Syndromes (Version 1.2018, Aug 29, 2017) states daily chelation therapy should be considered if > 20-30 RBC transfusions have been received to decrease iron overload, particularly for patients who have lower-risk MDS or who are potential transplant candidates LOW/INT-1

Definitions:

The Child-Pugh classification system:
The Child-Pugh classification is a scoring system used to determine the prognosis of individuals with cirrhosis. Scoring is based upon several factors: albumin, ascites, total bilirubin, prothrombin time, and encephalopathy, as follows:

	Score: 1 point	Score: 2 points	Score: 3 points
Serum Albumin (g/dL)	>3.5	3.0 - 3.5	<3.0
Serum Bilirubin (mg/dL)	<2.0	2.0 - 3.0	>3.0
Prothrombin time (seconds)	1 - 4	4 - 6	>6
Ascites	none	moderate	severe
Encephalopathy	none	mild	severe

The three classes and their scores are:
- **Class A** is score 5 – 6: Well compensated
- **Class B** is score 7 – 9: Significant functional compromise
- **Class C** is score >9: Decompensated disease

Methods for measuring iron overload:
Liver iron concentration (LIC) by biopsy
Magnetic resonance imaging with R2* or T2*
R2 technique

Thalassemia syndromes:
Alpha-thalassemia silent carrier
Alpha-thalassemia trait (minor)
Hemoglobin H disease
Hemoglobin Bart's Hydrops fetalis syndrome
Beta-thalassemia trait (minor)
Thalassemia intermedia
Beta-thalassemia major (Cooley's anemia)
Beta-thalassemia minor
Hemoglobin E (Hb-E) thalassemia
Mild Hb-E / Beta-thalassemia
Moderately severe Hb-E / Beta-thalassemia
Severe Hb-E / Beta-thalassemia
Delta-thalassemia
Hemoglobin S thalassemia
Hemoglobin C thalassemia
Hemoglobin D thalassemia
Delta-thalassemia
Hereditary persistence of fetal hemoglobin (HPFH)

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Myelodysplastic syndrome (MDS):
A heterogeneous group of clonal hematopoietic disorders with the potential to transform into acute myelocytic leukemia (AML). MDS include, *but are not limited to:*

- del 5q syndrome
- Refractory anemia
- Refractory anemia with:
  - Ringed sideroblasts
  - Excess blasts 1 and 2
- Refractory cytopenia with multilineage dysplasia or ring sideroblasts

International Prognostic Scoring System for MDS:

International Prognostic Scoring System (IPSS)					
Survival and AML evolution					
	Score value				
Prognostic variable	0	0.5	1	1.5	2
Bone marrow blasts (%)	< 5	5-10	--	11-20	21-30
Karyotype	Good	Intermediate	Poor	--	--
Cytopenias	0/1	2/3	--	--	--
Prognosis					
Overall Score	**IPSS Group**	**Median survival (y)**	**25% AML progression (y)**		
0	Low	5.7	9.4		
0.5-1	Intermediate-1	3.5	3.3		
1.5-2	Intermediate-2	1.1	1.1		
> 2.5	High	0.4	0.2		

Scoring system: A score from 0 to 2 is determined for each of the three variables; the three values are added to obtain the IPSS score. Example, a patient with 12 percent bone marrow blasts (score 1.5), complex chromosomal changes (poor karyotype score 1), neutrophil count of 1000/microL, and platelet count of 50,000/microL (two cytopenias = score 0.5) would have an IPSS score of 3 (= high risk).
Patients with 20-30% blasts may be considered to have MDS (FAB) or AML (WHO)
Karyotype-Cytogenetics: [Excludes karyotypes t(8;21), inv16, and t(15;17) which are considered to be AML and not MDS]
Good = normal, -Y alone, del(5q) alone, or del(20q) alone
Poor = complex (≥ 3 abnormalities) or chromosome 7 anomalies
Intermediate = other abnormalities
Cytopenias:
Absolute neutrophil count < 1,800/mcL
Platelets < 100,000 mcL
Hb < 10 g/dL (100 g/L

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Revised International Prognostic Scoring System (IPSS-R)							
Prognostic variable	0	0.5	1	1.5	2	3	4
Cytogenetic	Very good	-	Good	-	Intermediate	Poor	Very poor
Bone marrow blasts (%)	≤ 2	-	> 2- < 5	-	5-10	> 10	-
Hemoglobin	≥ 10	-	8- < 10	< 8	-	-	-
Platelets	≥ 100	50- < 100	< 50	-	-	-	-
ANC	≥ 0.8	< 0.8	-	-	-	-	-

Prognosis			
Overall Score	**IPSS-R Group**	**Median survival (y)**	**25% AML progression (y)**
≤ 1.5	Very low	8.8	Not reached
> 1.5- ≤ 3	Low	5.3	10.8
> 3- ≤ 4.5	Intermediate	3	3.2
> 4.5- ≤ 6	High	1.6	1.4
> 6	Very high	0.8	0.7

Cytogenetic risks:
Very good = -Y, del(11q)
Good = normal del(5q), del(12p), del(20q), double including del(5q)
Intermediate = del(7q), +8, +19, i(17q), any single or double independent clones
Poor = -7, inv(3)/t(3q)/del(3q), double including -7/del(7q), complex: 3 abnormalities
Very poor = complex: 3 abnormalities

Performance scores:

Eastern Cooperative Oncology Group (ECOG) Score (also known as Zubrod Score)	
0	Asymptomatic, fully active, able to carry on all pre-disease performance without restriction
1	Symptomatic, fully ambulatory, restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, for example light house work or office work
2	Symptomatic, in bed less than 50% of the day, ambulatory and capable of all self-care but unable to carry out any work activities
3	Symptomatic, confined to bed or chair more than 50% of the day but not bedridden, capable of only limited self-care
4	Bedridden, cannot perform any self-care, completely disabled
5	Dead

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Karnofsky Performance Score:	
100%	Able to carry on normal activity, no evidence of disease
90%	Able to carry on normal activity, minor signs or symptoms of disease
80%	Normal activity with effort, some signs and symptoms of disease
70%	Cares for self, unable to carry on normal activity or to work
60%	Requires occasional assistance from others but able to care for most needs
50%	Requires considerable assistance from others and frequent medical care
40%	Disabled, requires special care and assistance
30%	Severely disabled, hospitalization indicated, though death not imminent
20%	Very sick, hospitalization indicated, active support treatment necessary
10%	Moribund
0%	Dead

Lansky Play Score (Also known as Lansky Play - Performance Scale):	
100	Fully active, normal
90	Minor restrictions in physically strenuous activity
80	Active, but tires more quickly
70	Both greater restriction of and less time spent in play activity
60	Up and around, but minimal active play; keeps busy with quieter activities
50	Gets dressed but lies around much of the day, no active play but able to participate in all quiet play and activities
40	Mostly in bed; participates in quiet activities
30	In bed; needs assistance even for quiet play
20	Often sleeping; play entirely limited to very passive activities
10	No play; does not get out of bed
0	Unresponsive

Exjade (deferasirox) tablets for oral suspension
Jadenu (deferasirox) tablets for oral use
Jadenu Sprinkles (deferasirox) granules for oral use

Medication class:
Chelating agent

FDA-approved indication(s):
- Treatment of chronic iron overload caused by blood transfusions (transfusional hemosiderosis) in patients 2 years and older
- Treatment of chronic iron overload in patients 10 years and older with non-transfusion-dependent thalassemia (NTDT) syndromes and with a liver iron concentration (LIC) of at least 5 mg of iron per gram of liver dry weight (mg Fe/g dry weight) and a serum ferritin greater than 300 mcg/L

Limitations of use:
- Safety and efficacy of deferasirox in combination with other iron chelation therapies have not been established
- Controlled trials of deferasirox in myelodysplastic syndromes and chronic iron overload due to transfusions have not been conducted

Recommended Dose:
- Exjade:
  - Transfusional iron overload: 20 mg/kg once daily as oral suspension, calculate dose to nearest whole tablet
  - NTDT: 10 mg/kg once daily as oral suspension, calculate dose to nearest whole tablet
- Jadenu:
  - Transfusional iron overload: 14 mg/kg once daily calculate dose to nearest whole tablet or sachet
  - NTDT: 7 mg/kg once daily calculate dose to nearest whole tablet or sachet

- Note: For patients who are currently on Exjade tablets for oral suspension and converting to Jadenu, the dose should be about 30% lower, rounded to the nearest whole tablet or nearest whole sachet content for granules

Maximum dosage
- Exjade: 40 mg/kg once daily for transfusional hemosiderosis and 20 mg/kg once daily for NTDT
- Jadenu: 28 mg/kg once daily for transfusional hemosiderosis and 14 mg/kg once daily for NTDT

Available Dosage Forms:
- Exjade: 125 mg, 250 mg, and 500 mg tablets for oral suspension
- Jadenu: 90 mg, 180 mg, and 360 mg film coated tablets & granules in a sachet in a box with 30 sachets

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Warnings and Precautions:

- Avoid use in patients with severe hepatic impairment (Child-Pugh Class C)
- Reduce starting dose by 50% in patients with moderate hepatic impairment (Child-Pugh Class B)
- Do not use in patients with serum creatinine > 2x the upper limit of normal or with CrCl < 40 mL/min (Cockroft-Gault equation)
- Reduce starting dose by 50% in patients with renal impairment (CrCl 40-60 mL/min)
- Dose adjust for other degrees of renal dysfunction based on increases in serum creatinine & age
- May induce CYP3A4, may inhibit CYP1A2, CYP2C8, & is a substrate for UGT1A1
- Avoid use with aluminum-containing antacid preparations and theophylline
- Avoid use with phenobarbital, phenytoin, rifampicin, & ritonavir, if unavoidable increase initial dose of Exjade by 50%
- Avoid use with cholestyramine, colesevelam, & colestipol, if unavoidable increase initial dose of Exjade by 50%
- Avoid use with theophylline and tizanidine or other CYP1A2 substrates with a narrow therapeutic index
- Risk for GI ulceration, perforation, and hemorrhage is increased when used with drugs that have ulcerogenic or hemorrhagic potential (NSAIDS, corticosteroids, bisphosphonates, or anticoagulants)
- Interrupt therapy if cytopenias develop until the cause of the cytopenia is determined
- Discontinue permanently if serious and severe hypersensitivity reaction occurs
- Discontinue permanently if severe skin reactions including Stevens Johnson syndrome, toxic epidermal necrolysis, or erythema multiforme occur
- In transfusional iron overload, if serum ferritin < 500 mcg/L temporarily interrupt therapy
- In NTDT, if serum ferritin < 300 mcg/L interrupt therapy and get an LIC. If LIC < 3 mg Fe/g dw continue to hold therapy and monitor LIC. If LIC increases to more than 5 mg Fe/g dw, may restart therapy
- Woman who is breast feeding an infant or child should stop breast feeding

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Criteria:

- **Criteria for initial therapy:** Exjade (deferasirox) or Jadenu (deferasirox) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Prescriber is a Hematologist or Oncologist

2. A confirmed diagnosis of chronic iron overload due to **ONE** of the following:
   - Transfusional hemosiderosis in an individual 2 years of age or older with **ALL** of the following:
     - Evidence of transfusion related iron overload
       1. Evidence from **ONE** of the following:
          a. Receives blood transfusions on a regular basis **or** is participating in blood transfusion program
          b. Transfused with at least 100 mL/kg of packed red blood cells (PRBC) (at least 20 units of PRBC for a 40-kg person) **or** a history of frequent blood transfusions that have resulted in chronic iron overload
     - Serum ferritin consistently > 1,000 mcg/L

   - Non-transfusional thalassemia (NTDT) syndromes in an individual is 10 years of age or older with **ALL** of the following:
     - Serum ferritin consistently > 300 mcg/L on at least 2 measurements at least one month apart
     - Liver iron concentration (LIC) is ≥ 5 mg Fe/g dw by biopsy or by an FDA-approved method

3. **ALL** of the following baseline tests have been obtained before initiation of therapy:
   - Serum transaminase and bilirubin
   - Auditory examination
   - Ophthalmic examination including slit lamp examination and dilated fundoscopy
   - When used for iron overload in myelodysplastic syndrome (MDS), **ALL** of the following:
     - IPSS or IPSS-R score (score must be submitted with request)
     - Performance status (score must be submitted with request) using **ONE** of the following:
       1. ECOG **or** Karnofsky score **or** for age ≤ 10 a Lansky Play score

4. There are **NO** contraindications:
   - Contraindications include:
     - Known hypersensitivity to deferasirox
     - Serum creatinine > 2x the age-appropriate upper limit of normal **OR** CrCl < 40 mL/min
     - Individual with a platelet count of < 50 x 10^9/L
     - High-risk MDS defined by either IPSS or IPSS-R
     - Individuals with advanced malignancies

- Poor performance status defined by **ONE** of the following:
  1. ECOG score ≥ 3 **or** Karnofsky score < 70% **or** for age ≤ 10, Lansky Play < 70%

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Exjade (deferasirox) or Jadenu (deferasirox) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Individual continues to be seen by Hematologist or Oncologist

2. Individual's condition responded while on therapy
   - Response is defined as:
     - For transfusional hemosiderosis:
       - Serum ferritin decreased over baseline but is still > 500 mcg/L, if ferritin is consistently < 500 mcg/L, Exjade or Jadenu must be discontinued
       - Platelet count is > 50 x 10^9/L
       - CrCl > 40 mL/min
     - For NTDT: (if a serum ferritin and LIC is submitted, the LIC is used for determination)
       - Serum ferritin decreased over baseline but is still > 300 mcg/L, if ferritin is consistently < 300 mcg/L, Exjade or Jadenu must be discontinued
       - LIC decreased over baseline but is still ≥ 5 mg Fe/g dw, if LIC is consistently < 3 mg Fe/g dw, Exjade or Jadenu must be discontinued
       - Platelet count is > 50 x 10^9/L
       - CrCl > 40 mL/min

3. Individual has been adherent with the medication

4. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use
   - Contraindications as listed in the criteria for initial therapy section
   - Significant adverse effect:
     - Severe skin reactions including Stevens Johnson syndrome, toxic epidermal necrolysis, or erythema multiforme, signs and symptoms may include:
       - Progressive skin rash, blistering, oral ulcers
     - Severe hypersensitivity reaction, signs and symptoms may include:
       - Hives over neck and face, itching, nasal congestion, difficulty breathing, edema of throat, swelling of lips, mouth or tongue

5. There are no significant interacting drugs

Renewal duration: 12 months

Ferriprox (deferiprone) oral tablet and oral solution

Medication class:
Chelating agent

FDA-approved indication(s):
- Treatment of transfusional iron overload due to thalassemia syndromes when current chelation therapy is inadequate

Limitations of use:
- Safety and effectiveness have not been established for the treatment of transfusional iron overload in patients with other chronic anemias

Recommended Dose:
- Tablet: 25-33 mg/kg three times daily, dose should be rounded to the nearest 250 mg
- Oral solution: 25-33 mg/kg three times daily, dose should be rounded to the nearest 2.5 mL

- Note: Drug absorption of the solution and tablet formulation have been shown to be equivalent

Maximum dosage
- Tablet and Oral solution: 99 mg/kg/day

Available Dosage Forms:
- 500 mg film-coated tablets with a functional score (can be broken in half)
- 100 mg/mL in 500 mL bottle

Warnings and Precautions:
- Manage agranulocytosis / neutropenia prior to starting therapy
- Avoid use of drugs known to be associated with neutropenia or agranulocytosis, if unavoidable monitor ANC more frequently
- Do not resume Ferriprox in patients who developed agranulocytosis unless benefit outweigh risk
- Do not re-challenge patients who develop neutropenia with Ferriprox unless benefit outweighs risk
- Interrupt therapy if absolute neutrophil count $< 1.5 \times 10^9$/L (or 1,500/µL or 1,500mm^3) develops
- Interrupt therapy for acute infection
- Safety and efficacy have not been evaluated in patients with severe hepatic impairment (Child-Pugh Class C)
- Consider interruption of therapy for persistent increase in serum transaminase levels
- Zinc deficiency may occur with use and may require zinc supplementation
- Allow a 4-hour interval between Ferriprox and medications containing polyvalent cations (aluminum, antacids, zinc)
- Avoid concomitant use of UGT1A6 inhibitors (diclofenac, probenecid, or silymarin (milk thistle))
- Urine may appear reddish/brown due to excretion of iron-deferiprone complex
- If serum ferritin < 500 mcg/L temporarily interrupt therapy until it rises above 500 mcg/L

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- Woman of child bearing potential should avoid pregnancy
- Woman who is breast feeding an infant or child should stop breast feeding

Criteria:

- **Criteria for initial therapy:** Ferriprox (deferiprone) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met :

1. Prescriber is a Hematologist or Oncologist
2. Individual is 18 years of age or older
3. A confirmed diagnosis of transfusional iron overload due to thalassemia syndromes and serum ferritin levels are consistently > 2,500 mcg/L
4. Current chelation therapy with Exjade or Jadenu resulted in an inadequate response, or significant intolerance, or are contraindicated
5. **All** of the following baseline tests have been obtained before initiation of therapy:
   - Serum ferritin
   - Complete blood count with differential
   - Liver enzymes
6. There are **NO** contraindications
   - Contraindications include:
     - Hypersensitivity to deferiprone or any of the excipients

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Ferriprox (deferiprone) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Individual continues to be seen by a Hematologist or Oncologist
2. Individual's condition responded while on therapy
   - Response is defined as:
     - Serum ferritin decreased over baseline but is still > 500 mcg/L, if ferritin is consistently less than 500 mcg/L, Ferrirox must be discontinued
     - ANC is > 1.5 x 10^9/L
3. Individual has been adherent with the medication

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4. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use
    - Contraindications as listed in the criteria for initial therapy section
    - Significant adverse effect:
        - Agranulocytosis, signs and symptoms may include:
            - Any symptoms of infection such as fever, sore throat, mouth sores, chills, severe shaking or flu-like symptoms

5. There are no significant interacting drugs

Renewal duration: 12 months

Resources:

Exjade package Insert. Revised by manufacturer 10/2013. Accessed 05-08-2015. Reviewed on 06-20-2015.

Jadenu package Insert. Revised by manufacturer 03/2015. Accessed 05-08-2015. Reviewed on 06-20-2015.

Ferriprox package Insert. Revised by manufacturer 02/2015. Accessed 05-08-2015. Reviewed on 10-10-2015.

Kwiatkowski JL. Management of transfusional iron overload – differential properties and efficacy of iron chelating agents. J Blood Med 2011 Sept 20; 2:135-149

St. Pierre TG, Clark PR, Chua-anusom W, et al. Noninvasive measurement and imaging of liver iron concentrations using proton magnetic resonance. Blood 2005 Jan; 105 (2):855-861

Hoffbrand AV, Taher A, Cappellini MD. How I treat transfusional iron overload. Blood 2012 Nov; 120(18): 3657-3669

National Comprehensive Cancer Network Guidelines Clinical Practice Guidelines in Oncology: Myelodysplastic Syndromes; version 1.2017, August 18, 2016

UpToDate: Approach to the patient with suspected iron overload. Current through Sep 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/approach-to-the-patient-with-suspected-iron-overload?source=search_result&search=transfusional%20iron%20overload&selectedTitle=1~33

UpToDate: Iron chelators: Choice of agent, dosing, and adverse effects. Current through Sep 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/iron-chelators-choice-of-agent-dosing-and-adverse-effects?source=search_result&search=transfusional%20iron%20overload&selectedTitle=2~33

IRON CHELATING AGENTS:
EXJADE® (deferasirox) tablet for oral suspension
FERRIPROX® (deferiprone) tablet for oral use and oral solution
JADENU® (deferasirox) tablet for oral use
JADENU® Sprinkle (deferasirox) granules for oral use (cont.)

NCCN Clinical Practice Guidelines in Oncology: Myelodysplastic Syndromes. Version 1.2018, Aug 29, 2017. https://www.nccn.org/professionals/physician_gls/pdf/mds.pdf

UpToDate: Management of the complications of the myelodysplastic syndromes. Current through Sep 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/management-of-the-complications-of-the-myelodysplastic-syndromes?source=search_result&search=transfusional%20iron%20overload&selectedTitle=3~33#H2104230

BlueCross BlueShield of Arizona

An Independent Licensee of the Blue Cross and Blue Shield Association

Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:	Dosage Form:
Directions for Use:	Quantity: / Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.