Department:	Pharmacy Management	**Original Approval:**	01/09/2017
Policy #:	PM140	**Last Approval:**	07/11/2019
Title:	Darbepoetin alfa (Aranesp®) injection		
Approved By:	UM Pharmacy Subcommittee		

REQUIRED CLINICAL DOCUMENTATION FOR REVIEW

Documentation required to determine medical necessity for Darbepoetin alfa: History and/or physical examination notes and relevant specialty consultation notes that address the problem and need for the service: -Diagnosis -Labs/Diagnostics -Medication list (current and past) -Dosing and duration requested -Weight -Initial/Extended approval -Age -Prescribed by or in consultation with a hematologist, oncologist or specialist, when indicated.

BACKGROUND

Endogenous erythropoietin (EPO) is used to stimulate red blood cell (RBC) production in the bone marrow. Suppression of erythropoietin production or suppression of the bone marrow response to erythropoietin results in anemia in several disease processes, including chronic kidney disease (CKD), many types of cancer treatment, other chronic diseases, and use of certain drugs.

INDICATIONS/CRITERIA

Medicaid Members	For non-preferred agents in this class/category, patients must have had an inadequate response or have had a documented intolerance due to severe adverse reaction or contraindication to at least TWO* preferred agents. *If there is only one preferred agent in the class/category documentation of inadequate response to ONE preferred agent is needed If a new-to-market drug falls into an existing class/category, the drug will be considered non-preferred and subject to this class/category prior authorization (PA) criteria ***Continue to criteria for approval below.***
Medicare Members	***Step-utilization of Part D drugs not required.***

RECOMMENDED AUTHORIZATION CRITERIA
Erythropoiesis-Stimulating Agents may be considered medically necessary when used for ONE of the following conditions:

1. Treatment of anemia of prematurity for less than 6 months of age; OR

2. Treatment of anemia associated with chronic kidney disease (CKD) – (including patients on dialysis and not on dialysis); OR
3. Anemia associated with zidovudine-treated HIV-infected patients; OR
4. Treatment of anemia of cancer patients on chemotherapy, where the intent of treatment is palliative; OR
5. Treatment of anemia associated with myelodysplastic syndrome to reduce transfusion dependency; OR
6. Treatment of patients after allogeneic bone marrow transplantation; OR
7. Treatment of anemia due to ribavirin in patients who did not experience an improvement in hemoglobin level with ribavirin dose reduction; OR
8. To reduce the need for blood transfusions in anemic patients scheduled to undergo high-risk surgery who are at increased risk or intolerant to transfusions; OR
9. Special circumstance patients who will not or cannot receive whole blood or components as replacement for traumatic or surgical loss

1. **Anemia associated with chronic kidney disease (CKD) – (including patients on dialysis and not on dialysis)**

Criteria for Initial Approval:
The patient must meet all of the following criteria):

1. Diagnosis of chronic kidney disease (CKD); AND
2. Most recent hemoglobin level less than 10 g/dL; AND
3. Documentation of adequate iron stores as indicated by current (within the last 3 months) serum ferritin level greater than or equal to 100mcg/L or serum transferrin saturation greater than or equal to 20%.

If ALL criteria are met, the request will be approved for 6 months

Criteria for Reauthorization:

1. Hemoglobin level less than 11 g/dL documented in the previous 3 months; AND
2. Documentation of positive clinical response (e.g., as evidenced by decrease in blood transfusions) submitted by the prescriber.

If ALL criteria are met, the request will be approved for 12 months

Dosing in Patients with CKD who are on Dialysis. *Dosing must meet the following (A OR B):*

- **A)** For adults or children, initiate therapy at 0.45 mcg/kg subcutaneously (SC) or intravenously (IV) as a single injection once weekly; OR
- **B)** For adults, initiate therapy at 0.75 mcg/kg SC or IV once every 2 weeks.

Note: The IV route is recommended for patients on hemodialysis. For adult and pediatric patients receiving epoetin alfa ≥ 1,500 units once weekly, doses for conversion from epoetin alfa to Aranesp are available in the prescribing information. If the Hb approaches or exceeds 11.5 g/dL for adults or 12.0 g/dL for children, reduce or interrupt the Aranesp dose. Refer to the prescribing information insert regarding titration of Aranesp.[1] Use the lowest dose that will maintain a Hb level sufficient to reduce the need for red blood cell (RBC) transfusions.[1]

2. **Anemia of prematurity**

Clinical Criteria for Initial Approval

The patient must meet all of the following criteria):

1. Documentation of refusal of transfusion due to religious or cultural reasons; AND
2. Patient is less than 6 months of age; AND
3. Most recent hemoglobin level less than 10 g/dL.

If ALL criteria are met, the request will be approved for 3 months

Criteria for Reauthorization

1. Patient is less than 6 months of age; AND
2. Hemoglobin level is less than 11 g/dL; AND
3. Documentation of positive clinical response submitted by the prescriber.

If ALL criteria are met, the request will be approved for 3 months

3. **Other specific anemia indications**

1. Patient must have at least ONE of the following conditions:
   a. anemia associated with zidovudine-treated HIV-infected patients; OR
   b. anemia of cancer patients on chemotherapy, where the intent of treatment is palliative; OR
   c. anemia associated with myelodysplastic syndrome to reduce transfusion dependency; OR
   d. anemia after allogeneic bone marrow transplantation; OR
   e. anemia due to ribavirin in patients who did not experience an improvement in hemoglobin level with ribavirin dose reduction; OR
   f. to reduce the need for blood transfusions in anemic participants scheduled to undergo high-risk surgery who are at increased risk or intolerant to transfusions; OR
   g. special circumstance patients who will not or cannot receive whole blood or components as replacement for traumatic or surgical loss; AND
2. Most recent hemoglobin level less than 10 g/dL

If ALL criteria are met, the request will be approved for 3 months

Criteria for Reauthorization

1. Hemoglobin level less than 11 g/dL documented in the previous 3months; AND
2. Documentation of positive clinical response (e.g., as evidenced bydecrease in blood transfusions) submitted by the prescriber.

If ALL criteria are met, the request will be approved for 6 months

Dosage and quantity limits

J0881	500 units (500 mcg) per DOS
J0882	300 billing units (300 mcg) per DOS

HCPCS Code	**Description**

J0881	Injection, darbepoetin alfa, 1 mcg (non-ESRD use)
J0882	Injection, darbepoetin alfa, 1 microgram (for ESRD on dialysis)

Waste Management for All Indications.
Single-dose vials and syringes are available in many different strengths. The dose should be calculated and the number of vials/syringes needed assessed. Refer to the Aranesp prescribing information for more information. http://www.aranesp.com

Conditions Not Recommended for Approval
Aranesp has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Anemia Associated with Cancer in Patients not Receiving Myelosuppressive Cancer Chemotherapy.** Aranesp is not indicated in patients with cancer who are not receiving cancer chemotherapy.[1] The American Society of Clinical Oncology (ASCO)/American Society of Hematology (ASH) guidelines for the use of epoetin alfa and Aranesp in adult patients with cancer recommend that ESAs not be used in treatment of anemia associated with malignancy in those who are not receiving concurrent myelosuppressive chemotherapy.[4]

2. **Anemia Associated with Acute Myelogenous Leukemia (AML), Chronic Myelogenous Leukemia (CML), or other Myeloid Cancers.** Aranesp is indicated for use in non-myeloid cancers. AML and CML are examples of myeloid cancers.[1]

3. **Anemia Associated with Radiotherapy in Cancer.** Aranesp is not indicated for use in cancer patients who are given only radiation therapy.[1]

4. **To Enhance Athletic Performance.** Aranesp is not recommended for approval because this indication is excluded from coverage in a typical pharmacy benefit.

5. **Anemia in Patients due to Acute Blood Loss.** Use of Aranesp is not appropriate in these types of situations.

6. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

SPECIAL CONSIDERATIONS

BOXED WARNING: ESAs INCREASE THE RISK OF DEATH, MYOCARDIAL INFARCTION, STROKE, VENOUS THROMBOEMBOLISM, THROMBOSIS OF VASCULAR ACCESS AND TUMOR PROGRESSION OR RECURRENCE. See full prescribing information for complete boxed warning.[1]

Contraindications include[1]:

1. Uncontrolled hypertension
2. Pure red cell aplasia (PRCA) that begins after treatment with Aranesp or other erythropoietin protein drugs
3. Serious allergic reactions to Aranesp

LIMITATIONS/EXCLUSIONS

Please refer to a product line's certificate of coverage for benefit limitations and exclusions for these services:

PRODUCT LINE	LINK TO CERTIFICATE OF COVERAGE
MEDICARE ADVANTAGE	http://healthfirst.chpw.org/for-members/resource-library/handbooks-and-guides
WASHINGTON APPLE HEALTH	http://chpw.org/our-plans/apple-health/
INTEGRATED MANAGED CARE	http://chpw.org/our-plans/apple-health/

Citations & References

References	
	1. Product Information: ARANESP® intravenous injection, subcutaneous injection, darbepoetin alfa intravenous injection, subcutaneous injection. Amgen Inc (per FDA), Thousand Oaks, CA, 2017. 2. Product Information: Epogen® intravenous injection, subcutaneous injection, epoetin alfa intravenous injection, subcutaneous injection. Amgen Inc (per FDA), Thousand Oaks, CA, 2017 3. Product Information: Procrit® intravenous injection, subcutaneous injection, epoetin alfa intravenous injection, subcutaneous injection. Janssen Products LP (per FDA), Horsham, PA, 2017

	4. Product Information: RETACRIT™ intravenous, subcutaneous injection, epoetin alfa-epbx intravenous,subcutaneous injection. Hospira, Inc (per FDA), Lake Forest, IL, 2018 5. Product Information: Mircera® intravenous injection, subcutaneous injection, methoxy polyethylene glycol epoetin beta intravenous injection, subcutaneous injection. Hoffmann-La Roche Inc. (per FDA),South San Francisco, CA, 2015 6. KDIGO Clinical Practice Guidelines for Anemia in Chronic Kidney Disease. Kidney International Supplements. 2012; 2(4): 279-335. National Comprehensive Cancer Network Guidelines Version 3.2018. Cancer- and Chemotherapy-Induced Anemia.	
CFR	42 CFR § 438.210	
WAC	WAC 284-43-2050	
RCW		
Contract Citation	☒ WAH	AH section 17.3.2.1 General Description of Contracted Services - Pharmacy Benefit and Services - Apple Health Preferred Drug List and Plan Formularies
	☒ IMC	IMC section 16.12.2 General Description of Contracted Services - Pharmacy Benefit and Services - Apple Health Preferred Drug List and Plan Formularies
	☒ MA	https://healthfirst.chpw.org/our-plans/2018-medicare-plans/
Other Requirements		
NCQA Elements		

Revision History

Revision Date	Revision Description	Revision Made By
01/09/2017	NEW	Sophia Yun, PharmD
01/10/2017	Approval	MMLT
03/06/2017	Medication name formatting revision	Sophia Yun, PharmD
03/06/2017	Approval	MMLT
02/12/2018	Updated review	Catherine Vu, PharmD
03/01/2018	Approval	MMLT
03/09/2018	Reassigned from UM to Pharmacy	Cindy Bush
07/16/2018	Minor revisions	Jennifer Farley, PharmD
03/08/2019	Approval	UM Pharmacy Subcommittee
03/12/2019	Minor revisions	Ivan Figueira, PharmD

07/05/2019	Criteria revised to match HCA Medical policy no.82.40.1	Jennifer Farley, PharmD
07/11/2019	Approval	UM Pharmacy Subcommittee