University of Michigan Health Plan

DRUG DETERMINATION POLICY

Title: DDP-18 Erythropoietin-Stimulating Agents (ESAs)

Effective Date: 4/23/25

Important Information - Please Read Before Using This Policy

The following policy applies to health benefit plans administered by UM Health Plan and may not be covered by all UM Health Plan. Please refer to the member's benefit document for specific coverage information. If there is a difference between this general information and the member's benefit document, the member's benefit document will be used to determine coverage. For example, a member's benefit document may contain a specific exclusion related to a topic addressed in a coverage policy.

Benefit determinations for individual requests require consideration of:

1. The terms of the applicable benefit document in effect on the date of service.
2. Any applicable laws and regulations.
3. Any relevant collateral source materials including coverage policies.
4. The specific facts of the particular situation.

Contact UM Health Plan Customer Service to discuss plan benefits more specifically.

1.0 Policy:

This policy describes the determination process for coverage of specific drugs that require prior approval.

This policy does not guarantee or approve benefits. Coverage depends on the specific benefit plan. Drug Determination Policies are not recommendations for treatment and should not be used as treatment guidelines.

2.0 Background or Purpose:

Erythropoiesis-stimulating agents are drugs indicated for a number of diagnoses and are associated with significant toxicity. These criteria were developed and implemented to ensure appropriate use for the intended diagnoses and mitigation of toxicity, if possible.

3.0 Clinical Determination Guidelines:

Document the following with chart notes:

I. General Considerations

   A. Appropriate medication use [must meet all below]

      1. Diagnosis: meets standard diagnostic criteria that designates signs, symptoms, and test results to support specific diagnosis.

      2. Food and Drug Administration (FDA) approval status [must meet one listed below]

         a. FDA approved: product, indication, and/or dosage regimen.

         b. Non-FDA approved: compendium support (Lexicomp) for the use of a drug for a nnon-FDA approved indication or dosage regimen.

      3. Place in therapy: sequence of therapy supported by national of international accepted guidelines and/or relevant clinical studies.

B. Required site-of-care as determined by the Health Plan (DDP008 Site of Care for Administration of Parenteral Specialty Drugs)

C. Pharmaceutical sample use: the plan does not recognize samples as a medication trial or for continuation of therapy.

D. Adherence to requested medications required for re-approval [must meet one listed below]:

1. Medications processed under the medical benefit: consistent (at least 80% of days covered) based on medical claims history or chart notes.

2. Medications processed under the pharmacy benefit: consistent (at least 80% of days covered) fill history electronically or verbally from the pharmacy.

E. Non-Preferred (Epogen, Procrit and Retacrit): contraindicated, failed or had significant adverse effects to Aranesp and Mircera.

F. Exclusions

1. Cancer patients

a. Receiving myelosuppressive chemotherapy when the anticipated outcome is cure.

b. Receiving hormonal treatment, therapeutic biologicals, or radiation (unless on concurrent myelosuppressive chemotherapy)

2. Surgical patients:

a. Willing to donated autologous blood

b. Undergoing cardiac or vascular surgery

3. As a substitute for red blood cells transfusion in patients requiring immediate correction of anemia.

II. Chronic kidney disease (CKD)-induced anemia [must meet all listed below]:

A. Diagnosis and severity [must meet both listed below]:

1. Requiring blood transfusions in dialysis and non-dialysis patients.

2. Hemoglobin at or below 10gm per dL or hematocrit at or below 30 percent.

B. Dosage regimen: intravenous administration preferred for patients on dialysis [must meet both listed below]:

1. Initial [must meet one listed below]:

a. Epogen/Procrit/Retacrit intravenous or subcutaneous (epoetin alfa): 50 to 100 units per kg three times per week.

b. Mircera intravenous or subcutaneous (methoxy polyethylene glycol-epoetin beta): 0.6mg per kg every two weeks or 1.2mg per kg every four weeks in stabilized patients.

2. Titration [must meet one listed below]:

a. Maintain hemoglobin below 11g per dL.

b. Inadequate or lack of response over 12-week escalation: further increase not justified.

C. Approval:

1. Initial: six months.
2. Re-approval:
    a. Hemoglobin below 11g per dL or hematocrit below 33 percent.
    b. Six months.

III. Anemia due to chemotherapy in cancer patients [must meet all listed below]:

A. Diagnosis and severity [must meet both listed below]:

1. Patient receiving myelosuppressive chemotherapy to treat non-myeloid malignancies for more than two months.
2. Hemoglobin below 10g per dL.

B. Dosage regimen:

1. Initial: Epogen/Procrit/Retacrit intravenous or subcutaneous (epoetin alpha IV or SQ): 150 units per kg three times per week or 40,000 units one time per week until completion of chemotherapy.
2. Titration: maintain hemoglobin below 11g per dL.

C. Approval:

1. Initial: six months.
2. Re-approval:
    a. Hemoglobin below 11g per dL.
    b. Six months.

IV. Myelodysplastic Syndromes

A. Diagnosis and Severity

1. Predominant cytopenia: Isolated or predominant anemia
2. IPSS-M prognostic category: Lower-Risk (Calculator: **IPSS-M** online calculator)
3. Erythropoietin: ≤200mU/mL

B. Dosage regimen

1. Mircera subcutaneous (Epoetin alfa SQ): 40,000-60,000 units/week or in divided doses.
2. Ananesp subcutaneous (darbepoeitin alfa SQ): 150-300mcg SQ every other week

C. Approval: six months

V. Zidovudine use in human immunodeficiency virus (HIV) infection-induced anemia [must meet all listed below]:

A. Diagnosis and severity [must meet both listed below]:

1. Endogenous erythropoietin levels equal or below 500mu per mL and zidovudine doses at or below 4,200mg per week.

2. Hemoglobin at or below 12g per dL.

B. Dosage regimen:

1. Initial: Epogen/Procrit/Retacrit intravenous or subcutaneous (epoetin alpha methoxy polyethylene glycol-epoetin beta IV or SQ) – 100 units per kg.

2. Titration:

a. Maintain hemoglobin below 12g per dL.

b. Maximum dose: Epogen/Procrit/Retacrit intravenous or subcutaneous (epoetin IV or SQ) 300 units/kg; discontinue if hemoglobin goal not reached in eight weeks.

C. Approval.

1. Initial: four months.

2. Re-approval:

a. Hemoglobin at or below 12g per dL.

b. Four months.

VI. Surgery [must meet all listed below]:

A. Indication: to reduce allogenic red blood cell transfusions [must meet both listed below]:

1. Elective non-cardiac, non-vascular surgery.

2. Hemoglobin above 10g per dL and less than or equal to 13g per dL.

B. Dosage regimen: Epogen/Procrit/Retacrit intravenous or subcutaneous (epoetin alpha IV or SQ) [must meet one listed below]:

1. 300 units/kg daily for 15 doses; given ten days pre-op, day of surgery, and four days post-operative

2. 600 units/kg one time per week for four doses; given three, two, and one week pre-op and day of surgery.

4.0 Coding:

COVERED CODES - MEDICAL BENEFIT				
HCPCS Code	**Brand Name**	**Generic Name**	**Billing (1 Unit)**	**Prior Approval**
J0887	Mircera (for ESRD on dialysis)	methoxy polyethylene glycol-epoetin beta	1 mcg	Y
J0888	Mircera (for non-ESRD use)	methoxy polyethylene glycol-epoetin beta	1 mcg	Y

COVERED PRODUCTS - PHARMACY BENEFIT		
Brand Name	**Generic Name**	**Prior Approval**
Aranesp	darbepoetin alfa	Y
Epogen	epoetin alfa	Y
Procrit	epoetin alfa	Y
Retacrit	epoetin alpha-epbx	Y

EXCLUDED CODES AND PRODUCTS			
HCPCS Code	**Brand Name**	**Generic Name**	**Benefit Plan Reference/Reason**
J0885	Epogen/Procrit	epoetin alpha	Covered on the pharmacy benefit with prior approval
Q5105	Retacrit (ESRD on dialysis use)	epoetin alpha-epbx	Covered on the pharmacy benefit with prior approval
Q5106	Retacrit (non-ESRD use)	epoetin alpha-epbx	Covered on the pharmacy benefit with prior approval

5.0 References, Citations & Resources:

1. National Government Services. Erythropoietin Stimulating Agents (ESA) – Supplemental Instructions (DRUG-AC-07-06-02)12/01/07.
2. FDA Alert 11/8/07: Information for Healthcare Professionals: Erythropoiesis Stimulating Agents (ESA).
3. Lexicomp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Epoetin Alpha, Aranesp and Mircera accessed March 2025.
4. Management of cancer-associated anemia with erythropoiesis-stimulating agents: ASCO/ASH clinical practice guideline update. Blood Adv 2019; 3 (8): 1197–1210. doi: https://doi.org/10.1182/bloodadvances.2018030387
5. Kidney Disease: Improving Global Outcomes Anemia Work Group. KDIGO clinical practice guideline for anemia in chronic kidney disease. Kidney Int Suppl. 2012;2:S1–S335.
6. UpToDate: Treatment of lower-risk myelodysplastic syndrome/neoplasms (MDS)

   ptodate.com/contents/treatment-of-lower-risk-myelodysplastic-syndromes-neoplasms-mds?search=myelodysplastic%20syndrome%20treatment&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2#H3903616320

6.0 Appendices:

~~See page 5.~~

7.0 Revision History:

Original Effective Date: 08/13/2008

Next Review Date: 05/01/2026

Revision Date	Reason for Revision
4/19	Moving to new format; presented and approved at P&T Committee.
3/20	Annual review; replaced abbreviations, added drug Retacrit

Revision Date	Reason for Revision
2/21	Annual review; reformatting, replaced abbreviations, added appropriate use section; approved at 4/28/21 P&T
2/22	Annual review, added compendium reference in appropriate use section
2/23	Annual review, formatting changes for consistency, updated non preferred section to be reflective of current PDL, added guideline citation, added exclusion of curative chemotherapy
2/24	Annual review; updated coding, added guideline reference citation, removed Patient Safety and Monitoring appendix
2/25	Annual review; added general considerations section and moved appropriate use/non-preferred agents /exclusion as well as added samples, site of care and adherence, added myelodysplastic syndrome