Drug Policy:

Erythropoiesis Stimulating Agents

POLICY NUMBER UM ONC_1138	**SUBJECT** Erythropoiesis Stimulating Agents (ESAs): Epogen and Procrit (epoetin alfa), Aranesp (darbepoetin alfa), Mircera (epoetin beta), and Retacrit (epoetin alfa-epbx)		**DEPT/PROGRAM** UM Dept	**PAGE 1 of 4**
DATES COMMITTEE REVIEWED 07/22/11, 09/12/12, 06/13/13, 07/10/13, 07/24/14, 06/22/16, 07/26/16, 08/24/16, 09/12/16, 03/04/17, 05/10/17, 09/13/17, 08/08/18, 07/10/19, 12/11/19, 03/11/20, 08/12/20, 01/13/21, 02/10/21, 07/14/21, 11/15/21, 05/11/22, 06/08/22, 03/08/23, 04/12/23, 04/10/24	**APPROVAL DATE** April 10, 2024	**EFFECTIVE DATE** April 26, 2024	**COMMITTEE APPROVAL DATES** 07/22/11, 09/12/12, 06/13/13, 07/10/13, 07/24/14, 06/22/16, 07/26/16, 08/24/16, 09/12/16, 03/04/17, 05/10/17, 09/13/17, 08/08/18, 07/10/19, 12/11/19, 03/11/20, 08/12/20, 01/13/21, 02/10/21, 07/14/21, 11/15/21, 05/11/22, 06/08/22, 03/08/23, 04/12/23, 04/10/24	
PRIMARY BUSINESS OWNER: UM		**COMMITTEE/BOARD APPROVAL** Utilization Management Committee		
NCQA STANDARDS UM 2		**ADDITIONAL AREAS OF IMPACT**		
CMS REQUIREMENTS	**STATE/FEDERAL REQUIREMENTS**		**APPLICABLE LINES OF BUSINESS** Commercial, Exchange, Medicaid	

I. PURPOSE

To define and describe the accepted indications for Erythropoiesis Stimulating Agents (ESAs) Epogen and Procrit (epoetin alfa), Aranesp (darbepoetin alfa), and Retacrit (epoetin alfa-epbx) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

A. Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided:

1. The requested medication was used within the last year, AND
2. The member has not experienced disease progression and/or no intolerance to the requested medication, AND

3. Additional medication(s) are not being added to the continuation request.

B. Anemia of Chronic Kidney Disease (CKD)

1. Erythropoiesis Stimulating Agents (ESAs) may be used in Anemia of Chronic Kidney Disease as follows:
   a. The member has chronic kidney disease defined as GFR less than 60 ml/min over a period of at least three months AND
   b. Concomitant iron deficiency has been ruled out with a serum ferritin greater than or equal to 30 ng/mL AND/OR transferrin saturation greater than or equal to 20% with levels obtained within the last 12 months) AND
   c. For initiation of therapy, a Hgb of less than 10 g/dL is required (levels are obtained within the last 4 weeks) OR
   d. For continuation of therapy, a Hgb of 11 g/dL or less is required (levels are obtained within the last 4 weeks).

C. Chemotherapy induced anemia (CIA)

1. Erythropoiesis Stimulating Agents (ESAs) may be used in members at risk of requiring red blood cell transfusions within 30 days of anemia with solid tumors or non-myeloid malignancies receiving myelosuppressive chemotherapy without curative intent and such chemotherapy is ongoing or has been completed less than or equal to 8 weeks prior to initiation or continuation of ESA and the member meets the following criteria:
   a. For initial/continuation requests the baseline Hgb less than 10 g/dL or HCT less than 30 prior to the initiation of ESA therapy (levels are obtained within the last 4 weeks) AND
   b. Prior to initiating ESA therapy concomitant iron deficiency has been ruled out and serum ferritin is greater than or equal to 30 ng/mL AND/OR transferrin saturation is greater than or equal to 20%. For continuation requests, the above levels should be available at least 12 months prior to the continuation request.

D. Myelodysplastic Syndrome (MDS)

1. The member has lower risk MDS (IPSS Low and INT-1) AND Erythropoiesis Stimulating Agents (ESAs) may be used for the following:
   a. For member with symptomatic anemia with serum erythropoietin level less than or equal to 500 mU/mL AND
   b. For initiation of Erythropoiesis Stimulating Agents (ESAs): Hgb less than 10 g/dL or HCT less than 30 (levels are obtained within the last 4 weeks) OR
   c. For Continuation of Therapy: Hgb is 11g/dL or less (levels are obtained within the last 4 weeks) AND
   d. Serum ferritin greater than or equal to 30 ng/mL AND/OR transferrin saturation greater than or equal to 20% (levels are obtained within the last 12 months) OR if iron stains in the bone marrow show adequate iron AND
   e. Member's bone marrow biopsy shows less than 10% blasts in the bone marrow OR
   f. Erythropoiesis Stimulating Agents (ESAs) may be used in combination with filgrastim in members with less than 10% blasts in the bone marrow and the Hgb is unresponsive to a trial of ESA therapy.

III. EXCLUSION CRITERIA

A. For MDS: Lack of response after 12 weeks trial (response defined as 1 g/dL hemoglobin increase or decrease of transfusion requirements).

B. The member is on chemotherapy with curative intent.

C. The member completed myelosuppressive chemotherapy more than 8 weeks prior to initiation of Erythropoiesis Stimulating Agents (ESAs) for CIA.

D. Erythropoiesis Stimulating Agent (ESA) is not used for myeloid malignancies (e.g., acute, and chronic myeloid leukemia, myelofibrosis, polycythemia vera, or essential thrombocytopenia) or intermediate risk and high risk MDS OR MDS with a bone marrow blast count of greater than or equal to 10%.

E. The member has any of the following causes of anemia:

1. Deficiencies in B12, folate, or iron
2. Hemolysis, occult blood loss, hypothyroidism, or nutritional deficiency.

F. Erythropoiesis Stimulating Agent (ESA) is being used for the acute correction of anemia or as a substitute for RBC transfusions.

G. Investigational use of Erythropoiesis Stimulating Agents (ESAs) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:

1. Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
2. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
3. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
4. Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
5. That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
6. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
7. That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

IV. MEDICATION MANAGEMENT

A. Requests for ESAs shall be reviewed for appropriateness as per FDA approved product labeling, NKF KDOQI anemia in CKD guidelines, ASCO and NCCN clinical practice guidelines, or CMS approved compendia.

V. APPROVAL AUTHORITY

A. Review – Utilization Management Department

B. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

A. None

VII. REFERENCES

A. Aranesp Product Information. Amgen, Inc. Thousand Oaks, CA. 2019.

B. Epogen Product Information. Amgen, Inc. Thousand Oaks, CA. 2018.

C. Procrit Product Information. Janssen Products, LP Horsham, PA 2020.

D. Retacrit Product Information. Pfizer Laboratories Div Pfizer Inc. New York, NY 2020

E. Clinical Pharmacology Elsevier Gold Standard 2023.

F. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2023.

G. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2023.

H. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2023.

I. Bohlius J, Bohlke K, Castelli R, Djulbegovic B, Lustberg MB, Martino M, Mountzios G, Peswani N, Porter L, Tanaka TN, Trifirò G, Yang H, Lazo-Langner A. Management of Cancer-Associated Anemia With Erythropoiesis-Stimulating Agents: ASCO/ASH Clinical Practice Guideline Update. J Clin Oncol. 2019 May 20;37(15):1336-1351. doi: 10.1200/JCO.18.02142. Epub 2019 Apr 10. PMID: 30969847.

J. Tobian AA, Heddle NM, Wiegmann TL, Carson JL. Red blood cell transfusion: 2016 clinical practice guidelines from AABB. Transfusion. 2016 Oct;56(10):2627-2630. doi: 10.1111/trf.13735. PMID: 27739152.

K. Kliger AS, et al. KDOQI US commentary on the 2012 KDIGO Clinical Practice Guideline for Anemia in CKD. Am J Kidney Dis. 2013 Nov;62(5):849-59.

L. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. J Clin Oncol. 2014 Apr 20;32(12):1277-80.

M. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf.