Clinical Pharmacy Agreement: ESA dosing in the Ambulatory Setting

Effective Date: 4/27/2023 Next Review Date: 4/27/2026

PURPOSE:

To provide framework to pharmacists to independently dose Erythropoiesis Stimulating Agents when a clinical pharmacy agreement has been indicated by a medical provider. The goal is to utilize the pharmacists' drug therapy expertise, to manage and optimize therapy and patient outcomes, in addition to providing adequate medication education and reduce the risk of adverse events.

PERSONS AFFECTED:

This applies to OHSU Healthcare Pharmacy workforce personnel; pharmacists who manage ESAs in the ambulatory setting.

DEFINITIONS:

AML: acute myeloid leukemia
ACML: atypical chronic myelogenous leukemia
CBC: complete blood count
CKD: chronic kidney disease
CKTEC: Clinical Knowledge and Therapeutic Evaluation Committee
CML: chronic myelogenous leukemia
CMS: Center for Medicare and Medicaid Services
ESA: erythropoiesis stimulating agents
FDA: Food and Drug Administration
GFR: glomerular filtration rate
Hgb: hemoglobin
Hct: hematocrit
IBW: ideal body weight
IV: Intravenous
JMML: Juvenile myelomonocytic leukemia
MDS: myelodysplastic syndrome
SBP: systolic blood pressure
WHO: World Health Organization

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CLINICAL PHARMACY AGREEMENT:

1. The provider will determine whether specific medications are “pharmacist managed” or “provider managed” when ordering ESAs.
2. The provider must specify the indication intended for the clinical pharmacist agreement.
3. If ESA orders are to be managed by the pharmacist, the pharmacist is responsible for both dosing and monitoring, as well as appropriate laboratories needed to ensure accurate monitoring and dose adjustments (i.e. renal panel with electrolytes and BUN/ SCr).
4. The pharmacist performing monitoring and dose adjustments is responsible for both placing updated medication orders and documenting these recommendations/activities within a monitoring consult note.
5. The minimum required information in the pharmacy consult note, otherwise utilize developed template:
    - Initial Dosing
    - Monitoring & Dose Adjustments
    - Laboratory monitoring

RESPONSIBILITIES:

1. Pharmacist will utilize the treatment algorithm for the following indications:
    a. Anemia in CKD (non-dialysis)
        i. Intermittent Iron Repletion Protocol
    b. Anemia in CKD, post-renal transplant patients (non-dialysis)
    c. Symptomatic anemia due to MDS
    d. Chemotherapy induced anemia
    e. Peri-operative reduction of transfusion for elective, noncardiac, nonvascular surgery
2. When the treatment indication does not align with qualifying indications above or includes CMS non-approved criteria (reference below), the pharmacist will inform the ordering clinician to self-manage ESA therapy and document this change in a consult note. The provider will then follow the ESA Use Restriction and Dosing Policy in the Ambulatory Setting (HC-CKT-131-POL)
3. Pharmacist will contact provider if any deviations from management plan should occur based on clinical judgment.
4. Pharmacist will monitor lab appropriateness per treatment parameters and insurance approval.
5. Pharmacist will inform the Managed Care Team of all new plans and dosing changes (if approved under a prior authorization). Pharmacy will not be involved in the authorization process.

CMS NON-APPROVED CRITERIA:

1. Anemia in cancer or cancer treatment patient due to folate, B-12, or iron deficiency, hemolysis, bleeding, or bone marrow fibrosis
2. Anemia associated with the treatment of acute or chronic myelogenous leukemias (AML, CML), or erythroid cancers
3. Anemia of cancer not related to cancer treatment
4. Any anemia associated only with radiotherapy
5. Prophylactic use to prevent chemotherapy-induced anemia
6. Prophylactic use to reduce tumor hypoxia
7. Patients with erythropoietin-type resistance due to neutralizing antibodies
8. Anemia due to cancer treatment if patients have uncontrolled hypertension
9. Reference ICD-10 Dx Description ESA in Cancer Spreadsheet for correlating diagnosis and ICD-10 codes. Refer to appendix (section I).

1. **Anemia in Chronic Kidney Disease Treatment Algorithm:**

a. CMS Approved Criteria
   i. Anemia due to CKD Stage III-IV CKD (non-dialysis)

b. Special Populations
   i. Patients on hemodialysis will be managed in dialysis and deferred to provider. Pharmacist will not be involved in dosing adjustments or monitoring.
   ii. For CKD patients with post-renal transplant anemia in the setting of delayed graft function see dosing policy & algorithm listed under subsection 2.

c. Contraindications
   i. SBP > 180 mm Hg
   ii. DBP > 100 mm Hg

d. Initiation
   i. Requirements
      1. Diagnosis of stage III-V CKD
      2. Hgb < 10 g/dL or Hct < 30% (within 1 week of initiation)
      3. GFR < 60 ml/min (within 1 month of initiation)
      4. Iron studies (within 3 months of initiation)
         a. Ferritin ≥ 100 ng/mL
         b. Iron saturation ≥ 20%

e. Initiation Dose (Dose level 0, week 0)
   i. Darbepoetin alfa
      1. CKD NOT on dialysis
         a. ≥ 60 kg: 40 mcg subcutaneously every 4 weeks
         b. < 60 kg: 25 mcg subcutaneously every 4 weeks
   ii. Epoetin alfa-epbx
      1. CKD NOT on dialysis
         a. ≥ 60 kg: 20,000 units subcutaneously every 2 weeks
         b. < 60 kg: 10,000 units subcutaneously every 2 weeks

f. Monitoring
   i. Hemoglobin & Hematocrit
      1. Every 2 weeks for epoetin-alfa (within 72 hours of maintenance dose)
      2. Every 4 weeks for darbepoetin-alfa (within 72 hours of maintenance dose
   ii. Iron studies
      1. Baseline and every 3 months
   iii. GFR
      1. Baseline and every year

g. Maintenance Dose Considerations
   i. Assess changes in Hgb and make dose adjustments as detailed below (see table 1: Anemia due to CKD for quick reference)

ii. For patients being treated under a prior authorization and dose increase indicated: pharmacy will verify current dose level and place increased dose level in treatment plan for future visit and request a new authorization
iii. For dosing levels, reference Table 5: ESA Darbepoetin and Epoetin simplified dosing weight stratified (sect: RELATED DOCUMENTS/EXTERNAL LINKS pg 17-19)
iv. Only continue if Hgb remains ≤ 11 g/dL
v. If Hgb > 11 g/dL hold therapy
    1. Re-check Hgb and reinitiate when Hgb < 11 g/dL
    2. When reinitiating, decrease dose to next dose level (e.g. dose level 0 reduce to dose level -1)
vi. Dose adjustments
    1. In any 2 week increment at current dose level:
        a. Hgb increase > 1 g/dL
            i. Decrease dose to next dose level (e.g. dose level 0 decrease to dose level -1)
        b. Hgb increase ≤ 1g/dL
            1. Maintain dose
    2. In any 4 week increment at current dose level:
        a. Do not increase dose more frequently than once every 4 weeks
        b. Decrease indicated in most-recent 2-week interval as above
            i. Decrease dose as above
            ii. No increase assessment at 4-week interval
        c. Hgb increases ≥ 1 g/dL
            i. Maintain dose
        d. Hgb increases < 1 g/dL
            i. Hgb < 10 g/dL
                1. Increase dose to next dose level (e.g. dose level 0 increase to dose level 1)
            ii. And Hgb 10-11 g/dL
                1. Maintain dose
vii. If dosing interrupted for iron administration or missed appointments, resume dose at most recent previous dose given
viii. By week 12 after initiation, if there is no improvement in Hgb to 10-11 g/dL
    1. Maintain lowest dose to avoid transfusions
    2. If no improvement in transfusion requirement, discontinue ESA

Table 1: Anemia due to CKD Quick Reference

Hgb	ESA Dose Adjustments	
Initiation dose (Dose level 0, week 0)		
if Hgb < 10 g/dL	**Give corresponding dose at level 0 for week 0**	
Maintenance Dosing (week 2 onward)		
if Hgb > 11 g/dL at **ANY time**	HOLD dose, pt follow up at regular interval	
If Hgb ≤ 11 g/dL		
ESA previously held for Hgb > 11 g/dL ?	YES	Resume at one decreased dose level (ex: dose level –1)
	NO	See below
Assess Hgb change for most recent **2 week interval** at CURRENT dose level (ex: week 2 to week 4)		
Did the Hgb increase > 1g/dL?	YES	Decrease by one dose level (ex: dose level –1) do NOT assess 4-week dosing interval.
	NO	See below
Did Hgb increase ≤ 1 g/dL ?	• If at current dose for < 4 weeks => maintain current dose • If at current dose ≥ 4 weeks => assess 4-week interval below	
Assess Hgb change for most recent **4-week interval** at CURRENT dose level (ex: week 0 to week 4) <u>(Do not increase the dose more frequently than once every 4 weeks)</u>		
Did the Hgb increase ≥ 1 g/dL?	YES	Maintain dose
	NO	See below
If Hgb < 10 g/dL		
Did Hgb increase < 1 g/dL ?	Increase by one dose level (ex: dose level +1)	

h. Intermittent Iron Repletion Protocol
    i. Utilized by consulting pharmacist pool (ESA/IVIG/HIP pharmacist) in follow-up to iron studies not meeting treatment requirements
    ii. Restricted to anemia due to CKD patients only
    iii. If IV iron is indicated, put ESA plan on hold
    iv. Contraindications
        1. Documented IV iron allergy
        2. Active Infection
    v. Absolute Iron Deficiency Anemia due to CKD
        1. Initiation Requirements: Ferritin < 100 ng/mL
        2. Apply Infusion Plan: Iron dextran 1000 mg IV
        3. Monitoring: Recheck iron studies 28 days after iron infusion
            a. Ferritin ≥ 100 ng/dL and TSAT ≥ 20%
                i. Discontinue iron plan
                ii. Resume ESA plan
            b. Ferritin < 100 ng/mL or TSAT < 20%
                i. Refer to provider
    vi. Function Iron Deficiency Anemia due to CKD
        1. Initiation Requirements: TSAT < 20% and Ferritin 100-500 ng/mL
            a. Refer to Provider if TSAT < 20% and Ferritin > 500 ng/mL
        2. Apply Infusion Plan: Iron dextran 500 mg IV
        3. Monitoring: Recheck iron studies 7 days after iron infusion
            a. TSAT ≥ 20%
                i. Discontinue iron plan
                ii. Resume ESA plan
            b. TSAT < 20 % and Ferritin 100-500 ng/mL
                i. Order second dose of iron dextran 500 mg IV
                ii. Recheck iron studies 7 days after 2nd Iron infusion
                    1. Ferritin < 20% persists
                        a. Refer to provider
            c. TSAT < 20% and Ferritin > 500 ng/mL
                i. Refer to provider
    vii. Therapeutic interchange per Insurance requirement (reference Table 2: Therapeutic Interchange per Insurance Requirement, Alternative Option)
        1. Pharmacist to select appropriate admixture options including (as applicable) formulation, fluid base type, volume, concentration, administer-over time, and rate according to the package insert, drug information references, and facility policies, procedures, and practice standards.

Table 2: Therapeutic Interchange per Insurance Requirement, Alternative Options

OHSU ESA CPA Preferred	Dosing	
	Absolute Iron Deficiency	Functional Iron Deficiency
Iron Dextran	1000 mg IV	500 mg IV
Insurance Required Formulation	Alternative Dosing	
	Absolute Iron Deficiency	Function Iron Deficiency
Iron Sucrose (Venofer)	300 mg IV x3 doses (every 2-3 days)	200 mg IV x2 doses (every 2-3 days)
Ferumoxytol (Feraheme)	510 mg IV x2 doses (repeat dose 3-8 days after initial dose)	510 mg IV x1 dose
Ferric Carboxymaltose (Injectafer)	Weight ≥ 50 kg	
	750 mg IV x2 doses at least 7 days apart	750 mg IV x1 dose
	Weight < 50 kg	
	15 mg/kg IV x2 doses at least 7 days apart	15 mg/kg IV x1 dose

2. Anemia due to CKD Stage III-IV CKD (non-dialysis), Post-Renal Transplant Treatment Algorithm:

a. Special Populations
   i. Patients on hemodialysis will be managed in dialysis and deferred to provider. Clinic pharmacist will not be involved in dosing adjustments or monitoring.

b. Contraindications
   i. SBP > 180 mm Hg
   ii. DBP > 100 mm Hg

c. Initiation
   i. Requirements
      1. Kidney transplant or simultaneous kidney pancreas transplant recipient
      2. Persistent anemia with hemoglobin < 9 g/dL or hematocrit below 27% since transplant
      3. eGFR < 60 mL/min/1.73 m^2
      4. Iron studies (within 2 months)
         a. Ferritin ≥ 100 ng/mL
         b. TSAT ≥ 20%
      5. Recent CBC (within 7 days prior to initiation)
   ii. If initiation requirements not met with first appointment, pharmacist will contact referring provider and ESA pharmacist to assess if future appointments are needed

b. Dosing
   i. Darbepoetin alfa
      1. ≥60 kg: Darbepoetin alfa 40 mcg subcutaneously once weekly for 3 doses
      2. < 60 kg: Darbepoetin alfa 25 mcg subcutaneously once weekly for 3 doses
      3. Referring provider (including credentialed transplant pharmacist) may order different dose based on patient specific factors and clinical assessment.

d. Monitoring
   i. CBC (hemoglobin, hematocrit)
      1. With transplant labs, twice weekly for 1-month post-transplant followed by weekly
   ii. Iron studies (serum iron, TIBC, TSAT, ferritin)
      1. Prior to initiation of therapy unless available from previous 2 months
      2. Monthly

e. Maintenance Dosing Considerations
   i. Hold darbepoetin-alfa at any time if:
      1. Hemoglobin ≥ 11 g/dL
      2. HCT ≥ 33%
      3. If maintenance requirements not met, pharmacist will discontinue infusion plan and contact the referring provider and ESA consult pharmacist to get future appointments cancelled.
   ii. Infusion pharmacist will not assess for dose adjustments.
   iii. Referring provider may extended doses past 3 treatments if Hgb goal not met.

3. Symptomatic anemia due to MDS Treatment Algorithm:

a. CMS Approved Criteria
    i. Symptomatic anemia due to MDS
b. Special Populations
    i. MDS/MPN overlap syndromes are recognized by WHO as 5 different clonal subtypes or diseases and an ESA treatment algorithm is not uniformly adopted. In these cases, the CPA will use the MDS ESA treatment algorithm to dose ESAs. In cases where GCSF is warranted, the pharmacist will contact the primary oncologist for appropriateness.
    ii. MDS/MPN overlap syndromes subtypes JMML and aCML are excluded from this algorithm per previously defined exclusion criteria (pediatric and CMS non-approved criteria respectively)
c. Contraindications
    i. SBP > 180 mm Hg
    ii. DBP > 100 mm Hg
d. Initiation
    i. Requirements
        1. Diagnosis of MDS
            a. On bone marrow biopsy
        2. Rule out of AML
            a. Marrow blast < 5%
        3. Life expectancy > 3 months
        4. Symptomatic anemia
            a. Fatigue, weakness, shortness of breath, lightheadedness, dizziness, cold hands and feet
        5. Currently NOT receiving chemotherapy – if so refer to chemotherapy induced anemia
        6. Hgb < 10 g/dL (within 1 week of initiation)
        7. Erythropoietin level < 500 mU/mL (within 1 month of initiation)
        8. Iron studies (within 3 months of initiation)
            a. Ferritin ≥ 100 ng/ml
            b. Iron saturation ≥ 20%
e. Initiation Dose (Dose level 0, week 0)
    i. Darbepoetin alfa
        1. ≥ 60 kg: 300 mcg subcutaneously every 2 weeks
        2. < 60 kg: 200 mcg subcutaneously every 2 weeks
    ii. Epoetin alfa-epbx
        1. ≥ 60 kg: 40,000 units subcutaneously once weekly
        2. < 60 kg: 24,000 units subcutaneously once weekly
f. Monitoring
    i. Hemoglobin & Hematocrit
        1. Once weekly for epoetin alfa-epbx (within 72 hours of maintenance dosing)
        2. Every 2 weeks for darbepoetin alfa (within 72 hours of maintenance dosing)
    ii. Iron studies
        1. Baseline and every 3 month

iii. Transfusion requirement

g. Maintenance Dose Considerations:
   i. Assess changes in Hgb and make dose adjustments as detailed below (see table 3: Symptomatic anemia due to MDS for quick reference)
   ii. For patients being treated under a prior authorization and dose increase indicated: pharmacy will verify current dose level and place increased dose level in treatment plan for future visit and request a new authorization
   iii. For dosing levels, reference Table 5: ESA Darbepoetin and Epoetin simplified dosing weight stratified (sect: RELATED DOCUMENTS/EXTERNAL LINKS pg 17-19)
   iv. Only continue if Hgb remains < 12 g/dL
   v. If Hgb ≥ 12 g/dL hold therapy
      1. Re-check Hgb and reinitiate when Hgb < 10 g/dL
      2. When reinitiating, decrease dose to next dose level (e.g. dose level 0 reduce to dose level -1
   vi. Dose adjustments
      1. In any 2 week increment at current dose level:
         a. Hgb increase > 1g/dL
            i. Decrease dose to next dose level (e.g. dose level 0 decrease to dose level -1)
         b. Hgb increase ≤ 1 g/dL
            i. Maintain dose
      2. If in any 4 week increment at current dose level:
         a. Do not increase dose more frequently than once every 4 weeks
         b. Decrease indicated in most-recent 2-week interval as above
            i. Decrease dose as above
            ii. No increase assessment at 4-week interval
         c. Hgb increase ≥ 1g/dL
            i. Maintain dose
         d. Hgb increases < 1 g/dL
            i. Hgb < 10 g/dL
               1. Increase dose to next dose level (e.g. dose level 0 increase to dose level 1)
            ii. Hgb 10-12 g/dL
               1. Maintain dose
   vii. If dosing interrupted for iron administration or missed appointments, resume dose at most recent previous dose given
   viii. And By week 12 after initiation, if increase in Hgb < 1.5 g/dL, Hgb < 10 g/dL, or no decrease in transfusion needs, contact provider to recommend adding GCSF 300 mcg 1-3x per week
   ix. By week 16 after initiation, if increase in Hgb < 1.5 g/dL, or unable to reach target Hgb of 10-12 g/dL
      1. Maintain lowest dose to avoid transfusions
      2. If no improvement in transfusion needs, discontinue ESA (and GCSF if initiated)

Table 3: Symptomatic anemia due to MDS Quick Reference

Hgb	ESA Dose Adjustments	
Initiation dose (Dose level 0, week 0)		
if Hgb < 10 g/dL	**Give corresponding dose at level 0 for week 0**	
Maintenance Dosing (week 2 onward)		
If Hgb ≥ 12 g/dL at **ANY time**	HOLD dose, pt follow up at regular interval	
Is Hgb 10 g/dL-12 g/dL?	YES	Maintain dose
	NO	See below
If Hgb < 11 g/dL		
ESA previously held for Hgb ≥ 12 g/dL ?	YES	Resume at one decreased dose level (ex: dose level –1)
	NO	See below
Assess Hgb change for most recent **2-week interval** at CURRENT dose level (ex: week 2 to week 4)		
Did the Hgb increase > 1g/dL?	YES	Decrease by one dose level (ex: dose level –1) do NOT assess 4-week dosing interval.
	NO	See below
Did Hgb increase ≤ 1 g/dL ?	• If at current dose for < 4 weeks => maintain current dose • If at current dose ≥ 4 weeks => assess 4-week interval below	
Assess Hgb change for most recent **4-week interval** at CURRENT dose level (ex: week 0 to week 4) <u>(Do not increase the dose more frequently than once every 4 weeks)</u>		
Did the Hgb increase ≥ 1 g/dL?	YES	Maintain dose
	NO	See below
If Hgb < 10 g/dL		
Did Hgb increase < 1 g/dL ?	Increase by one dose level (ex: dose level +1)	
<u>By week 12 after initiation:</u> if increase in Hgb < 1.5 g/dL, Hgb < 10 g/dL, or no decrease in transfusion needs, contact provider to recommend adding GCSF 300 mcg 1-3x per week		

4. Chemotherapy Induced Anemia Treatment Algorithm:

a. CMS Approved Criteria
    i. Anemia secondary to myelosuppressive anticancer chemotherapy in solid tumors, multiple myeloma, lymphoma, lymphocytic leukemia
b. Contraindications
    i. SBP > 180 mm Hg
    ii. DBP > 100 mm Hg
c. Initiation Requirements
    i. Must have received myelosuppressive chemotherapy in the last 8 weeks
    ii. Minimum of 2 additional months of planned myelosuppressive chemotherapy
    iii. Anemia cannot be managed by transfusion
    iv. Intent of chemotherapy treatment is palliative
    v. Hgb < 10 g/dL or Hct <30% (within 1 week of initiation)
    vi. Iron studies (within 3 months of initiation)
        1. Ferritin ≥ 100 ng/mL
        2. Iron saturation ≥ 20%
d. Initiation Dose (Dose level 0, week 0)
    i. Darbepoetin alfa
        1. ≥ 60 kg: 300 mcg subcutaneously every 2 weeks
        2. < 60 kg: 200 mcg subcutaneously every 2 weeks
    ii. Epoetin alfa-epbx
        1. ≥ 60 kg: 40,000 units subcutaneously once weekly
        2. < 60 kg: 24,000 units subcutaneously once weekly
e. Monitoring
    i. Hemoglobin & Hematocrit
        1. Once weekly for epoetin alfa-epbx (within 72 hours of maintenance)
        2. Every 2 weeks for darbepoetin alfa (within 72 hours of maintenance)
    ii. Iron studies
        1. Baseline and every 3 months
    iii. Transfusion requirement
f. Maintenance Dose Considerations
    i. Assess changes in Hgb and make dose adjustments as detailed below (see table 4: Table 4: Chemotherapy Induced Anemia for quick reference)
    ii. For patients being treated under a prior authorization and dose increase indicated: pharmacy will verify current dose level and place increased dose level in treatment plan for future visit and request a new authorization
    iii. For dosing levels, reference Table 5: ESA Darbepoetin and Epoetin simplified dosing weight stratified (sect: RELATED DOCUMENTS/EXTERNAL LINKS pg 17-19)
    iv. Only continue if Hgb remains < 10 g/dL
    v. If Hgb ≥ 10 g/dl hold therapy
        1. Re-check Hgb and reinitiate when Hgb < 10 g/dL

2. When reinitiating, decrease dose to next dose level (e.g. dose level 0 reduce to dose level -1)

vi. Dose adjustments
   1. In any 2 week increment at current dose level:
      a. Hgb increase > 1g/dL
         i. Decrease dose to next dose level (e.g. dose level 0 decrease to dose level -1)
      b. Hgb increase ≤ 1 g/dL
         i. Maintain dose
   2. If in any 4 week increment at current dose level:
      a. Do not increase dose more frequently than once every 4 weeks
      b. Decrease indicated in most-recent 2-week interval as above
         i. Decrease dose as above
         ii. No increase assessment at 4-week interval
      c. Hgb increase ≥ 1g/dL
         i. Maintain dose
      d. Hgb increases < 1 g/dL
         i. Increase dose to next dose level (e.g. dose level 0 increase to dose level 1)

g. If dosing interrupted for iron administration or missed appointments, resume dose at most recent previous dose given

h. If dosing interrupted for iron administration or missed appointments, resume dose at most recent previous dose given

i. By week 8 after initiation, if increase in Hgb < 1 g/dL or Hgb < 10 g/dL:
   i. Maintain lowest dose to avoid transfusions
   ii. If no improvement in transfusion needs, discontinue ESA
   iii. Discontinue on completion of chemotherapy

Table 4: Chemotherapy Induced Anemia Quick Reference

Hgb		**ESA Dose Adjustments**
if Hgb ≥ 10 g/dL at **ANY time**		HOLD dose, pt follow up at regular interval
Initiation dose (Dose level 0, week 0)		
if Hgb < 10 g/dL		**Give corresponding dose at level 0 for week 0**
Maintenance Dosing (week 2 onward)		
If Hgb < 10 g/dL		
ESA previously held for Hgb ≥ 10 g/dL ?	YES	Resume at one decreased dose level (ex: dose level –1)
	NO	See below
Assess Hgb change for most recent **2-week interval** at CURRENT dose level (ex: week 2 to week 4)		
Did the Hgb increase > 1g/dL?	YES	Decrease by one dose level (ex: dose level –1) do NOT assess 4-week dosing interval.
	NO	See below
Did Hgb increase ≤ 1 g/dL ?		• If at current dose for < 4 weeks => maintain current dose • If at current dose ≥ 4 weeks => assess 4-week interval below
Assess Hgb change for most recent **4-week interval** at CURRENT dose level (ex: week 0 to week 4) (Do not increase the dose more frequently than once every 4 weeks)		
Did the Hgb increase ≥ 1 g/dL?	YES	Maintain dose
	NO	See below
Did Hgb increase < 1 g/dL ?		Increase by one dose level (ex: dose level +1)

5. Perioperative Allogeneic Red Blood Cell Transfusion Reduction Treatment Algorithm:

a. CMS Approved Criteria

i. elective, noncardiac, nonvascular surgery

b. Contraindications
   i. SBP > 180 mm Hg
   ii. DBP > 100 mmHg
c. Initiation Requirements
   i. Surgery must be elective, noncardiac, and nonvascular
   ii. Patient must be unwilling to donate autologous blood
   iii. Perioperative Hgb >10 g/dL and ≤ 13 g/dL
   iv. Iron studies (within 1 month of initiation)
      1. Ferritin ≥ 100 ng/mL
      2. Iron saturation ≥ 20%
d. Dosing
   i. Epoetin alfa <u>weekly</u>
      1. ≥ 60 kg: 40,000 units subcutaneously once weekly for 3 doses beginning 3 weeks prior to procedure (approximately 3 weeks, 2 weeks, and 1 week prior)
      2. < 60 kg: 30,000 units subcutaneously once weekly 3 doses beginning 3 weeks prior to procedure (approximately 3 weeks, 2 weeks, and 1 week prior)
e. Monitoring
   i. Hemoglobin & Hematocrit
      1. Once weekly for epoetin alfa-epbx
f. Maintenance Dosing Considerations
   i. Treatment Parameters for 2 weeks and 1 week prior to surgery
   ii. Only continue if Hgb remains < 14 g/dL
   iii. If Hgb ≥ 14 g/dL hold therapy
   iv. <u>If maintenance dosing requirements not met, pharmacist will discontinue infusion plan and contact the referring provider and ESA consult pharmacist to get future appointments cancelled.</u>

RELATED DOCUMENTS/EXTERNAL LINKS:

Table 5: ESA Darbepoetin and Epoetin simplified dosing weight stratified

Darbepoetin								
Indication	**Weight**	**Dose Level 0 (Starting Dose)**	**Dose Decrease**		**Dose Increase**			
			Dose level -1	**Dose level -2**	**Dose level +1**	**Dose level +2**	**Adjunctive agent**	**Notes**
MDS	≥ 60 kg (or flat dose)	300 mcg every 2 weeks	200 mcg every 2 weeks	150 mcg every 2 weeks	400 mcg every 2 weeks	500 mcg every 2 weeks	By week 12 if no response, contact provider to add GCSF 300 mcg 1-3x per week	By week 16 if no increase in Hgb by 1.5 or reach target of 10-12 g/dL or decrease in transfusion needs discontinue
	< 60 kg	200 mcg every 2 weeks	150 mcg every 2 weeks	100 mcg every 2 weeks	300 mcg every 2 weeks	400 mcg every 2 weeks		
Chemo induced	≥ 60 kg (or flat dose)	300 mcg every 2 weeks	200 mcg every 2 weeks	150 mcg every 2 weeks	400 mcg every 2 weeks			By week 8 if no improvement in Hgb, maintain lowest dose to avoid transfusions, if no improvement in transfusion requirements discontinue
	< 60 kg	200 mcg every 2 weeks	150 mcg every 2 weeks	100 mcg every 2 weeks	300 mcg every 2 weeks			
CKD (no HD)	≥ 60 kg (or flat dose)	40 mcg every 4 weeks	25 mcg every 4 weeks	20 mcg every 4 weeks	60 mcg every 4 weeks	80 mcg every 4 weeks		By week 12 if no improvement in Hgb, maintain lowest dose to avoid transfusions, if no improvement in transfusion requirements discontinue
	< 60 kg	25 mcg every 4 weeks	20 mcg every 4 weeks	12.5 mcg every 4 weeks	40 mcg every 4 weeks	60 mcg every 4 weeks		
Post-renal transplant (no HD)	≥ 60 kg	40 mcg weekly for 3 doses	HOLD if Hemoglobin ≥ 11 g/dL OR HCT ≥ 33%		Per discussion with transplant nephrology attending			
	< 60 kg	25 mcg weekly for 3 doses	HOLD if Hemoglobin ≥ 11 g/dL OR HCT ≥ 33%					

Epoetin								
Indication	**Weight**	**Dose level 0 (Starting Dose)**	**Dose Decrease**		**Dose Increase**			
			Dose level -1	**Dose level -2**	**Dose level +1**	**Dose level +2**	**Adjunctive agent**	**Notes**
MDS	≥ 60 kg (or flat dose)	40,000 units weekly	30,000 units weekly	22,000 units weekly	50,000 units weekly	60,000 units weekly	By week 12 if no response, contact provider to add GCSF 300 mcg 1-3x per week	By week 16 if no increase in Hgb by 1.5 or reach target of 10-12 g/dL or decrease in transfusion needs discontinue
	< 60 kg	24,000 units weekly	18,000 units weekly	14,000 units weekly	40,000 units weekly	60,000 units weekly		
Chemo induced	≥ 60 kg (or flat dose)	40,000 units weekly	30,000 units weekly	22,000 units weekly	60,000 units weekly			By week 8 if no improvement in Hgb, maintain lowest dose to avoid transfusions, if no improvement in transfusion requirements discontinue
	< 60 kg	24,000 units weekly	18,000 units weekly	14,000 units weekly	40,000 units weekly			
CKD (no HD)	≥ 60 kg (or flat dose)	20,000 units every 2 weeks	14,000 units every 2 weeks	10,000 units every 2 weeks	24,000 units every 2 weeks	30,000 units every 2 weeks		By week 12 if no improvement in Hgb, maintain lowest dose to avoid transfusions, if no improvement in transfusion requirements discontinue
	< 60 kg	10,000 units every 2 weeks	8,000 units every 2 weeks	6,000 units every 2 weeks	12,000 units every 2 weeks	16,000 units every 2 weeks		

APPENDIX:

I. ICD-10 Dx Description ESA in Cancer

ICD-10 CM	ICD-10 DX Description
C92.00	Acute myeloblastic leukemia, not having achieved remission
C92.40	Acute promyelocytic leukemia, not having achieved remission
C92.50	Acute myelomonocytic leukemia, not having achieved remission
C92.60	Acute myeloid leukemia with 11q23-abnormality not having achieved remission
C92.A0	Acute myeloid leukemia with multilineage dysplasia, not having achieved remission
C92.01	Acute myeloblastic leukemia, in remission
C92.41	Acute promyelocytic leukemia, in remission
C92.51	Acute myelomonocytic leukemia, in remission
C92.61	Acute myeloid leukemia with 11q23-abnormality in remission
C92.A1	Acute myeloid leukemia with multilineage dysplasia, in remission
C92.02	Acute myeloblastic leukemia, in relapse
C92.42	Acute promyelocytic leukemia, in relapse
C92.52	Acute myelomonocytic leukemia, in relapse
C92.62	Acute myeloid leukemia with 11q23-abnormality in relapse
C92.A2	Acute myeloid leukemia with multilineage dysplasia, in relapse
C92.10	Chronic myeloid leukemia, BCR/ABL-positive, not having achieved remission
C92.11	Chronic myeloid leukemia, BCR/ABL-positive, in remission
C92.12	Chronic myeloid leukemia, BCR/ABL-positive, in relapse
C92.20	Atypical chronic myeloid leukemia, BCR/ABL-negative, not having achieved remission
C92.21	Atypical chronic myeloid leukemia, BCR/ABL-negative, in remission
C92.Z0	Other myeloid leukemia not having achieved remission
C92.Z1	Other myeloid leukemia, in remission
C92.Z2	Other myeloid leukemia, in relapse
C92.90	Myeloid leukemia, unspecified, not having achieved remission
C92.91	Myeloid leukemia, unspecified in remission
C94.00	Acute erythroid leukemia, not having achieved remission
C94.01	Acute erythroid leukemia, in remission
C94.02	Acute erythroid leukemia, in relapse
C94.20	Acute megakaryoblastic leukemia not having achieved remission
C94.21	Acute megakaryoblastic leukemia, in remission
C94.22	Acute megakaryoblastic leukemia, in relapse
C94.30	Mast cell leukemia not having achieved remission
C94.80	Other specified leukemias not having achieved remission
C94.31	Mast cell leukemia, in remission
C94.81	Other specified leukemias, in remission
D45	Polycythemia vera
D50.0	Iron deficiency anemia secondary to blood loss (chronic)
D50.8	Other iron deficiency anemias
D50.1	Sideropenic dysphagia
D50.9	Iron deficiency anemia, unspecified
D51.0	Vitamin B12 deficiency anemia due to intrinsic factor deficiency

D51.1	Vitamin B12 deficiency anemia due to selective vitamin B12 malabsorption with proteinuria
D51.2	Transcobalamin II deficiency
D51.3	Other dietary vitamin B12 deficiency anemia
D51.8	Other vitamin B12 deficiency anemias
D51.9	Vitamin B12 deficiency anemia, unspecified
D52.0	Dietary folate deficiency anemia
D52.1	Drug-induced folate deficiency anemia
D52.8	Other folate deficiency anemias
D52.9	Folate deficiency anemia, unspecified
D53.1	Other megaloblastic anemias, not elsewhere classified
D58.0	Hereditary spherocytosis
D55.0	Anemia due to glucose-6-phosphate dehydrogenase [G6PD] deficiency
D55.1	Anemia due to other disorders of glutathione metabolism
D58.9	Hereditary hemolytic anemia, unspecified
D59.0	Drug-induced autoimmune hemolytic anemia
D59.10	Autoimmune hemolytic anemia, unspecified
D59.11	Warm autoimmune hemolytic anemia
D59.12	Cold autoimmune hemolytic anemia
D59.13	Mixed type autoimmune hemolytic anemia
D59.19	Other autoimmune hemolytic anemia
D59.4	Other nonautoimmune hemolytic anemias
D59.2	Drug-induced nonautoimmune hemolytic anemia
D59.5	Paroxysmal nocturnal hemoglobinuria [Marchiafava-Micheli]
D59.6	Hemoglobinuria due to hemolysis from other external causes
D59.8	Other acquired hemolytic anemias
D59.9	Acquired hemolytic anemia, unspecified
D60.0	Chronic acquired pure red cell aplasia
D60.1	Transient acquired pure red cell aplasia
D60.8	Other acquired pure red cell aplasias
D60.9	Acquired pure red cell aplasia, unspecified
D61.01	Constitutional (pure) red blood aplasia
D61.09	Other constitutional aplastic anemia
D61.2	Aplastic anemia due to other external agents
D61.3	Idiopathic aplastic anemia
D61.810	Antineoplastic chemotherapy induced pancytopenia
D61.811	Other drug-induced pancytopenia
D61.818	Other pancytopenia
D61.82	Myelophthisis
D61.89	Other specified aplastic anemias and other bone marrow failure syndromes
D61.9	Aplastic anemia, unspecified
D62	Acute posthemorrhagic anemia
D63.0	Anemia in neoplastic disease
D64.0	Hereditary sideroblastic anemia

D64.1	Secondary sideroblastic anemia due to disease
D64.2	Secondary sideroblastic anemia due to drugs and toxins
D64.3	Other sideroblastic anemias
D64.9	Anemia, unspecified
D73.1	Hypersplenism
E53.1	Pyrioxine deficiency
T45.1X5A	Adverse effect of antineoplastic and immunosuppresive drugs, initial encounter

TRAINING/COMPETENCIES:

1. Complete CPA competency
2. Complete Clinical Pharmacy Agreement: Erythropoietin Stimulating Agents privileging checklist prior to provisioning services as described in this CPA

QUALITY ASSURANCE:

1. Peer review of 1-5 charts every 12 months will be conducted with a standard peer review form to assess the quality of the clinical pharmacist's encounters.

RELEVANT REFERENCES:

Policy # HC-CKT-131-POL "Erythropoiesis Stimulating Agents Use Restriction and Dosing Policy in the Ambulatory Setting"
Policy #HC-PHR-149-POL "Pharmacist review of prescriptions and medication orders"

1. Gafter-Gvili A, Schechter A, Rozen-Zvi B. Iron deficiency anemia in chronic kidney disease. *Acta Haematol*. 2019;142(1):44-50.
2. International Society of Nephrology. KDIGO Clinical Practice Guideline for Anemia in Chronic Kidney Disease. 2012. 2(4) 279-335.

TITLE, POLICY OWNER:

Department of Pharmacy Services

APPROVING COMMITTEE(S):

Clotting Anticoagulation Transfusion Committee
Clinical Knowledge and Therapeutics Executive Committee

FINAL APPROVAL:

Clinical Knowledge and Therapeutics Executive Committee