Erythropoietic Agents

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Instructions for Use

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Related Policies

- N/A

Coverage Rationale

This policy refers to the following erythropoietic agents:

- Aranesp® (darbepoetin alfa)
- Epogen® (epoetin alfa)
- Mircera® (methoxy polyethylene glycol-epoetin beta)
- Procrit® (epoetin alfa)

Anemia Due to Chronic Kidney Disease (CKD)

For initial coverage of Aranesp, Epogen, or Procrit for Anemia Due to Chronic Kidney Disease (CKD), the following will be required:

- Diagnosis of chronic kidney disease (CKD) **and**
- Verification of iron evaluation for adequate iron stores **and**
- Verification of anemia as defined by one of the following laboratory values collected within 30 days of the request:
    - Hematocrit (Hct) less than 30%
    - Hemoglobin (Hgb) less than 10 g/dL **and**
- One of the following:
    - Patient is on dialysis **or**
    - All of the following:
        - Patient is NOT on dialysis **and**
        - The rate of hemoglobin decline indicates the likelihood of requiring a red blood cell (RBC) transfusion **and**
        - Reducing the risk of alloimmunization and/or other RBC transfusion-related risks is a goal

For initial coverage of Mircera for Anemia Due to Chronic Kidney Disease (CKD), the following will be required:

- Diagnosis of chronic kidney disease (CKD) **and**
- Verification of iron evaluation for adequate iron stores **and**
- One of the following:
    - All of the following:
        - Patient is greater than or equal to 18 years of age **and**
        - Verification of anemia as defined by one of the following laboratory values collected within 30 days of the request:
            - Hematocrit (Hct) less than 30%
            - Hemoglobin (Hgb) less than 10 g/dL **and**
        - One of the following:
            - Patient is on dialysis **or**
            - All of the following**:**
                - Patient is NOT on dialysis **and**
                - The rate of hemoglobin decline indicates the likelihood of requiring a red blood cell (RBC) transfusion **and**
                - Reducing the risk of alloimmunization and/or other RBC transfusion-related risks is a goal **or**
    - All of the following:
        - Patient is between 3 months and 17 years of age **and**
        - Patient's hemoglobin level has been stabilized by treatment with another erythropoietin stimulating agent (ESA) (e.g., Aranesp, Retacrit) **and**
        - Patient is converting to Mircera from another ESA (e.g., Aranesp, Retacrit)

For reauthorization coverage of Aranesp, Epogen, Mircera or Procrit for Anemia Due to Chronic Kidney Disease (CKD), the following will be required:

- Diagnosis of chronic kidney disease (CKD) **and**
- One of the following:
    - Both of the following:
        - Patient is on dialysis
        - Most recent or average Hct over 3 months is 33% or less (Hgb 11 g/dL or less) **or**
    - Both of the following:
        - Patient is not on dialysis
        - Most recent or average (avg) Hct over 3 months is 30% or less (Hgb 10 g/dL or less) **or**
    - Both of the following:
        - Request is for a pediatric patient
        - Most recent or average Hct over 3 months is 36% or less (Hgb 12 g/dL or less) **and**
- One of the following:
    - Decrease in the need for blood transfusion **or**
    - Hemoglobin (Hgb) increased greater than or equal to 1g/dL from pre-treatment level **and**
- Verification of iron evaluation for adequate iron stores

Anemia in Patients with HIV-infection

For initial coverage of Epogen or Procrit for Anemia in Patients with HIV-infection, the following will be required:

- Verification of iron evaluation for adequate iron stores **and**
- Verification of anemia as defined by one of the following laboratory values collected within 30 days of the request:

    - Hemoglobin (Hgb) less than 12 g/dL
    - Hematocrit (Hct) less than 36% **and**
- Serum erythropoietin level less than or equal to 500 mU/mL **and**
- One of the following:
    - Patient is receiving zidovudine therapy **or**
    - Diagnosis of HIV infection [off-label]

For reauthorization coverage of Epogen and Procrit for Anemia in Patients with HIV-infection, the following will be required:

- Verification of anemia as defined by one of the following:
    - Most recent or average hematocrit (Hct) over a 3-month period was below 36%
    - Most recent or average hemoglobin (Hgb) over a 3-month period was below 12 g/dL **and**
- One of the following:
    - Decrease in the need for blood transfusion **or**
    - Hemoglobin (Hgb) increased greater than or equal to 1g/dL from pre-treatment level.

Anemia Due to Chemotherapy in Patients with Cancer

For initial coverage of Aranesp, Epogen, and Procrit for Anemia Due to Chemotherapy in Patients with Cancer, the following will be required:

- Verification that other causes of anemia have been ruled out **and**
- Verification of anemia as defined by one of the following laboratory values collected within the prior two weeks of the request:
    - Hematocrit (Hct) less than 30%
    - Hemoglobin (Hgb) less than 10 g/dL **and**
- Verification of iron evaluation for adequate iron stores **and**
- Verification that the cancer is a non-myeloid malignancy **and**
- Patient is receiving chemotherapy.

For reauthorization coverage of Aranesp, Epogen, or Procrit for Anemia Due to Chemotherapy in Patients with Cancer, the following will be required:

- Verification of anemia as defined by one of the following laboratory values collected within the prior two weeks of the request:
    - Hemoglobin (Hgb) less than 10 g/dL
    - Hematocrit (Hct) less than 30% **and**
- One of the following:
    - Decrease in the need for blood transfusion **or**
    - Hemoglobin (Hgb) increased greater than or equal to 1 g/dL from pre-treatment level **and**
- Patient is receiving chemotherapy.

Preoperative use for reduction of allogeneic blood transfusion in patients undergoing surgery

For initial coverage of Epogen or Procrit for Preoperative use for reduction of allogeneic blood transfusion in patients undergoing surgery, the following will be required:

- Patient is scheduled to undergo elective, non-cardiac, non-vascular surgery **and**
- Hemoglobin (Hgb) is greater than 10 to less than or equal to 13 g/dL **and**
- Patient is at high risk for perioperative transfusions **and**
- Patient is unwilling or unable to donate autologous blood pre-operatively **and**
- Verification of iron evaluation for adequate iron stores

Anemia in Myelodysplastic Syndrome (MDS) patients [off-label]

For initial coverage of Aranesp, Epogen or Procrit for Anemia in Myelodysplastic Syndrome (MDS) patients, the following will be required:

- Diagnosis of Myelodysplastic Syndrome (MDS) **and**
- One of the following:
  - Serum erythropoietin level less than or equal to 500 mU/mL
  - Diagnosis of transfusion-dependent MDS **and**
- Verification of iron evaluation for adequate iron stores

For reauthorization coverage of Aranesp, Epogen and Procrit for Anemia in Myelodysplastic Syndrome (MDS) patients [off-label], the following will be required:

- Verification of anemia as defined by one of the following:
  - Most recent or average hematocrit (Hct) over a 3-month period was less than or equal to 36%
  - Most recent or average hemoglobin (Hgb)over a 3-month period was less than or equal to 12 g/dL **and**
- One of the following:
  - Decrease in the need for blood transfusion **or**
  - Hemoglobin (Hgb) increased greater than or equal to 1 g/dL from pre-treatment level.

Anemia in HCV-infected patients due to ribavirin in combination with interferon or peg-interferon

For initial coverage of Epogen or Procrit for Anemia in HCV-infected patients due to ribavirin in combination with interferon or peg-interferon, the following will be required:

- Diagnosis of hepatitis C viral (HCV) infection **and**
- Verification of iron evaluation for adequate iron stores **and**
- Verification of anemia as defined by one of the following laboratory values collected within 30 days of the request:
  - Hematocrit (Hct) less than 36%
  - Hemoglobin (Hgb) less than 12 g/dL **and**
- Verification of both of the following:
  - Patient is receiving ribavirin **and**
  - Patient is receiving one of the following:
    - interferon alfa-2b
    - interferon alfacon-1
    - peginterferon alfa-2b
    - peginterferon alfa-2a

For reauthorization coverage of Epogen or Procrit for Anemia in HCV-infected patients due to ribavirin in combination with interferon or peg-interferon, the following will be required:

- Verification of anemia as defined by one of the following:
  - Most recent or average hematocrit (Hct) over a 3-month period was 36% or less
  - Most recent or average hemoglobin (Hgb) over a 3-month period was 12 g/dL or less **and**
- One of the following:
  - Decrease in the need for blood transfusion **or**
  - Hemoglobin (Hgb) increased greater than or equal to 1 g/dL from pre-treatment level.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J0881	Injection, darbepoetin alfa, 1 mcg (non-ESRD use)
J0882	Injection, darbepoetin alfa, 1 mcg (for ESRD on dialysis)
J0885	Injection, epoetin alfa, (for non-ESRD use), 1000 units
J0887	Injection, epoetin beta, 1 microgram, (for ESRD on dialysis)
J0888	Injection, epoetin beta, 1 microgram, (for non-ESRD use)
Q4081	Injection, epoetin alfa, 100 units (for ESRD on dialysis)

ICD-10 Code	Description
B20	Human immunodeficiency virus [HIV] disease
B97.35	Human immunodeficiency virus, type 2 [HIV 2] as the cause of diseases classified elsewhere
C00.0	Malignant neoplasm of external upper lip
C00.1	Malignant neoplasm of external lower lip
C00.2	Malignant neoplasm of external lip, unspecified
C00.3	Malignant neoplasm of upper lip, inner aspect
C00.4	Malignant neoplasm of lower lip, inner aspect
C00.5	Malignant neoplasm of lip, unspecified, inner aspect
C00.6	Malignant neoplasm of commissure of lip, unspecified
C00.8	Malignant neoplasm of overlapping sites of lip
C01	Malignant neoplasm of base of tongue
C02.0	Malignant neoplasm of dorsal surface of tongue
C02.1	Malignant neoplasm of border of tongue
C02.2	Malignant neoplasm of ventral surface of tongue
C02.3	Malignant neoplasm of anterior two-thirds of tongue, part unspecified
C02.4	Malignant neoplasm of lingual tonsil
C02.8	Malignant neoplasm of overlapping sites of tongue
C03.0	Malignant neoplasm of upper gum
C03.1	Malignant neoplasm of lower gum
C04.0	Malignant neoplasm of anterior floor of mouth
C04.1	Malignant neoplasm of lateral floor of mouth
C04.8	Malignant neoplasm of overlapping sites of floor of mouth
C05.0	Malignant neoplasm of hard palate
C05.1	Malignant neoplasm of soft palate
C05.2	Malignant neoplasm of uvula
C05.8	Malignant neoplasm of overlapping sites of palate
C06.0	Malignant neoplasm of cheek mucosa
C06.1	Malignant neoplasm of vestibule of mouth
C06.2	Malignant neoplasm of retromolar area
C06.89	Malignant neoplasm of overlapping sites of other parts of mouth
C07	Malignant neoplasm of parotid gland

ICD-10 Code	Description
C08.0	Malignant neoplasm of submandibular gland
C08.1	Malignant neoplasm of sublingual gland
C09.0	Malignant neoplasm of tonsillar fossa
C09.1	Malignant neoplasm of tonsillar pillar (anterior) (posterior)
C09.8	Malignant neoplasm of overlapping sites of tonsil
C10.0	Malignant neoplasm of vallecula
C10.1	Malignant neoplasm of anterior surface of epiglottis
C10.2	Malignant neoplasm of lateral wall of oropharynx
C10.3	Malignant neoplasm of posterior wall of oropharynx
C10.4	Malignant neoplasm of branchial cleft
C10.8	Malignant neoplasm of overlapping sites of oropharynx
C11.0	Malignant neoplasm of superior wall of nasopharynx
C11.1	Malignant neoplasm of posterior wall of nasopharynx
C11.2	Malignant neoplasm of lateral wall of nasopharynx
C11.3	Malignant neoplasm of anterior wall of nasopharynx
C11.8	Malignant neoplasm of overlapping sites of nasopharynx
C12	Malignant neoplasm of pyriform sinus
C13.0	Malignant neoplasm of postcricoid region
C13.1	Malignant neoplasm of aryepiglottic fold, hypopharyngeal aspect
C13.2	Malignant neoplasm of posterior wall of hypopharynx
C13.8	Malignant neoplasm of overlapping sites of hypopharynx
C14.0	Malignant neoplasm of pharynx, unspecified
C14.2	Malignant neoplasm of Waldeyer's ring
C14.8	Malignant neoplasm of overlapping sites of lip, oral cavity and pharynx
C15.3	Malignant neoplasm of upper third of esophagus
C15.4	Malignant neoplasm of middle third of esophagus
C15.5	Malignant neoplasm of lower third of esophagus
C15.8	Malignant neoplasm of overlapping sites of esophagus
C16.0	Malignant neoplasm of cardia
C16.1	Malignant neoplasm of fundus of stomach
C16.2	Malignant neoplasm of body of stomach
C16.3	Malignant neoplasm of pyloric antrum
C16.4	Malignant neoplasm of pylorus
C16.5	Malignant neoplasm of lesser curvature of stomach, unspecified
C16.6	Malignant neoplasm of greater curvature of stomach, unspecified
C16.8	Malignant neoplasm of overlapping sites of stomach
C17.0	Malignant neoplasm of duodenum
C17.1	Malignant neoplasm of jejunum
C17.2	Malignant neoplasm of ileum

ICD-10 Code	Description
C17.3	Meckel's diverticulum, malignant
C17.8	Malignant neoplasm of overlapping sites of small intestine
C18.0	Malignant neoplasm of cecum
C18.1	Malignant neoplasm of appendix
C18.2	Malignant neoplasm of ascending colon
C18.3	Malignant neoplasm of hepatic flexure
C18.4	Malignant neoplasm of transverse colon
C18.5	Malignant neoplasm of splenic flexure
C18.6	Malignant neoplasm of descending colon
C18.7	Malignant neoplasm of sigmoid colon
C18.8	Malignant neoplasm of overlapping sites of colon
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
C21.1	Malignant neoplasm of anal canal
C21.2	Malignant neoplasm of cloacogenic zone
C21.8	Malignant neoplasm of overlapping sites of rectum, anus and anal canal
C22.0	Liver cell carcinoma
C22.1	Intrahepatic bile duct carcinoma
C22.2	Hepatoblastoma
C22.3	Angiosarcoma of liver
C22.4	Other sarcomas of liver
C22.7	Other specified carcinomas of liver
C22.8	Malignant neoplasm of liver, primary, unspecified as to type
C22.9	Malignant neoplasm of liver, not specified as primary or secondary
C23	Malignant neoplasm of gallbladder
C24.0	Malignant neoplasm of extrahepatic bile duct
C24.1	Malignant neoplasm of ampulla of Vater
C24.8	Malignant neoplasm of overlapping sites of biliary tract
C25.0	Malignant neoplasm of head of pancreas
C25.1	Malignant neoplasm of body of pancreas
C25.2	Malignant neoplasm of tail of pancreas
C25.3	Malignant neoplasm of pancreatic duct
C25.4	Malignant neoplasm of endocrine pancreas
C25.7	Malignant neoplasm of other parts of pancreas
C25.8	Malignant neoplasm of overlapping sites of pancreas
C26.1	Malignant neoplasm of spleen
C30.0	Malignant neoplasm of nasal cavity
C30.1	Malignant neoplasm of middle ear
C31.0	Malignant neoplasm of maxillary sinus

ICD-10 Code	Description
C31.1	Malignant neoplasm of ethmoidal sinus
C31.2	Malignant neoplasm of frontal sinus
C31.3	Malignant neoplasm of sphenoid sinus
C31.8	Malignant neoplasm of overlapping sites of accessory sinuses
C32.0	Malignant neoplasm of glottis
C32.1	Malignant neoplasm of supraglottis
C32.2	Malignant neoplasm of subglottis
C32.3	Malignant neoplasm of laryngeal cartilage
C32.8	Malignant neoplasm of overlapping sites of larynx
C33	Malignant neoplasm of trachea
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
C37	Malignant neoplasm of thymus
C38.0	Malignant neoplasm of heart
C38.1	Malignant neoplasm of anterior mediastinum
C38.2	Malignant neoplasm of posterior mediastinum
C38.4	Malignant neoplasm of pleura
C38.8	Malignant neoplasm of overlapping sites of heart, mediastinum and pleura
C40.01	Malignant neoplasm of scapula and long bones of right upper limb
C40.02	Malignant neoplasm of scapula and long bones of left upper limb
C40.11	Malignant neoplasm of short bones of right upper limb
C40.12	Malignant neoplasm of short bones of left upper limb
C40.21	Malignant neoplasm of long bones of right lower limb
C40.22	Malignant neoplasm of long bones of left lower limb
C40.31	Malignant neoplasm of short bones of right lower limb
C40.32	Malignant neoplasm of short bones of left lower limb
C40.81	Malignant neoplasm of overlapping sites of bone and articular cartilage of right limb
C40.82	Malignant neoplasm of overlapping sites of bone and articular cartilage of left limb
C41.0	Malignant neoplasm of bones of skull and face
C41.1	Malignant neoplasm of mandible
C41.2	Malignant neoplasm of vertebral column
C41.3	Malignant neoplasm of ribs, sternum and clavicle

ICD-10 Code	Description
C41.4	Malignant neoplasm of pelvic bones, sacrum and coccyx
C43.0	Malignant melanoma of lip
C43.111	Malignant melanoma of right upper eyelid, including canthus
C43.112	Malignant melanoma of right lower eyelid, including canthus
C43.121	Malignant melanoma of left upper eyelid, including canthus
C43.122	Malignant melanoma of left lower eyelid, including canthus
C43.21	Malignant melanoma of right ear and external auricular canal
C43.22	Malignant melanoma of left ear and external auricular canal
C43.31	Malignant melanoma of nose
C43.39	Malignant melanoma of other parts of face
C43.4	Malignant melanoma of scalp and neck
C43.51	Malignant melanoma of anal skin
C43.52	Malignant melanoma of skin of breast
C43.59	Malignant melanoma of other part of trunk
C43.61	Malignant melanoma of right upper limb, including shoulder
C43.62	Malignant melanoma of left upper limb, including shoulder
C43.71	Malignant melanoma of right lower limb, including hip
C43.72	Malignant melanoma of left lower limb, including hip
C43.8	Malignant melanoma of overlapping sites of skin
C4A.0	Merkel cell carcinoma of lip
C4A.111	Merkel cell carcinoma of right upper eyelid, including canthus
C4A.112	Merkel cell carcinoma of right lower eyelid, including canthus
C4A.121	Merkel cell carcinoma of left upper eyelid, including canthus
C4A.122	Merkel cell carcinoma of left lower eyelid, including canthus
C4A.21	Merkel cell carcinoma of right ear and external auricular canal
C4A.22	Merkel cell carcinoma of left ear and external auricular canal
C4A.31	Merkel cell carcinoma of nose
C4A.39	Merkel cell carcinoma of other parts of face
C4A.4	Merkel cell carcinoma of scalp and neck
C4A.51	Merkel cell carcinoma of anal skin
C4A.52	Merkel cell carcinoma of skin of breast
C4A.59	Merkel cell carcinoma of other part of trunk
C4A.61	Merkel cell carcinoma of right upper limb, including shoulder
C4A.62	Merkel cell carcinoma of left upper limb, including shoulder
C4A.71	Merkel cell carcinoma of right lower limb, including hip
C4A.72	Merkel cell carcinoma of left lower limb, including hip
C4A.8	Merkel cell carcinoma of overlapping sites
C44.01	Basal cell carcinoma of skin of lip
C44.02	Squamous cell carcinoma of skin of lip

ICD-10 Code	Description
C44.09	Other specified malignant neoplasm of skin of lip
C44.1121	Basal cell carcinoma of skin of right upper eyelid, including canthus
C44.1122	Basal cell carcinoma of skin of right lower eyelid, including canthus
C44.1191	Basal cell carcinoma of skin of left upper eyelid, including canthus
C44.1192	Basal cell carcinoma of skin of left lower eyelid, including canthus
C44.1221	Squamous cell carcinoma of skin of right upper eyelid, including canthus
C44.1222	Squamous cell carcinoma of skin of right lower eyelid, including canthus
C44.1291	Squamous cell carcinoma of skin of left upper eyelid, including canthus
C44.1292	Squamous cell carcinoma of skin of left lower eyelid, including canthus
C44.1321	Sebaceous cell carcinoma of skin of right upper eyelid, including canthus
C44.1322	Sebaceous cell carcinoma of skin of right lower eyelid, including canthus
C44.1391	Sebaceous cell carcinoma of skin of left upper eyelid, including canthus
C44.1392	Sebaceous cell carcinoma of skin of left lower eyelid, including canthus
C44.1921	Other specified malignant neoplasm of skin of right upper eyelid, including canthus
C44.1922	Other specified malignant neoplasm of skin of right lower eyelid, including canthus
C44.1991	Other specified malignant neoplasm of skin of left upper eyelid, including canthus
C44.1992	Other specified malignant neoplasm of skin of left lower eyelid, including canthus
C44.212	Basal cell carcinoma of skin of right ear and external auricular canal
C44.219	Basal cell carcinoma of skin of left ear and external auricular canal
C44.222	Squamous cell carcinoma of skin of right ear and external auricular canal
C44.229	Squamous cell carcinoma of skin of left ear and external auricular canal
C44.292	Other specified malignant neoplasm of skin of right ear and external auricular canal
C44.299	Other specified malignant neoplasm of skin of left ear and external auricular canal
C44.311	Basal cell carcinoma of skin of nose
C44.319	Basal cell carcinoma of skin of other parts of face
C44.321	Squamous cell carcinoma of skin of nose
C44.329	Squamous cell carcinoma of skin of other parts of face
C44.391	Other specified malignant neoplasm of skin of nose
C44.399	Other specified malignant neoplasm of skin of other parts of face
C44.41	Basal cell carcinoma of skin of scalp and neck
C44.42	Squamous cell carcinoma of skin of scalp and neck
C44.49	Other specified malignant neoplasm of skin of scalp and neck
C44.510	Basal cell carcinoma of anal skin
C44.511	Basal cell carcinoma of skin of breast
C44.519	Basal cell carcinoma of skin of other part of trunk
C44.520	Squamous cell carcinoma of anal skin
C44.521	Squamous cell carcinoma of skin of breast
C44.529	Squamous cell carcinoma of skin of other part of trunk
C44.590	Other specified malignant neoplasm of anal skin

ICD-10 Code	Description
C44.591	Other specified malignant neoplasm of skin of breast
C44.599	Other specified malignant neoplasm of skin of other part of trunk
C44.612	Basal cell carcinoma of skin of right upper limb, including shoulder
C44.619	Basal cell carcinoma of skin of left upper limb, including shoulder
C44.622	Squamous cell carcinoma of skin of right upper limb, including shoulder
C44.629	Squamous cell carcinoma of skin of left upper limb, including shoulder
C44.692	Other specified malignant neoplasm of skin of right upper limb, including shoulder
C44.699	Other specified malignant neoplasm of skin of left upper limb, including shoulder
C44.712	Basal cell carcinoma of skin of right lower limb, including hip
C44.719	Basal cell carcinoma of skin of left lower limb, including hip
C44.722	Squamous cell carcinoma of skin of right lower limb, including hip
C44.729	Squamous cell carcinoma of skin of left lower limb, including hip
C44.792	Other specified malignant neoplasm of skin of right lower limb, including hip
C44.799	Other specified malignant neoplasm of skin of left lower limb, including hip
C44.81	Basal cell carcinoma of overlapping sites of skin
C44.82	Squamous cell carcinoma of overlapping sites of skin
C44.89	Other specified malignant neoplasm of overlapping sites of skin
C45.0	Mesothelioma of pleura
C45.1	Mesothelioma of peritoneum
C45.2	Mesothelioma of pericardium
C45.7	Mesothelioma of other sites
C46.0	Kaposi's sarcoma of skin
C46.1	Kaposi's sarcoma of soft tissue
C46.2	Kaposi's sarcoma of palate
C46.3	Kaposi's sarcoma of lymph nodes
C46.4	Kaposi's sarcoma of gastrointestinal sites
C46.51	Kaposi's sarcoma of right lung
C46.52	Kaposi's sarcoma of left lung
C46.7	Kaposi's sarcoma of other sites
C47.0	Malignant neoplasm of peripheral nerves of head, face and neck
C47.11	Malignant neoplasm of peripheral nerves of right upper limb, including shoulder
C47.12	Malignant neoplasm of peripheral nerves of left upper limb, including shoulder
C47.21	Malignant neoplasm of peripheral nerves of right lower limb, including hip
C47.22	Malignant neoplasm of peripheral nerves of left lower limb, including hip
C47.3	Malignant neoplasm of peripheral nerves of thorax
C47.4	Malignant neoplasm of peripheral nerves of abdomen
C47.5	Malignant neoplasm of peripheral nerves of pelvis
C47.6	Malignant neoplasm of peripheral nerves of trunk, unspecified
C47.8	Malignant neoplasm of overlapping sites of peripheral nerves and autonomic nervous system

ICD-10 Code	Description
C48.0	Malignant neoplasm of retroperitoneum
C48.1	Malignant neoplasm of specified parts of peritoneum
C48.8	Malignant neoplasm of overlapping sites of retroperitoneum and peritoneum
C49.0	Malignant neoplasm of connective and soft tissue of head, face and neck
C49.11	Malignant neoplasm of connective and soft tissue of right upper limb, including shoulder
C49.12	Malignant neoplasm of connective and soft tissue of left upper limb, including shoulder
C49.21	Malignant neoplasm of connective and soft tissue of right lower limb, including hip
C49.22	Malignant neoplasm of connective and soft tissue of left lower limb, including hip
C49.3	Malignant neoplasm of connective and soft tissue of thorax
C49.4	Malignant neoplasm of connective and soft tissue of abdomen
C49.5	Malignant neoplasm of connective and soft tissue of pelvis
C49.6	Malignant neoplasm of connective and soft tissue of trunk, unspecified
C49.8	Malignant neoplasm of overlapping sites of connective and soft tissue
C49.A1	Gastrointestinal stromal tumor of esophagus
C49.A2	Gastrointestinal stromal tumor of stomach
C49.A3	Gastrointestinal stromal tumor of small intestine
C49.A4	Gastrointestinal stromal tumor of large intestine
C49.A5	Gastrointestinal stromal tumor of rectum
C49.A9	Gastrointestinal stromal tumor of other sites
C50.011	Malignant neoplasm of nipple and areola, right female breast
C50.012	Malignant neoplasm of nipple and areola, left female breast
C50.021	Malignant neoplasm of nipple and areola, right male breast
C50.022	Malignant neoplasm of nipple and areola, left male breast
C50.111	Malignant neoplasm of central portion of right female breast
C50.112	Malignant neoplasm of central portion of left female breast
C50.121	Malignant neoplasm of central portion of right male breast
C50.122	Malignant neoplasm of central portion of left male breast
C50.211	Malignant neoplasm of upper-inner quadrant of right female breast
C50.212	Malignant neoplasm of upper-inner quadrant of left female breast
C50.221	Malignant neoplasm of upper-inner quadrant of right male breast
C50.222	Malignant neoplasm of upper-inner quadrant of left male breast
C50.311	Malignant neoplasm of lower-inner quadrant of right female breast
C50.312	Malignant neoplasm of lower-inner quadrant of left female breast
C50.321	Malignant neoplasm of lower-inner quadrant of right male breast
C50.322	Malignant neoplasm of lower-inner quadrant of left male breast
C50.411	Malignant neoplasm of upper-outer quadrant of right female breast
C50.412	Malignant neoplasm of upper-outer quadrant of left female breast
C50.421	Malignant neoplasm of upper-outer quadrant of right male breast
C50.422	Malignant neoplasm of upper-outer quadrant of left male breast

ICD-10 Code	Description
C50.511	Malignant neoplasm of lower-outer quadrant of right female breast
C50.512	Malignant neoplasm of lower-outer quadrant of left female breast
C50.521	Malignant neoplasm of lower-outer quadrant of right male breast
C50.522	Malignant neoplasm of lower-outer quadrant of left male breast
C50.611	Malignant neoplasm of axillary tail of right female breast
C50.612	Malignant neoplasm of axillary tail of left female breast
C50.621	Malignant neoplasm of axillary tail of right male breast
C50.622	Malignant neoplasm of axillary tail of left male breast
C50.811	Malignant neoplasm of overlapping sites of right female breast
C50.812	Malignant neoplasm of overlapping sites of left female breast
C50.821	Malignant neoplasm of overlapping sites of right male breast
C50.822	Malignant neoplasm of overlapping sites of left male breast
C50.911	Malignant neoplasm of unspecified site of right female breast
C50.912	Malignant neoplasm of unspecified site of left female breast
C50.921	Malignant neoplasm of unspecified site of right male breast
C50.922	Malignant neoplasm of unspecified site of left male breast
C51.0	Malignant neoplasm of labium majus
C51.1	Malignant neoplasm of labium minus
C51.2	Malignant neoplasm of clitoris
C51.8	Malignant neoplasm of overlapping sites of vulva
C52	Malignant neoplasm of vagina
C53.0	Malignant neoplasm of endocervix
C53.1	Malignant neoplasm of exocervix
C53.8	Malignant neoplasm of overlapping sites of cervix uteri
C54.0	Malignant neoplasm of isthmus uteri
C54.1	Malignant neoplasm of endometrium
C54.2	Malignant neoplasm of myometrium
C54.3	Malignant neoplasm of fundus uteri
C54.8	Malignant neoplasm of overlapping sites of corpus uteri
C56.1	Malignant neoplasm of right ovary
C56.2	Malignant neoplasm of left ovary
C57.01	Malignant neoplasm of right fallopian tube
C57.02	Malignant neoplasm of left fallopian tube
C57.11	Malignant neoplasm of right broad ligament
C57.12	Malignant neoplasm of left broad ligament
C57.21	Malignant neoplasm of right round ligament
C57.22	Malignant neoplasm of left round ligament
C57.3	Malignant neoplasm of parametrium
C57.7	Malignant neoplasm of other specified female genital organs

ICD-10 Code	Description
C57.8	Malignant neoplasm of overlapping sites of female genital organs
C58	Malignant neoplasm of placenta
C60.0	Malignant neoplasm of prepuce
C60.1	Malignant neoplasm of glans penis
C60.2	Malignant neoplasm of body of penis
C60.8	Malignant neoplasm of overlapping sites of penis
C61	Malignant neoplasm of prostate
C62.01	Malignant neoplasm of undescended right testis
C62.02	Malignant neoplasm of undescended left testis
C62.11	Malignant neoplasm of descended right testis
C62.12	Malignant neoplasm of descended left testis
C63.01	Malignant neoplasm of right epididymis
C63.02	Malignant neoplasm of left epididymis
C63.11	Malignant neoplasm of right spermatic cord
C63.12	Malignant neoplasm of left spermatic cord
C63.2	Malignant neoplasm of scrotum
C63.7	Malignant neoplasm of other specified male genital organs
C63.8	Malignant neoplasm of overlapping sites of male genital organs
C64.1	Malignant neoplasm of right kidney, except renal pelvis
C64.2	Malignant neoplasm of left kidney, except renal pelvis
C65.1	Malignant neoplasm of right renal pelvis
C65.2	Malignant neoplasm of left renal pelvis
C66.1	Malignant neoplasm of right ureter
C66.2	Malignant neoplasm of left ureter
C67.0	Malignant neoplasm of trigone of bladder
C67.1	Malignant neoplasm of dome of bladder
C67.2	Malignant neoplasm of lateral wall of bladder
C67.3	Malignant neoplasm of anterior wall of bladder
C67.4	Malignant neoplasm of posterior wall of bladder
C67.5	Malignant neoplasm of bladder neck
C67.6	Malignant neoplasm of ureteric orifice
C67.7	Malignant neoplasm of urachus
C67.8	Malignant neoplasm of overlapping sites of bladder
C68.0	Malignant neoplasm of urethra
C68.1	Malignant neoplasm of paraurethral glands
C68.8	Malignant neoplasm of overlapping sites of urinary organs
C69.01	Malignant neoplasm of right conjunctiva
C69.02	Malignant neoplasm of left conjunctiva
C69.11	Malignant neoplasm of right cornea

ICD-10 Code	Description
C69.12	Malignant neoplasm of left cornea
C69.21	Malignant neoplasm of right retina
C69.22	Malignant neoplasm of left retina
C69.31	Malignant neoplasm of right choroid
C69.32	Malignant neoplasm of left choroid
C69.41	Malignant neoplasm of right ciliary body
C69.42	Malignant neoplasm of left ciliary body
C69.51	Malignant neoplasm of right lacrimal gland and duct
C69.52	Malignant neoplasm of left lacrimal gland and duct
C69.61	Malignant neoplasm of right orbit
C69.62	Malignant neoplasm of left orbit
C69.81	Malignant neoplasm of overlapping sites of right eye and adnexa
C69.82	Malignant neoplasm of overlapping sites of left eye and adnexa
C70.0	Malignant neoplasm of cerebral meninges
C70.1	Malignant neoplasm of spinal meninges
C71.0	Malignant neoplasm of cerebrum, except lobes and ventricles
C71.1	Malignant neoplasm of frontal lobe
C71.2	Malignant neoplasm of temporal lobe
C71.3	Malignant neoplasm of parietal lobe
C71.4	Malignant neoplasm of occipital lobe
C71.5	Malignant neoplasm of cerebral ventricle
C71.6	Malignant neoplasm of cerebellum
C71.7	Malignant neoplasm of brain stem
C71.8	Malignant neoplasm of overlapping sites of brain
C72.0	Malignant neoplasm of spinal cord
C72.1	Malignant neoplasm of cauda equina
C72.21	Malignant neoplasm of right olfactory nerve
C72.22	Malignant neoplasm of left olfactory nerve
C72.31	Malignant neoplasm of right optic nerve
C72.32	Malignant neoplasm of left optic nerve
C72.41	Malignant neoplasm of right acoustic nerve
C72.42	Malignant neoplasm of left acoustic nerve
C72.59	Malignant neoplasm of other cranial nerves
C73	Malignant neoplasm of thyroid gland
C74.01	Malignant neoplasm of cortex of right adrenal gland
C74.02	Malignant neoplasm of cortex of left adrenal gland
C74.11	Malignant neoplasm of medulla of right adrenal gland
C74.12	Malignant neoplasm of medulla of left adrenal gland
C75.0	Malignant neoplasm of parathyroid gland

ICD-10 Code	Description
C75.1	Malignant neoplasm of pituitary gland
C75.2	Malignant neoplasm of craniopharyngeal duct
C75.3	Malignant neoplasm of pineal gland
C75.4	Malignant neoplasm of carotid body
C75.5	Malignant neoplasm of aortic body and other paraganglia
C75.8	Malignant neoplasm with pluriglandular involvement, unspecified
C7A.010	Malignant carcinoid tumor of the duodenum
C7A.011	Malignant carcinoid tumor of the jejunum
C7A.012	Malignant carcinoid tumor of the ileum
C7A.020	Malignant carcinoid tumor of the appendix
C7A.021	Malignant carcinoid tumor of the cecum
C7A.022	Malignant carcinoid tumor of the ascending colon
C7A.023	Malignant carcinoid tumor of the transverse colon
C7A.024	Malignant carcinoid tumor of the descending colon
C7A.025	Malignant carcinoid tumor of the sigmoid colon
C7A.026	Malignant carcinoid tumor of the rectum
C7A.090	Malignant carcinoid tumor of the bronchus and lung
C7A.091	Malignant carcinoid tumor of the thymus
C7A.092	Malignant carcinoid tumor of the stomach
C7A.093	Malignant carcinoid tumor of the kidney
C7A.094	Malignant carcinoid tumor of the foregut, unspecified
C7A.095	Malignant carcinoid tumor of the midgut, unspecified
C7A.096	Malignant carcinoid tumor of the hindgut, unspecified
C7A.098	Malignant carcinoid tumors of other sites
C7A.1	Malignant poorly differentiated neuroendocrine tumors
C7A.8	Other malignant neuroendocrine tumors
C7B.01	Secondary carcinoid tumors of distant lymph nodes
C7B.02	Secondary carcinoid tumors of liver
C7B.03	Secondary carcinoid tumors of bone
C7B.04	Secondary carcinoid tumors of peritoneum
C7B.09	Secondary carcinoid tumors of other sites
C7B.1	Secondary Merkel cell carcinoma
C7B.8	Other secondary neuroendocrine tumors
C76.0	Malignant neoplasm of head, face and neck
C76.1	Malignant neoplasm of thorax
C76.2	Malignant neoplasm of abdomen
C76.3	Malignant neoplasm of pelvis
C76.41	Malignant neoplasm of right upper limb
C76.42	Malignant neoplasm of left upper limb

ICD-10 Code	Description
C76.51	Malignant neoplasm of right lower limb
C76.52	Malignant neoplasm of left lower limb
C76.8	Malignant neoplasm of other specified ill-defined sites
C77.0	Secondary and unspecified malignant neoplasm of lymph nodes of head, face and neck
C77.1	Secondary and unspecified malignant neoplasm of intrathoracic lymph nodes
C77.2	Secondary and unspecified malignant neoplasm of intra-abdominal lymph nodes
C77.3	Secondary and unspecified malignant neoplasm of axilla and upper limb lymph nodes
C77.4	Secondary and unspecified malignant neoplasm of inguinal and lower limb lymph nodes
C77.5	Secondary and unspecified malignant neoplasm of intrapelvic lymph nodes
C77.8	Secondary and unspecified malignant neoplasm of lymph nodes of multiple regions
C78.01	Secondary malignant neoplasm of right lung
C78.02	Secondary malignant neoplasm of left lung
C78.1	Secondary malignant neoplasm of mediastinum
C78.2	Secondary malignant neoplasm of pleura
C78.39	Secondary malignant neoplasm of other respiratory organs
C78.4	Secondary malignant neoplasm of small intestine
C78.5	Secondary malignant neoplasm of large intestine and rectum
C78.6	Secondary malignant neoplasm of retroperitoneum and peritoneum
C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct
C78.89	Secondary malignant neoplasm of other digestive organs
C79.01	Secondary malignant neoplasm of right kidney and renal pelvis
C79.02	Secondary malignant neoplasm of left kidney and renal pelvis
C79.11	Secondary malignant neoplasm of bladder
C79.19	Secondary malignant neoplasm of other urinary organs
C79.2	Secondary malignant neoplasm of skin
C79.31	Secondary malignant neoplasm of brain
C79.32	Secondary malignant neoplasm of cerebral meninges
C79.49	Secondary malignant neoplasm of other parts of nervous system
C79.51	Secondary malignant neoplasm of bone
C79.52	Secondary malignant neoplasm of bone marrow
C79.61	Secondary malignant neoplasm of right ovary
C79.62	Secondary malignant neoplasm of left ovary
C79.71	Secondary malignant neoplasm of right adrenal gland
C79.72	Secondary malignant neoplasm of left adrenal gland
C79.81	Secondary malignant neoplasm of breast
C79.82	Secondary malignant neoplasm of genital organs
C79.89	Secondary malignant neoplasm of other specified sites
C80.0	Disseminated malignant neoplasm, unspecified
C80.1	Malignant (primary) neoplasm, unspecified

ICD-10 Code	Description
C80.2	Malignant neoplasm associated with transplanted organ
C81.01	Nodular lymphocyte predominant Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.02	Nodular lymphocyte predominant Hodgkin lymphoma, intrathoracic lymph nodes
C81.03	Nodular lymphocyte predominant Hodgkin lymphoma, intra-abdominal lymph nodes
C81.04	Nodular lymphocyte predominant Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.05	Nodular lymphocyte predominant Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.06	Nodular lymphocyte predominant Hodgkin lymphoma, intrapelvic lymph nodes
C81.07	Nodular lymphocyte predominant Hodgkin lymphoma, spleen
C81.08	Nodular lymphocyte predominant Hodgkin lymphoma, lymph nodes of multiple sites
C81.09	Nodular lymphocyte predominant Hodgkin lymphoma, extranodal and solid organ sites
C81.11	Nodular sclerosis Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.12	Nodular sclerosis Hodgkin lymphoma, intrathoracic lymph nodes
C81.13	Nodular sclerosis Hodgkin lymphoma, intra-abdominal lymph nodes
C81.14	Nodular sclerosis Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.15	Nodular sclerosis Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.16	Nodular sclerosis Hodgkin lymphoma, intrapelvic lymph nodes
C81.17	Nodular sclerosis Hodgkin lymphoma, spleen
C81.18	Nodular sclerosis Hodgkin lymphoma, lymph nodes of multiple sites
C81.19	Nodular sclerosis Hodgkin lymphoma, extranodal and solid organ sites
C81.21	Mixed cellularity Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.22	Mixed cellularity Hodgkin lymphoma, intrathoracic lymph nodes
C81.23	Mixed cellularity Hodgkin lymphoma, intra-abdominal lymph nodes
C81.24	Mixed cellularity Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.25	Mixed cellularity Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.26	Mixed cellularity Hodgkin lymphoma, intrapelvic lymph nodes
C81.27	Mixed cellularity Hodgkin lymphoma, spleen
C81.28	Mixed cellularity Hodgkin lymphoma, lymph nodes of multiple sites
C81.29	Mixed cellularity Hodgkin lymphoma, extranodal and solid organ sites
C81.31	Lymphocyte depleted Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.32	Lymphocyte depleted Hodgkin lymphoma, intrathoracic lymph nodes
C81.33	Lymphocyte depleted Hodgkin lymphoma, intra-abdominal lymph nodes
C81.34	Lymphocyte depleted Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.35	Lymphocyte depleted Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.36	Lymphocyte depleted Hodgkin lymphoma, intrapelvic lymph nodes
C81.37	Lymphocyte depleted Hodgkin lymphoma, spleen
C81.38	Lymphocyte depleted Hodgkin lymphoma, lymph nodes of multiple sites
C81.39	Lymphocyte depleted Hodgkin lymphoma, extranodal and solid organ sites
C81.41	Lymphocyte-rich Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.42	Lymphocyte-rich Hodgkin lymphoma, intrathoracic lymph nodes

ICD-10 Code	Description
C81.43	Lymphocyte-rich Hodgkin lymphoma, intra-abdominal lymph nodes
C81.44	Lymphocyte-rich Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.45	Lymphocyte-rich Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.46	Lymphocyte-rich Hodgkin lymphoma, intrapelvic lymph nodes
C81.47	Lymphocyte-rich Hodgkin lymphoma, spleen
C81.48	Lymphocyte-rich Hodgkin lymphoma, lymph nodes of multiple sites
C81.49	Lymphocyte-rich Hodgkin lymphoma, extranodal and solid organ sites
C81.71	Other Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.72	Other Hodgkin lymphoma, intrathoracic lymph nodes
C81.73	Other Hodgkin lymphoma, intra-abdominal lymph nodes
C81.74	Other Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.75	Other Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.76	Other Hodgkin lymphoma, intrapelvic lymph nodes
C81.77	Other Hodgkin lymphoma, spleen
C81.78	Other Hodgkin lymphoma, lymph nodes of multiple sites
C81.79	Other Hodgkin lymphoma, extranodal and solid organ sites
C81.91	Hodgkin lymphoma, unspecified, lymph nodes of head, face, and neck
C81.92	Hodgkin lymphoma, unspecified, intrathoracic lymph nodes
C81.93	Hodgkin lymphoma, unspecified, intra-abdominal lymph nodes
C81.94	Hodgkin lymphoma, unspecified, lymph nodes of axilla and upper limb
C81.95	Hodgkin lymphoma, unspecified, lymph nodes of inguinal region and lower limb
C81.96	Hodgkin lymphoma, unspecified, intrapelvic lymph nodes
C81.97	Hodgkin lymphoma, unspecified, spleen
C81.98	Hodgkin lymphoma, unspecified, lymph nodes of multiple sites
C81.99	Hodgkin lymphoma, unspecified, extranodal and solid organ sites
C82.01	Follicular lymphoma grade I, lymph nodes of head, face, and neck
C82.02	Follicular lymphoma grade I, intrathoracic lymph nodes
C82.03	Follicular lymphoma grade I, intra-abdominal lymph nodes
C82.04	Follicular lymphoma grade I, lymph nodes of axilla and upper limb
C82.05	Follicular lymphoma grade I, lymph nodes of inguinal region and lower limb
C82.06	Follicular lymphoma grade I, intrapelvic lymph nodes
C82.07	Follicular lymphoma grade I, spleen
C82.08	Follicular lymphoma grade I, lymph nodes of multiple sites
C82.09	Follicular lymphoma grade I, extranodal and solid organ sites
C82.11	Follicular lymphoma grade II, lymph nodes of head, face, and neck
C82.12	Follicular lymphoma grade II, intrathoracic lymph nodes
C82.13	Follicular lymphoma grade II, intra-abdominal lymph nodes
C82.14	Follicular lymphoma grade II, lymph nodes of axilla and upper limb
C82.15	Follicular lymphoma grade II, lymph nodes of inguinal region and lower limb

ICD-10 Code	Description
C82.16	Follicular lymphoma grade II, intrapelvic lymph nodes
C82.17	Follicular lymphoma grade II, spleen
C82.18	Follicular lymphoma grade II, lymph nodes of multiple sites
C82.19	Follicular lymphoma grade II, extranodal and solid organ sites
C82.21	Follicular lymphoma grade III, unspecified, lymph nodes of head, face, and neck
C82.22	Follicular lymphoma grade III, unspecified, intrathoracic lymph nodes
C82.23	Follicular lymphoma grade III, unspecified, intra-abdominal lymph nodes
C82.24	Follicular lymphoma grade III, unspecified, lymph nodes of axilla and upper limb
C82.25	Follicular lymphoma grade III, unspecified, lymph nodes of inguinal region and lower limb
C82.26	Follicular lymphoma grade III, unspecified, intrapelvic lymph nodes
C82.27	Follicular lymphoma grade III, unspecified, spleen
C82.28	Follicular lymphoma grade III, unspecified, lymph nodes of multiple sites
C82.29	Follicular lymphoma grade III, unspecified, extranodal and solid organ sites
C82.31	Follicular lymphoma grade IIIa, lymph nodes of head, face, and neck
C82.32	Follicular lymphoma grade IIIa, intrathoracic lymph nodes
C82.33	Follicular lymphoma grade IIIa, intra-abdominal lymph nodes
C82.34	Follicular lymphoma grade IIIa, lymph nodes of axilla and upper limb
C82.35	Follicular lymphoma grade IIIa, lymph nodes of inguinal region and lower limb
C82.36	Follicular lymphoma grade IIIa, intrapelvic lymph nodes
C82.37	Follicular lymphoma grade IIIa, spleen
C82.38	Follicular lymphoma grade IIIa, lymph nodes of multiple sites
C82.39	Follicular lymphoma grade IIIa, extranodal and solid organ sites
C82.41	Follicular lymphoma grade IIIb, lymph nodes of head, face, and neck
C82.42	Follicular lymphoma grade IIIb, intrathoracic lymph nodes
C82.43	Follicular lymphoma grade IIIb, intra-abdominal lymph nodes
C82.44	Follicular lymphoma grade IIIb, lymph nodes of axilla and upper limb
C82.45	Follicular lymphoma grade IIIb, lymph nodes of inguinal region and lower limb
C82.46	Follicular lymphoma grade IIIb, intrapelvic lymph nodes
C82.47	Follicular lymphoma grade IIIb, spleen
C82.48	Follicular lymphoma grade IIIb, lymph nodes of multiple sites
C82.49	Follicular lymphoma grade IIIb, extranodal and solid organ sites
C82.51	Diffuse follicle center lymphoma, lymph nodes of head, face, and neck
C82.52	Diffuse follicle center lymphoma, intrathoracic lymph nodes
C82.53	Diffuse follicle center lymphoma, intra-abdominal lymph nodes
C82.54	Diffuse follicle center lymphoma, lymph nodes of axilla and upper limb
C82.55	Diffuse follicle center lymphoma, lymph nodes of inguinal region and lower limb
C82.56	Diffuse follicle center lymphoma, intrapelvic lymph nodes
C82.57	Diffuse follicle center lymphoma, spleen
C82.58	Diffuse follicle center lymphoma, lymph nodes of multiple sites

ICD-10 Code	Description
C82.59	Diffuse follicle center lymphoma, extranodal and solid organ sites
C82.61	Cutaneous follicle center lymphoma, lymph nodes of head, face, and neck
C82.62	Cutaneous follicle center lymphoma, intrathoracic lymph nodes
C82.63	Cutaneous follicle center lymphoma, intra-abdominal lymph nodes
C82.64	Cutaneous follicle center lymphoma, lymph nodes of axilla and upper limb
C82.65	Cutaneous follicle center lymphoma, lymph nodes of inguinal region and lower limb
C82.66	Cutaneous follicle center lymphoma, intrapelvic lymph nodes
C82.67	Cutaneous follicle center lymphoma, spleen
C82.68	Cutaneous follicle center lymphoma, lymph nodes of multiple sites
C82.69	Cutaneous follicle center lymphoma, extranodal and solid organ sites
C82.81	Other types of follicular lymphoma, lymph nodes of head, face, and neck
C82.82	Other types of follicular lymphoma, intrathoracic lymph nodes
C82.83	Other types of follicular lymphoma, intra-abdominal lymph nodes
C82.84	Other types of follicular lymphoma, lymph nodes of axilla and upper limb
C82.85	Other types of follicular lymphoma, lymph nodes of inguinal region and lower limb
C82.86	Other types of follicular lymphoma, intrapelvic lymph nodes
C82.87	Other types of follicular lymphoma, spleen
C82.88	Other types of follicular lymphoma, lymph nodes of multiple sites
C82.89	Other types of follicular lymphoma, extranodal and solid organ sites
C82.91	Follicular lymphoma, unspecified, lymph nodes of head, face, and neck
C82.92	Follicular lymphoma, unspecified, intrathoracic lymph nodes
C82.93	Follicular lymphoma, unspecified, intra-abdominal lymph nodes
C82.94	Follicular lymphoma, unspecified, lymph nodes of axilla and upper limb
C82.95	Follicular lymphoma, unspecified, lymph nodes of inguinal region and lower limb
C82.96	Follicular lymphoma, unspecified, intrapelvic lymph nodes
C82.97	Follicular lymphoma, unspecified, spleen
C82.98	Follicular lymphoma, unspecified, lymph nodes of multiple sites
C82.99	Follicular lymphoma, unspecified, extranodal and solid organ sites
C83.01	Small cell B-cell lymphoma, lymph nodes of head, face, and neck
C83.02	Small cell B-cell lymphoma, intrathoracic lymph nodes
C83.03	Small cell B-cell lymphoma, intra-abdominal lymph nodes
C83.04	Small cell B-cell lymphoma, lymph nodes of axilla and upper limb
C83.05	Small cell B-cell lymphoma, lymph nodes of inguinal region and lower limb
C83.06	Small cell B-cell lymphoma, intrapelvic lymph nodes
C83.07	Small cell B-cell lymphoma, spleen
C83.08	Small cell B-cell lymphoma, lymph nodes of multiple sites
C83.09	Small cell B-cell lymphoma, extranodal and solid organ sites
C83.11	Mantle cell lymphoma, lymph nodes of head, face, and neck
C83.12	Mantle cell lymphoma, intrathoracic lymph nodes

ICD-10 Code	Description
C83.13	Mantle cell lymphoma, intra-abdominal lymph nodes
C83.14	Mantle cell lymphoma, lymph nodes of axilla and upper limb
C83.15	Mantle cell lymphoma, lymph nodes of inguinal region and lower limb
C83.16	Mantle cell lymphoma, intrapelvic lymph nodes
C83.17	Mantle cell lymphoma, spleen
C83.18	Mantle cell lymphoma, lymph nodes of multiple sites
C83.19	Mantle cell lymphoma, extranodal and solid organ sites
C83.31	Diffuse large B-cell lymphoma, lymph nodes of head, face, and neck
C83.32	Diffuse large B-cell lymphoma, intrathoracic lymph nodes
C83.33	Diffuse large B-cell lymphoma, intra-abdominal lymph nodes
C83.34	Diffuse large B-cell lymphoma, lymph nodes of axilla and upper limb
C83.35	Diffuse large B-cell lymphoma, lymph nodes of inguinal region and lower limb
C83.36	Diffuse large B-cell lymphoma, intrapelvic lymph nodes
C83.37	Diffuse large B-cell lymphoma, spleen
C83.38	Diffuse large B-cell lymphoma, lymph nodes of multiple sites
C83.39	Diffuse large B-cell lymphoma, extranodal and solid organ sites
C83.51	Lymphoblastic (diffuse) lymphoma, lymph nodes of head, face, and neck
C83.52	Lymphoblastic (diffuse) lymphoma, intrathoracic lymph nodes
C83.53	Lymphoblastic (diffuse) lymphoma, intra-abdominal lymph nodes
C83.54	Lymphoblastic (diffuse) lymphoma, lymph nodes of axilla and upper limb
C83.55	Lymphoblastic (diffuse) lymphoma, lymph nodes of inguinal region and lower limb
C83.56	Lymphoblastic (diffuse) lymphoma, intrapelvic lymph nodes
C83.57	Lymphoblastic (diffuse) lymphoma, spleen
C83.58	Lymphoblastic (diffuse) lymphoma, lymph nodes of multiple sites
C83.59	Lymphoblastic (diffuse) lymphoma, extranodal and solid organ sites
C83.71	Burkitt lymphoma, lymph nodes of head, face, and neck
C83.72	Burkitt lymphoma, intrathoracic lymph nodes
C83.73	Burkitt lymphoma, intra-abdominal lymph nodes
C83.74	Burkitt lymphoma, lymph nodes of axilla and upper limb
C83.75	Burkitt lymphoma, lymph nodes of inguinal region and lower limb
C83.76	Burkitt lymphoma, intrapelvic lymph nodes
C83.77	Burkitt lymphoma, spleen
C83.78	Burkitt lymphoma, lymph nodes of multiple sites
C83.79	Burkitt lymphoma, extranodal and solid organ sites
C83.81	Other non-follicular lymphoma, lymph nodes of head, face, and neck
C83.82	Other non-follicular lymphoma, intrathoracic lymph nodes
C83.83	Other non-follicular lymphoma, intra-abdominal lymph nodes
C83.84	Other non-follicular lymphoma, lymph nodes of axilla and upper limb
C83.85	Other non-follicular lymphoma, lymph nodes of inguinal region and lower limb

ICD-10 Code	Description
C83.86	Other non-follicular lymphoma, intrapelvic lymph nodes
C83.87	Other non-follicular lymphoma, spleen
C83.88	Other non-follicular lymphoma, lymph nodes of multiple sites
C83.89	Other non-follicular lymphoma, extranodal and solid organ sites
C83.91	Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of head, face, and neck
C83.92	Non-follicular (diffuse) lymphoma, unspecified, intrathoracic lymph nodes
C83.93	Non-follicular (diffuse) lymphoma, unspecified, intra-abdominal lymph nodes
C83.94	Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of axilla and upper limb
C83.95	Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of inguinal region and lower limb
C83.96	Non-follicular (diffuse) lymphoma, unspecified, intrapelvic lymph nodes
C83.97	Non-follicular (diffuse) lymphoma, unspecified, spleen
C83.98	Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of multiple sites
C83.99	Non-follicular (diffuse) lymphoma, unspecified, extranodal and solid organ sites
C84.01	Mycosis fungoides, lymph nodes of head, face, and neck
C84.02	Mycosis fungoides, intrathoracic lymph nodes
C84.03	Mycosis fungoides, intra-abdominal lymph nodes
C84.04	Mycosis fungoides, lymph nodes of axilla and upper limb
C84.05	Mycosis fungoides, lymph nodes of inguinal region and lower limb
C84.06	Mycosis fungoides, intrapelvic lymph nodes
C84.07	Mycosis fungoides, spleen
C84.08	Mycosis fungoides, lymph nodes of multiple sites
C84.09	Mycosis fungoides, extranodal and solid organ sites
C84.11	Sezary disease, lymph nodes of head, face, and neck
C84.12	Sezary disease, intrathoracic lymph nodes
C84.13	Sezary disease, intra-abdominal lymph nodes
C84.14	Sezary disease, lymph nodes of axilla and upper limb
C84.15	Sezary disease, lymph nodes of inguinal region and lower limb
C84.16	Sezary disease, intrapelvic lymph nodes
C84.17	Sezary disease, spleen
C84.18	Sezary disease, lymph nodes of multiple sites
C84.19	Sezary disease, extranodal and solid organ sites
C84.41	Peripheral T-cell lymphoma, not elsewhere classified, lymph nodes of head, face, and neck
C84.42	Peripheral T-cell lymphoma, not elsewhere classified, intrathoracic lymph nodes
C84.43	Peripheral T-cell lymphoma, not elsewhere classified, intra-abdominal lymph nodes
C84.44	Peripheral T-cell lymphoma, not elsewhere classified, lymph nodes of axilla and upper limb
C84.45	Peripheral T-cell lymphoma, not elsewhere classified, lymph nodes of inguinal region and lower limb
C84.46	Peripheral T-cell lymphoma, not elsewhere classified, intrapelvic lymph nodes
C84.47	Peripheral T-cell lymphoma, not elsewhere classified, spleen
C84.48	Peripheral T-cell lymphoma, not elsewhere classified, lymph nodes of multiple sites

ICD-10 Code	Description
C84.49	Peripheral T-cell lymphoma, not elsewhere classified, extranodal and solid organ sites
C84.61	Anaplastic large cell lymphoma, ALK-positive, lymph nodes of head, face, and neck
C84.62	Anaplastic large cell lymphoma, ALK-positive, intrathoracic lymph nodes
C84.63	Anaplastic large cell lymphoma, ALK-positive, intra-abdominal lymph nodes
C84.64	Anaplastic large cell lymphoma, ALK-positive, lymph nodes of axilla and upper limb
C84.65	Anaplastic large cell lymphoma, ALK-positive, lymph nodes of inguinal region and lower limb
C84.66	Anaplastic large cell lymphoma, ALK-positive, intrapelvic lymph nodes
C84.67	Anaplastic large cell lymphoma, ALK-positive, spleen
C84.68	Anaplastic large cell lymphoma, ALK-positive, lymph nodes of multiple sites
C84.69	Anaplastic large cell lymphoma, ALK-positive, extranodal and solid organ sites
C84.71	Anaplastic large cell lymphoma, ALK-negative, lymph nodes of head, face, and neck
C84.72	Anaplastic large cell lymphoma, ALK-negative, intrathoracic lymph nodes
C84.73	Anaplastic large cell lymphoma, ALK-negative, intra-abdominal lymph nodes
C84.74	Anaplastic large cell lymphoma, ALK-negative, lymph nodes of axilla and upper limb
C84.75	Anaplastic large cell lymphoma, ALK-negative, lymph nodes of inguinal region and lower limb
C84.76	Anaplastic large cell lymphoma, ALK-negative, intrapelvic lymph nodes
C84.77	Anaplastic large cell lymphoma, ALK-negative, spleen
C84.78	Anaplastic large cell lymphoma, ALK-negative, lymph nodes of multiple sites
C84.79	Anaplastic large cell lymphoma, ALK-negative, extranodal and solid organ sites
C84.A1	Cutaneous T-cell lymphoma, unspecified lymph nodes of head, face, and neck
C84.A2	Cutaneous T-cell lymphoma, unspecified, intrathoracic lymph nodes
C84.A3	Cutaneous T-cell lymphoma, unspecified, intra-abdominal lymph nodes
C84.A4	Cutaneous T-cell lymphoma, unspecified, lymph nodes of axilla and upper limb
C84.A5	Cutaneous T-cell lymphoma, unspecified, lymph nodes of inguinal region and lower limb
C84.A6	Cutaneous T-cell lymphoma, unspecified, intrapelvic lymph nodes
C84.A7	Cutaneous T-cell lymphoma, unspecified, spleen
C84.A8	Cutaneous T-cell lymphoma, unspecified, lymph nodes of multiple sites
C84.A9	Cutaneous T-cell lymphoma, unspecified, extranodal and solid organ sites
C84.Z1	Other mature T/NK-cell lymphomas, lymph nodes of head, face, and neck
C84.Z2	Other mature T/NK-cell lymphomas, intrathoracic lymph nodes
C84.Z3	Other mature T/NK-cell lymphomas, intra-abdominal lymph nodes
C84.Z4	Other mature T/NK-cell lymphomas, lymph nodes of axilla and upper limb
C84.Z5	Other mature T/NK-cell lymphomas, lymph nodes of inguinal region and lower limb
C84.Z6	Other mature T/NK-cell lymphomas, intrapelvic lymph nodes
C84.Z7	Other mature T/NK-cell lymphomas, spleen
C84.Z8	Other mature T/NK-cell lymphomas, lymph nodes of multiple sites
C84.Z9	Other mature T/NK-cell lymphomas, extranodal and solid organ sites
C84.91	Mature T/NK-cell lymphomas, unspecified, lymph nodes of head, face, and neck
C84.92	Mature T/NK-cell lymphomas, unspecified, intrathoracic lymph nodes

ICD-10 Code	Description
C84.93	Mature T/NK-cell lymphomas, unspecified, intra-abdominal lymph nodes
C84.94	Mature T/NK-cell lymphomas, unspecified, lymph nodes of axilla and upper limb
C84.95	Mature T/NK-cell lymphomas, unspecified, lymph nodes of inguinal region and lower limb
C84.96	Mature T/NK-cell lymphomas, unspecified, intrapelvic lymph nodes
C84.97	Mature T/NK-cell lymphomas, unspecified, spleen
C84.98	Mature T/NK-cell lymphomas, unspecified, lymph nodes of multiple sites
C84.99	Mature T/NK-cell lymphomas, unspecified, extranodal and solid organ sites
C85.11	Unspecified B-cell lymphoma, lymph nodes of head, face, and neck
C85.12	Unspecified B-cell lymphoma, intrathoracic lymph nodes
C85.13	Unspecified B-cell lymphoma, intra-abdominal lymph nodes
C85.14	Unspecified B-cell lymphoma, lymph nodes of axilla and upper limb
C85.15	Unspecified B-cell lymphoma, lymph nodes of inguinal region and lower limb
C85.16	Unspecified B-cell lymphoma, intrapelvic lymph nodes
C85.17	Unspecified B-cell lymphoma, spleen
C85.18	Unspecified B-cell lymphoma, lymph nodes of multiple sites
C85.19	Unspecified B-cell lymphoma, extranodal and solid organ sites
C85.21	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of head, face, and neck
C85.22	Mediastinal (thymic) large B-cell lymphoma, intrathoracic lymph nodes
C85.23	Mediastinal (thymic) large B-cell lymphoma, intra-abdominal lymph nodes
C85.24	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of axilla and upper limb
C85.25	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of inguinal region and lower limb
C85.26	Mediastinal (thymic) large B-cell lymphoma, intrapelvic lymph nodes
C85.27	Mediastinal (thymic) large B-cell lymphoma, spleen
C85.28	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of multiple sites
C85.29	Mediastinal (thymic) large B-cell lymphoma, extranodal and solid organ sites
C85.81	Other specified types of non-Hodgkin lymphoma, lymph nodes of head, face, and neck
C85.82	Other specified types of non-Hodgkin lymphoma, intrathoracic lymph nodes
C85.83	Other specified types of non-Hodgkin lymphoma, intra-abdominal lymph nodes
C85.84	Other specified types of non-Hodgkin lymphoma, lymph nodes of axilla and upper limb
C85.85	Other specified types of non-Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C85.86	Other specified types of non-Hodgkin lymphoma, intrapelvic lymph nodes
C85.87	Other specified types of non-Hodgkin lymphoma, spleen
C85.88	Other specified types of non-Hodgkin lymphoma, lymph nodes of multiple sites
C85.89	Other specified types of non-Hodgkin lymphoma, extranodal and solid organ sites
C85.91	Non-Hodgkin lymphoma, unspecified, lymph nodes of head, face, and neck
C85.92	Non-Hodgkin lymphoma, unspecified, intrathoracic lymph nodes
C85.93	Non-Hodgkin lymphoma, unspecified, intra-abdominal lymph nodes
C85.94	Non-Hodgkin lymphoma, unspecified, lymph nodes of axilla and upper limb
C85.95	Non-Hodgkin lymphoma, unspecified, lymph nodes of inguinal region and lower limb

ICD-10 Code	Description
C85.96	Non-Hodgkin lymphoma, unspecified, intrapelvic lymph nodes
C85.97	Non-Hodgkin lymphoma, unspecified, spleen
C85.98	Non-Hodgkin lymphoma, unspecified, lymph nodes of multiple sites
C85.99	Non-Hodgkin lymphoma, unspecified, extranodal and solid organ sites
C86.0	Extranodal NK/T-cell lymphoma, nasal type
C86.1	Hepatosplenic T-cell lymphoma
C86.2	Enteropathy-type (intestinal) T-cell lymphoma
C86.3	Subcutaneous panniculitis-like T-cell lymphoma
C86.4	Blastic NK-cell lymphoma
C86.5	Angioimmunoblastic T-cell lymphoma
C86.6	Primary cutaneous CD30-positive T-cell proliferations
C88.2	Heavy chain disease
C88.3	Immunoproliferative small intestinal disease
C88.4	Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue [MALT-lymphoma]
C88.8	Other malignant immunoproliferative diseases
C90.00	Multiple myeloma not having achieved remission
C90.02	Multiple myeloma in relapse
C90.10	Plasma cell leukemia not having achieved remission
C90.12	Plasma cell leukemia in relapse
C90.20	Extramedullary plasmacytoma not having achieved remission
C90.22	Extramedullary plasmacytoma in relapse
C90.30	Solitary plasmacytoma not having achieved remission
C90.32	Solitary plasmacytoma in relapse
C91.00	Acute lymphoblastic leukemia not having achieved remission
C91.02	Acute lymphoblastic leukemia, in relapse
C91.10	Chronic lymphocytic leukemia of B-cell type not having achieved remission
C91.12	Chronic lymphocytic leukemia of B-cell type in relapse
C91.30	Prolymphocytic leukemia of B-cell type not having achieved remission
C91.32	Prolymphocytic leukemia of B-cell type, in relapse
C91.40	Hairy cell leukemia not having achieved remission
C91.42	Hairy cell leukemia, in relapse
C91.50	Adult T-cell lymphoma/leukemia (HTLV-1-associated) not having achieved remission
C91.52	Adult T-cell lymphoma/leukemia (HTLV-1-associated), in relapse
C91.60	Prolymphocytic leukemia of T-cell type not having achieved remission
C91.62	Prolymphocytic leukemia of T-cell type, in relapse
C91.A0	Mature B-cell leukemia Burkitt-type not having achieved remission
C91.A2	Mature B-cell leukemia Burkitt-type, in relapse
C91.Z0	Other lymphoid leukemia not having achieved remission
C91.Z2	Other lymphoid leukemia, in relapse

ICD-10 Code	Description
C91.90	Lymphoid leukemia, unspecified not having achieved remission
C91.92	Lymphoid leukemia, unspecified, in relapse
C96.0	Multifocal and multisystemic (disseminated) Langerhans-cell histiocytosis
C96.20	Malignant mast cell neoplasm, unspecified
C96.21	Aggressive systemic mastocytosis
C96.22	Mast cell sarcoma
C96.29	Other malignant mast cell neoplasm
C96.4	Sarcoma of dendritic cells (accessory cells)
C96.A	Histiocytic sarcoma
C96.Z	Other specified malignant neoplasms of lymphoid, hematopoietic and related tissue
D00.01	Carcinoma in situ of labial mucosa and vermilion border
D00.02	Carcinoma in situ of buccal mucosa
D00.03	Carcinoma in situ of gingiva and edentulous alveolar ridge
D00.04	Carcinoma in situ of soft palate
D00.05	Carcinoma in situ of hard palate
D00.06	Carcinoma in situ of floor of mouth
D00.07	Carcinoma in situ of tongue
D00.08	Carcinoma in situ of pharynx
D00.1	Carcinoma in situ of esophagus
D00.2	Carcinoma in situ of stomach
D01.0	Carcinoma in situ of colon
D01.1	Carcinoma in situ of rectosigmoid junction
D01.2	Carcinoma in situ of rectum
D01.3	Carcinoma in situ of anus and anal canal
D01.49	Carcinoma in situ of other parts of intestine
D01.5	Carcinoma in situ of liver, gallbladder and bile ducts
D01.7	Carcinoma in situ of other specified digestive organs
D02.0	Carcinoma in situ of larynx
D02.1	Carcinoma in situ of trachea
D02.21	Carcinoma in situ of right bronchus and lung
D02.22	Carcinoma in situ of left bronchus and lung
D02.3	Carcinoma in situ of other parts of respiratory system
D03.0	Melanoma in situ of lip
D03.111	Melanoma in situ of right upper eyelid, including canthus
D03.112	Melanoma in situ of right lower eyelid, including canthus
D03.121	Melanoma in situ of left upper eyelid, including canthus
D03.122	Melanoma in situ of left lower eyelid, including canthus
D03.21	Melanoma in situ of right ear and external auricular canal
D03.22	Melanoma in situ of left ear and external auricular canal

ICD-10 Code	Description
D03.39	Melanoma in situ of other parts of face
D03.4	Melanoma in situ of scalp and neck
D03.51	Melanoma in situ of anal skin
D03.52	Melanoma in situ of breast (skin) (soft tissue)
D03.59	Melanoma in situ of other part of trunk
D03.61	Melanoma in situ of right upper limb, including shoulder
D03.62	Melanoma in situ of left upper limb, including shoulder
D03.71	Melanoma in situ of right lower limb, including hip
D03.72	Melanoma in situ of left lower limb, including hip
D03.8	Melanoma in situ of other sites
D04.0	Carcinoma in situ of skin of lip
D04.111	Carcinoma in situ of skin of right upper eyelid, including canthus
D04.112	Carcinoma in situ of skin of right lower eyelid, including canthus
D04.121	Carcinoma in situ of skin of left upper eyelid, including canthus
D04.122	Carcinoma in situ of skin of left lower eyelid, including canthus
D04.21	Carcinoma in situ of skin of right ear and external auricular canal
D04.22	Carcinoma in situ of skin of left ear and external auricular canal
D04.39	Carcinoma in situ of skin of other parts of face
D04.4	Carcinoma in situ of skin of scalp and neck
D04.5	Carcinoma in situ of skin of trunk
D04.61	Carcinoma in situ of skin of right upper limb, including shoulder
D04.62	Carcinoma in situ of skin of left upper limb, including shoulder
D04.71	Carcinoma in situ of skin of right lower limb, including hip
D04.72	Carcinoma in situ of skin of left lower limb, including hip
D04.8	Carcinoma in situ of skin of other sites
D05.01	Lobular carcinoma in situ of right breast
D05.02	Lobular carcinoma in situ of left breast
D05.11	Intraductal carcinoma in situ of right breast
D05.12	Intraductal carcinoma in situ of left breast
D05.81	Other specified type of carcinoma in situ of right breast
D05.82	Other specified type of carcinoma in situ of left breast
D05.91	Unspecified type of carcinoma in situ of right breast
D05.92	Unspecified type of carcinoma in situ of left breast
D06.0	Carcinoma in situ of endocervix
D06.1	Carcinoma in situ of exocervix
D06.7	Carcinoma in situ of other parts of cervix
D07.0	Carcinoma in situ of endometrium
D07.1	Carcinoma in situ of vulva
D07.2	Carcinoma in situ of vagina

ICD-10 Code	Description
D07.39	Carcinoma in situ of other female genital organs
D07.4	Carcinoma in situ of penis
D07.5	Carcinoma in situ of prostate
D07.61	Carcinoma in situ of scrotum
D07.69	Carcinoma in situ of other male genital organs
D09.0	Carcinoma in situ of bladder
D09.19	Carcinoma in situ of other urinary organs
D09.21	Carcinoma in situ of right eye
D09.22	Carcinoma in situ of left eye
D09.3	Carcinoma in situ of thyroid and other endocrine glands
D09.8	Carcinoma in situ of other specified sites
D37.01	Neoplasm of uncertain behavior of lip
D37.02	Neoplasm of uncertain behavior of tongue
D37.030	Neoplasm of uncertain behavior of the parotid salivary glands
D37.031	Neoplasm of uncertain behavior of the sublingual salivary glands
D37.032	Neoplasm of uncertain behavior of the submandibular salivary glands
D37.039	Neoplasm of uncertain behavior of the major salivary glands, unspecified
D37.04	Neoplasm of uncertain behavior of the minor salivary glands
D37.05	Neoplasm of uncertain behavior of pharynx
D37.09	Neoplasm of uncertain behavior of other specified sites of the oral cavity
D37.1	Neoplasm of uncertain behavior of stomach
D37.2	Neoplasm of uncertain behavior of small intestine
D37.3	Neoplasm of uncertain behavior of appendix
D37.4	Neoplasm of uncertain behavior of colon
D37.5	Neoplasm of uncertain behavior of rectum
D37.6	Neoplasm of uncertain behavior of liver, gallbladder and bile ducts
D37.8	Neoplasm of uncertain behavior of other specified digestive organs
D38.0	Neoplasm of uncertain behavior of larynx
D38.1	Neoplasm of uncertain behavior of trachea, bronchus and lung
D38.2	Neoplasm of uncertain behavior of pleura
D38.3	Neoplasm of uncertain behavior of mediastinum
D38.4	Neoplasm of uncertain behavior of thymus
D38.5	Neoplasm of uncertain behavior of other respiratory organs
D39.0	Neoplasm of uncertain behavior of uterus
D39.11	Neoplasm of uncertain behavior of right ovary
D39.12	Neoplasm of uncertain behavior of left ovary
D39.2	Neoplasm of uncertain behavior of placenta
D39.8	Neoplasm of uncertain behavior of other specified female genital organs
D40.0	Neoplasm of uncertain behavior of prostate

ICD-10 Code	Description
D40.11	Neoplasm of uncertain behavior of right testis
D40.12	Neoplasm of uncertain behavior of left testis
D41.11	Neoplasm of uncertain behavior of right renal pelvis
D41.12	Neoplasm of uncertain behavior of left renal pelvis
D41.20	Neoplasm of uncertain behavior of unspecified ureter
D41.21	Neoplasm of uncertain behavior of right ureter
D41.22	Neoplasm of uncertain behavior of left ureter
D41.3	Neoplasm of uncertain behavior of urethra
D41.4	Neoplasm of uncertain behavior of bladder
D41.8	Neoplasm of uncertain behavior of other specified urinary organs
D42.0	Neoplasm of uncertain behavior of cerebral meninges
D42.1	Neoplasm of uncertain behavior of spinal meninges
D43.0	Neoplasm of uncertain behavior of brain, supratentorial
D43.1	Neoplasm of uncertain behavior of brain, infratentorial
D43.2	Neoplasm of uncertain behavior of brain, unspecified
D43.3	Neoplasm of uncertain behavior of cranial nerves
D43.4	Neoplasm of uncertain behavior of spinal cord
D43.8	Neoplasm of uncertain behavior of other specified parts of central nervous system
D44.0	Neoplasm of uncertain behavior of thyroid gland
D44.11	Neoplasm of uncertain behavior of right adrenal gland
D44.12	Neoplasm of uncertain behavior of left adrenal gland
D44.2	Neoplasm of uncertain behavior of parathyroid gland
D44.3	Neoplasm of uncertain behavior of pituitary gland
D44.4	Neoplasm of uncertain behavior of craniopharyngeal duct
D44.5	Neoplasm of uncertain behavior of pineal gland
D44.6	Neoplasm of uncertain behavior of carotid body
D44.7	Neoplasm of uncertain behavior of aortic body and other paraganglia
D46.1	Refractory anemia with ring sideroblasts
D46.20	Refractory anemia with excess of blasts, unspecified
D46.21	Refractory anemia with excess of blasts 1
D46.22	Refractory anemia with excess of blasts 2
D46.A	Refractory cytopenia with multilineage dysplasia
D46.B	Refractory cytopenia with multilineage dysplasia and ring sideroblasts
D46.C	Myelodysplastic syndrome with isolated del(5q) chromosomal abnormality
D46.Z	Other myelodysplastic syndromes
D47.01	Cutaneous mastocytosis
D47.02	Systemic mastocytosis
D47.09	Other mast cell neoplasms of uncertain behavior
D47.3	Essential (hemorrhagic) thrombocythemia

ICD-10 Code	Description
D47.Z9	Other specified neoplasms of uncertain behavior of lymphoid, hematopoietic and related tissue
D48.0	Neoplasm of uncertain behavior of bone and articular cartilage
D48.110	Desmoid tumor of head and neck
D48.111	Desmoid tumor of chest wall
D48.112	Desmoid tumor, intrathoracic
D48.113	Desmoid tumor of abdominal wall
D48.114	Desmoid tumor, intraabdominal
D48.115	Desmoid tumor of upper extremity and shoulder girdle
D48.116	Desmoid tumor of lower extremity and pelvic girdle
D48.117	Desmoid tumor of back
D48.118	Desmoid tumor of other site
D48.119	Desmoid tumor of unspecified site
D48.19	Other specified neoplasm of uncertain behavior of connective and other soft tissue
D48.2	Neoplasm of uncertain behavior of peripheral nerves and autonomic nervous system
D48.3	Neoplasm of uncertain behavior of retroperitoneum
D48.4	Neoplasm of uncertain behavior of peritoneum
D48.5	Neoplasm of uncertain behavior of skin
D48.61	Neoplasm of uncertain behavior of right breast
D48.62	Neoplasm of uncertain behavior of left breast
D48.7	Neoplasm of uncertain behavior of other specified sites
D49.0	Neoplasm of unspecified behavior of digestive system
D49.1	Neoplasm of unspecified behavior of respiratory system
D49.2	Neoplasm of unspecified behavior of bone, soft tissue, and skin
D49.3	Neoplasm of unspecified behavior of breast
D49.4	Neoplasm of unspecified behavior of bladder
D49.511	Neoplasm of unspecified behavior of right kidney
D49.512	Neoplasm of unspecified behavior of left kidney
D49.59	Neoplasm of unspecified behavior of other genitourinary organ
D49.6	Neoplasm of unspecified behavior of brain
D49.7	Neoplasm of unspecified behavior of endocrine glands and other parts of nervous system
D49.81	Neoplasm of unspecified behavior of retina and choroid
D49.89	Neoplasm of unspecified behavior of other specified sites
D61.1	Drug-induced aplastic anemia
D63.8	Anemia in other chronic diseases classified elsewhere
D75.81	Myelofibrosis
D75.84	Other platelet-activating anti-PF4 disorders
M16.0	Bilateral primary osteoarthritis of hip
M16.11	Unilateral primary osteoarthritis, right hip
M16.12	Unilateral primary osteoarthritis, left hip

ICD-10 Code	Description
M16.31	Unilateral osteoarthritis resulting from hip dysplasia, right hip
M16.32	Unilateral osteoarthritis resulting from hip dysplasia, left hip
M16.51	Unilateral post-traumatic osteoarthritis, right hip
M16.52	Unilateral post-traumatic osteoarthritis, left hip
M16.6	Other bilateral secondary osteoarthritis of hip
M16.7	Other unilateral secondary osteoarthritis of hip
M17.0	Bilateral primary osteoarthritis of knee
M17.11	Unilateral primary osteoarthritis, right knee
M17.12	Unilateral primary osteoarthritis, left knee
M17.2	Bilateral post-traumatic osteoarthritis of knee
M17.31	Unilateral post-traumatic osteoarthritis, right knee
M17.32	Unilateral post-traumatic osteoarthritis, left knee
M17.4	Other bilateral secondary osteoarthritis of knee
M17.5	Other unilateral secondary osteoarthritis of knee
N18.32	Chronic kidney disease, stage 3b
N18.4	Chronic kidney disease, stage 4 (severe)
N18.5	Chronic kidney disease, stage 5
N18.6	End stage renal disease
Q85.01	Neurofibromatosis, type 1
Q85.02	Neurofibromatosis, type 2
Q85.03	Schwannomatosis
Q85.09	Other neurofibromatosis
Z01.818	Encounter for other preprocedural examination

Background

Erythropoietin is a naturally occurring glycoprotein hormone that stimulates the production and maturation of erythrocytes in the bone marrow. Erythrocytes are responsible for transporting oxygen from the lungs to the peripheral tissues. Erythropoietin is primarily produced and released into the bloodstream by the kidneys. Renal production of erythropoietin is stimulated when the renal oxygen sensor is triggered by hypoxia or low tissue oxygen (*Hörl 2013*).

The erythropoiesis-stimulating agents (ESAs) approved by the Food and Drug Administration (FDA) in the United States (U.S.) include Epogen (epoetin alfa), Procrit (epoetin alfa), Aranesp (darbepoetin alfa), Retacrit (epoetin alfa-epbx), and Mircera (methoxy polyethylene glycol-epoetin beta). Retacrit is the first and only FDA-approved ESA biosimilar in the U.S. The ESAs work like human protein erythropoietin, which stimulates bone marrow to make red blood cells (*FDA news release 2017*).

ESAs were first introduced in the early 1980's to provide a treatment option for anemia in patients with chronic kidney disease (CKD). Later trials indicated that ESAs were also effective in patients with chemotherapy-induced anemia; however, their use has become more controversial due to data linking ESA use to inferior survival and worse cancer outcomes (*Patnaik 2024*). Although ESAs may decrease the need for RBC transfusions, multiple meta-analyses of randomized controlled trials (RCTs) have demonstrated an increase in mortality, cardiovascular events, and cancer

progression without significant improvements in morbidity or quality of life (QoL) for patients receiving therapy (*Collister et al 2016, Grant et al 2013, Palmer et al 2014a, Tonia et al 2012*).

Clinical Evidence

Anemia in CKD

According to a Cochrane review, use of ESAs in pre-dialysis patients corrected anemia and avoided blood transfusions compared to placebo or no treatment (*Cody et al 2016*). A total of 19 studies (N = 993) evaluated ESAs, with most of the studies being published prior to 2000. ESAs improved Hemoglobin (Hb) (mean difference [MD] 1.90 g/dL; 95% confidence interval [CI], -2.34 to -1.47) and decreased the number of patients with blood transfusions (risk ratio [RR], 0.32; 95% CI, 0.12 to 0.83). No differences with the measure of kidney disease progression were observed. Endpoints of QoL and change in exercise capacity were not measured in a manner which was suitable for analysis.

The Correction of Anemia with Epoetin Alfa in Chronic Kidney Disease (CHOIR) trial was a notable trial that found that patients with CKD (n = 1432) treated to a higher target Hb (13.5 g/dL) had higher risk for the composite outcome of death, nonfatal myocardial infarction, stroke, and hospitalization for congestive heart failure (CHF) than patients treated to a lower Hb target (11.3 g/dL) (17.5 vs 13.5%; hazard ratio [HR], 1.34; 95% CI, 1.03 to 1.74; p = 0.03) (*Singh et al 2006*). Analysis of study data in the intent-to-treat (ITT) population and including all events from randomization until study termination or 30 days after the last dose showed a higher incidence of events in the high-Hb group (HR, 1.3; 95% CI, 1.01 to 1.62; p = 0.04). Even though the trial was halted early, evidence suggested that higher Hb levels led to an increased rate of adverse events (AEs). The prescribing information and warnings for all drugs of this class were updated to reflect these findings. Findings were similar to the Normal Hematocrit Study performed in patients with CKD on dialysis with CHF or ischemic heart disease (*Besarab et al 1998*).

A systematic review evaluated 9 trials comparing epoetin alfa and darbepoetin alfa for all-cause mortality in adult patients with anemia with CKD including those on dialysis (N = 2024). Duration of the trials was 20 to 52 weeks. All studies were powered to compare an anemia treatment parameter, usually Hb. None of the studies were powered for hard safety endpoints such as mortality or nonfatal cardiovascular events. Meta-analysis found no significant difference in mortality between epoetin and darbepoetin (odds ratio [OR] 1.33; 95% CI, 0.88 to 2.01) (*Wilhelm-Leen et al 2015*).

Numerous trials have evaluated extended dosing intervals of epoetin for patients with CKD. In general, larger doses given less frequently demonstrated similar outcomes with epoetin alfa and darbepoetin (*Benz et al 2007, Patel et al 2012, Pergola et al 2009, Pergola et al 2010, Provenzano et al 2004, Provenzano et al 2005, Spinowitz et al 2008a*, *Warady et al 2018*). A systematic review confirmed that various dosing frequencies of darbepoetin and epoetin resulted in similar mean final Hb values in patients receiving hemodialysis (*Hahn et al 2014*). Many of these dosing regimen studies were completed in small patient populations and open-label (OL) design. The FDA-approved dosing regimen for epoetin alfa is 3 times weekly for patients with CKD.

ESA treatment may be administered via subcutaneous (SC) or intravenous (IV) injection in patients with CKD on dialysis. Comparisons of the method of administration (IV vs SC) have been completed with epoetin and darbepoetin. In an OL German study, switching patients on dialysis from SC darbepoetin to IV administration led to stable mean Hb levels and mean weekly darbepoetin doses (*Bommer et al 2008*). Another OL study showed that switching patients on dialysis from SC epoetin to IV darbepoetin resulted in stable mean Hb levels at stable darbepoetin doses after 3 months (*Chazot et al 2009*).

In a double-blind (DB), multicenter (MC), placebo-controlled (PC), randomized clinical trial, the safety of darbepoetin in patients with type 2 diabetes mellitus, CKD, and anemia were evaluated (*Pfeffer et al 2009*). The patients had a baseline Hb level of ≤ 11 g/dL. The primary endpoint of the TREAT study was the composite of death or a non-fatal cardiovascular event (nonfatal myocardial infarction, CHF, stroke, or hospitalization for myocardial ischemia) and death or end-stage renal disease. The primary cardiovascular composite outcome of death or nonfatal cardiovascular event occurred in 632 patients (31.4%) of the darbepoetin group, and 602 patients (29.7%) treated with placebo (HR for darbepoetin vs placebo, 1.05; 95% CI, 0.94 to 1.17; p = 0.41). For the individual endpoints contributing to the composite, there were no statistically significant differences between the groups for any parameter except for fatal and non-fatal stroke which occurred more frequently with darbepoetin (5% vs 2.6%; HR, 1.92; 95% CI, 1.38 to 2.68; p < 0.001). For the composite

endpoint of death or end-stage renal disease, no significant difference was detected (darbepoetin 32.4% vs placebo 30.5%; HR, 1.06; 95% CI, 0.95 to 1.19; p = 0.29). The study was performed from 2004 to 2007, when the standard of care target Hb level was 13 g/dL. Additional notification was sent to investigators and participants of the adverse outcomes with higher Hb targets; however, the study protocol was not modified. A third-party vendor assayed Hb levels and reported the dosage adjustment necessary for patients receiving darbepoetin. At baseline, the darbepoetin group had a lower proportion of patients with a history of CHF (31.5 vs 35.2%; unadjusted p = 0.01). In summary, darbepoetin in patients with anemia, diabetes, and chronic renal disease did not increase the risk of the composite outcome of death or cardiovascular outcome and death or end-stage renal disease. It was noted that stroke, fatal or non-fatal, occurred more frequently in patients who received darbepoetin compared to placebo.

A systematic review evaluated darbepoetin and the other ESAs in 21 studies in patients with CKD for the effect on blood transfusion (*Palmer et al 2014b*). Darbepoetin reduced the need for blood transfusions compared to placebo or no treatment; however, in 3 studies comparing darbepoetin to epoetin, darbepoetin had uncertain effects on RBC transfusions and all-cause mortality compared to epoetin. Darbepoetin and Mircera were similar for risk of RBC transfusions.

A Cochrane review compared the efficacy and safety of the ESAs (Mircera, epoetin alfa, epoetin beta [not available in U.S.], darbepoetin alfa, and biosimilar ESAs) in adults with CKD. A total of 56 studies (N = 15,596) were included in the analysis. In network analyses, there was moderate to low confidence that the ESAs prevented blood transfusions compared to placebo. The authors concluded that there was insufficient evidence to suggest superiority of any ESA formulation based on available safety and efficacy data (*Palmer et al 2014a*).

A systematic review evaluated 17 studies (N = 10,049) with ESAs for effects on health-related quality of life (HRQoL) in CKD patients (*Collister et al 2016*). Higher Hb target levels (range: 10.2 to 13.6 g/dL) resulted in no statistically significant improvements in Short-Form 36 (SF-36) domains or for the Kidney Disease Questionnaire (KDQ) compared to patients on placebo or lower Hb target levels (range: 7.4 to 12 g/dL). For the KDQ, patients with higher Hb targets had an improvement of 0.5 (95% CI, -2.2 to 1.2) points in the physical symptom domain, a 0.5-point improvement in the fatigue domain (95% CI, -1.6 to 0.5), and 0.2-point improvement in the depression domain (95% CI, -1.1 to 0.8). A clinically meaningful benefit is considered a minimum of a 0.5-point improvement on the KDQ. The systematic review is consistent with the prescribing information and previously published reports.

Very few RCTs comparing darbepoetin and epoetin alfa have been published. Two non-inferiority studies comparing epoetin alfa to darbepoetin alfa in the treatment of anemia of CKD demonstrated no difference in efficacy between the 2 agents. In a study of adult patients with CKD by *Nissenson et al*, the mean changes in Hb levels from baseline to the evaluation period were similar between the darbepoetin alfa (0.16 to 0.09 g/dL) and epoetin alfa (0 to 0.06 g/dL) groups (difference, 0.16 g/dL; 95% CI, -0.06 to 0.38; p value not reported). In a second study by *Vanrenterghem et al* (N = 522) of patients with CKD on dialysis, the mean change in Hb was 0.05 g/dL in the darbepoetin alfa group compared to 0 g/dL in the epoetin alfa group (difference, 0.05 g/dL; 95% CI, -0.14 to 0.24; p values not reported). No statistically significant differences in the mean change in Hb levels from baseline, the primary endpoint, were reported. In addition, in both studies there were no differences in safety profiles, and no antibodies detected to either treatment (*Nissenson et al 2002, Vanrenterghem et al 2002*). An OL trial comparing darbepoetin SC 0.45 mcg/kg once weekly and epoetin SC 50 units/kg twice weekly found similar efficacy in achieving a Hb response and similar safety profile in 166 patients with CKD not on dialysis (*Locatelli et al 2001*).

The safety and efficacy of Mircera was established in several Phase 3, MC, OL, active-controlled trials that randomized patients with CKD with anemia to treatment with either Mircera or a comparator ESA. Four clinical trials assessed Mircera in the maintenance of Hb levels among patients currently treated with other ESAs for anemia of CKD (*Canaud et al 2008, Levin et al 2007, Spinowitz et al 2008b, Sulowicz et al 2007*). Patients were randomized to receive Mircera administered either once every 2 weeks or once every 4 weeks, or to continue their current ESA schedule and dose. Throughout the trials, treatment with Mircera consistently maintained Hb concentrations within the targeted range (10 to 13.5 g/dL) and demonstrated non-inferiority compared to other ESAs. In addition, an extension trial was conducted that demonstrated the long-term safety and efficacy of Mircera administered every 4 weeks in maintaining stable Hb levels in patients with CKD not on dialysis following correction with Mircera administered every 2 weeks (*Kessler et al 2010*).

Other direct-comparative trials have been conducted to evaluate the safety and efficacy of Mircera relative to other ESAs. In the trials, mean Hb concentrations remained constant within the recommended target range in all treatment groups and further confirmed the efficacy and safety of once monthly Mircera for treatment and maintenance of Hb (*Al-Ali et al 2015, Carrera et al 2010, Roger et al 2011*).

A systematic review compared the efficacy and tolerability of Mircera with darbepoetin alfa for the treatment of anemia in non-dialysis dependent patients (N = 1155) with CKD (*Alsalimy et al 2014*). Based on the analysis, changes in Hb level from baseline demonstrated that Mircera was clinically non-inferior to darbepoetin alfa.

Two studies evaluated Mircera for the treatment of anemia in patients with CKD who were not treated with an ESA at baseline. In the ARCTOS study, patients (N = 324) not currently receiving dialysis were randomized to Mircera administered every 2 weeks or darbepoetin alfa administered once a week for 28 weeks. Hb response rate, defined as an increase ≥ 1 g/dL vs baseline and a concentration ≥ 11 g/dL, was achieved in 97.5% of patients treated with Mircera and 96.3% of patients treated with darbepoetin alfa (*Macdougall et al 2008*). In the second study, patients who were receiving either peritoneal dialysis or hemodialysis were randomized to Mircera IV every 2 weeks or epoetin alfa or beta IV administered 3 times weekly for 24 weeks. Hb response rate was achieved in 93.3% of patients treated with Mircera and 91.3% of patients treated with epoetin (*Klinger et al 2007*). Peak Hb levels were 12.28 g/dL for Mircera and 12.19 g/dL for epoetin.

A Cochrane systematic review and meta-analysis evaluated the effect of treatment with continuous erythropoiesis receptor activator (Mircera) on health outcomes from 27 RCTs in 5410 adults with anemia and CKD, vs a different ESA (darbepoetin alfa or epoetin alfa or beta) or placebo (*Saglimbene et al 2017*). The analysis demonstrated that overall, there was low certainty evidence that Mircera had little or no effects on mortality (RR, 1.07; 95% CI, 0.73 to 1.57; RR, 1.11; 95% CI, 0.75 to 1.65), major adverse cardiovascular events (MACE) (RR, 5.09; 95% CI, 0.25 to 105.23; RR, 5.56; 95% CI, 0.99 to 31.30), need for blood transfusion (RR, 1.02; 95% CI, 0.72 to 1.46; RR, 0.94; 95% CI, 0.55 to 1.61), or additional iron therapy (RR, 1.03; 95% CI, 0.91 to 1.15; RR, 0.99; 95% CI, 0.95 to 1.03) vs epoetin alfa/beta or darbepoetin alfa, respectively. There was insufficient evidence to compare the effect of Mircera to placebo on clinical outcomes. No studies reported comparative treatment effects of different ESAs on HRQoL.

A systematic review and meta-analysis of 30 RCTs in adults with CKD did not find statistically significant differences for efficacy and safety between ESA biosimilars and their originators. Compared with ESA biosimilars, epoetin alfa did not statistically differ for any of the 10 measured outcomes (ie, blood transfusion, fatigue, breathlessness, all-cause mortality, cardiovascular mortality, MI, stroke, hypertension, vascular access thrombosis). When comparing epoetin alfa and darbepoetin alfa, darbepoetin alfa had more favorable results for blood transfusions (RR, 2.18; 95% CI, 1.31 to 3.62) (*Amato et al 2018*).

Anemia associated with chemotherapy

ESAs provided an attractive solution to decreasing the number of allogeneic blood transfusions in patients with chemotherapy-induced anemia; however, multiple meta-analyses of RCTs have demonstrated an increase in mortality, cardiovascular events, and cancer progression without improvement in morbidity or QoL for patients receiving therapy (*Collister et al 2016, Grant et al 2013, Palmer et al 2014a*). In patients with anemia due to chemotherapy, ESAs should be avoided when the anticipated outcome of chemotherapy is cure. The use of ESAs for anemia from myelosuppressive chemotherapy should be at the lowest dose to avoid RBC transfusions and should be discontinued upon the completion of chemotherapy. The Agency for Healthcare Research and Quality (AHRQ) performed an updated meta-analysis of 59 RCTs, 5 of which directly compared epoetin alfa to darbepoetin alfa in patients diagnosed with malignant disease that were anemic or at risk for anemia from chemotherapy and/or radiotherapy or the underlying malignant disease. Of the endpoints evaluated, AHRQ found that the evidence did not show any clinically significant differences between epoetin alfa and darbepoetin alfa with regard to transfusion risk (pooled RR, 1.14; 95% CI, 0.82 to 1.59; I2 = 43%; 5 trials; N = 2005), on-study mortality (pooled HR, 0.9; 95% CI, 0.67 to 1.2; I2 = 72%; 2 trials; N = 1567) and thromboembolic events (pooled RR, 0.86; 95% CI, 0.61 to 1.21; I2 = 0%; 3 trials; N = 1873). ESA therapy was associated with higher thromboembolic event rates (pooled RR, 1.51; 95% CI, 1.3 to 1.74; I2 = 0%; 37 trials; N = 12,570) and rates of on-study mortality (pooled HR, 1.17; 95% CI, 1.04 to 1.31; I2 = 0%; 37 trials; N = 11,266) compared to controls. Of the other endpoints evaluated, it was determined that the evidence was not sufficient for conclusions on effects of either epoetin

alfa or darbepoetin alfa compared to control on HRQoL, tumor response and progression, overall survival, or adverse outcomes (*Grant et al 2013*).

A systematic review assessed the effects of ESAs to either prevent or treat anemia in cancer patients with or without concurrent anti-cancer therapy. ESAs were associated with a hematological response (defined as ≥ 2 g/dL increase in Hb or ≥ 6% increase in hematocrit) compared to control (RR, 3.39; 95% CI, 3.1 to 3.71; 31 trials; N = 6413). However, there was significant heterogeneity between trials (I2 = 53%). It was noted that all trials indicated a beneficial effect of ESAs on hematological response (*Tonia et al 2012*). Other meta-analyses have reported similar findings (*Bohlius et al 2009*).

In a patient-level meta-analysis, the effectiveness of darbepoetin in improving Hb levels and reducing need for blood transfusions was evaluated in patients with chemotherapy-induced anemia with an initial Hb of ≤ 10 g/dL (*Pirker et al 2016*). Patient-level data were obtained from four Phase 3, DB, PC RCTs of darbepoetin that were 12 to 18 weeks in duration; for this analysis, data were extracted for patients with baseline Hb ≤ 10 g/dL (n = 261 for darbepoetin; n = 273 for placebo). This represented only 33% of the enrolled population. A second analysis evaluated darbepoetin only and identified 15 studies (n = 3768) without front loading and 6 studies (n = 901) with front loading. For the endpoint of Hb increase of ≥ 1 g/dL or ≥ 2 g/dL vs placebo, darbepoetin improved Hb levels (HR, 2.07; 95% CI, 1.62 to 2.63) and (HR, 2.91; 95% CI, 2.09 to 4.06), respectively. Mean time to ≥ 1 g/dL increase in Hb was 43 days (95% CI, 37 to 50) for darbepoetin and not evaluable for placebo. Median time to ≥ 2 g/dL increase was 78 days (95% CI, 71 to not evaluable) for darbepoetin and not evaluable for placebo. Transfusions were more commonly required between the start of week 5 and end of week 12 in patients who received placebo than in patients who received darbepoetin. Note that only Amgen-sponsored studies were included in this analysis, and Amgen supported the meta-analysis.

In an OL, MC, randomized non-inferiority trial, the impact of epoetin 40,000 units weekly on tumor outcomes was compared with the best supportive care for the treatment of anemia in 2098 patients receiving chemotherapy for metastatic breast cancer (*Leyland-Jones et al 2016*). The median progression-free survival (based on investigator-determined disease progression) was 7.4 months in both groups (HR, 1.089; 95% CI, 0.988 to 1.200) with the upper bound exceeding the prespecified non-inferiority margin of 1.15. There was a reduction in the number of RBC transfusions in the epoetin-treated patients vs best supportive care (5.8 vs 11.4%; $p < 0.001$), while the rate of thrombotic vascular events was higher (2.8 vs 1.4%, respectively; $p = 0.038$). Overall, the non-inferiority of treatment with epoetin was not established, and RBC transfusion was shown to be the best approach to manage anemia in patients with metastatic breast cancer receiving chemotherapy.

RCTs have shown that extended dosing intervals (e.g., every 2 weeks or every 3 weeks) of darbepoetin have achieved comparable clinical outcomes in many types of cancers compared with weekly epoetin alfa (*Glaspy et al 2006*, *Schwartzberg et al 2004, Senecal et al 2005, Steensma et al 2015*).

A randomized, DB, PC, Phase 3 non-inferiority trial (N = 2516) evaluated the long-term safety and efficacy of darbepoetin for chemotherapy-induced anemia in patients with advanced non-small cell lung cancer with a primary endpoint of overall survival. Darbepoetin and placebo were administered SC every 3 weeks to a Hb ceiling of 12.0 g/dL and were discontinued within 3 weeks after the last dose of chemotherapy, or upon disease progression, whichever occurred first. The study was stopped early (median duration of follow up, 30 months for darbepoetin and 33 months for placebo) with results demonstrating non-inferiority of darbepoetin vs placebo for overall survival (HR, 0.92; 95% CI, 0.83 to 1.01). Darbepoetin also showed superiority to placebo in reducing the incidence of RBC transfusions or Hb ≤ 8.0 g/dL from week 5 to the end of the treatment period (*Gascón et al 2020*).

A systematic review of 17 RCTs evaluated the effectiveness of ESAs in treating cancer-related anemia, the overall risk of cardiovascular events, and the overall impact on prognosis (e.g., overall survival). While ESAs increased Hb and reduced the need for blood transfusions, there was no demonstrated benefit in overall survival, even with an increased association of cardiovascular AEs compared to placebo. The review also noted higher rates of cardiovascular AEs in patients with uncontrolled hypertension and aggressive ESA dosing (*Rao et al 2021*).

Anemia associated with zidovudine in patients with HIV

Early trials with epoetin in HIV were performed when zidovudine was one of only a few antiretrovirals available for treatment of HIV. Since the late 1980's and 1990's, numerous antiretroviral treatment options have become available

and resulted in limited use of zidovudine. A meta-analysis of 4 small, DB, RCTs evaluated the efficacy and safety of epoetin compared to placebo in improving hematocrit values in patients with HIV or acquired immunodeficiency syndrome (AIDS) (*Henry et al 1992*). In the 12-week trials, epoetin significantly increased hematocrit from baseline compared to placebo in patients with an endogenous erythropoietin level of ≤ 500 IU/L (mean change, 4.6 vs 0.5, respectively; p = 0.0002; MD, 3.9; 95% CI, 1.8 to 6.0). A meta-analysis of 6 randomized, clinical trials with 537 patients evaluated the risk of death associated with epoetin or placebo in patients with HIV or AIDS and anemia (*Martí-Carvajal et al 2011*). None of the included studies evaluated death as a primary outcome. The risk of death was not statistically significant for epoetin vs placebo or when comparing epoetin once weekly vs 3 times weekly. Studies had significant attrition bias.

Reduced need for transfusions associated with surgery

Clinical trials have evaluated the use of epoetin in reducing the need for blood transfusions in adults undergoing elective surgeries (*de Andrade et al 1996, Faris et al 1996, Goldberg et al 1996, Zhao et al 2016*). Epoetin is associated with an increased risk of deep venous thrombosis; therefore, appropriate preventative measures should be utilized. In a DB, MC, PC trial, the efficacy and safety of epoetin 300 units/kg and 100 units/kg were compared to placebo in 316 adult patients scheduled for elective orthopedic surgery. The primary outcome was the rate of transfusion which was significantly lower in patients receiving epoetin 300 units/kg with a pretreatment Hb of > 10 to ≤ 13 g/dL (epoetin 300 units/kg,16%; epoetin 100 units/kg, 23%; placebo, 45%; p = 0.024) (*de Andrade et al 1996*).

Epoetin has been shown to reduce the need for blood transfusions in 200 patients undergoing elective orthopedic surgeries compared to placebo (*Faris et al 1996*). Epoetin 100 units/kg/day (17%) and epoetin 300 units/kg/day (25%) led to a reduction in the percentage of patients who required a blood transfusion following a major elective orthopedic surgery compared to control (54%; p ≤ 0.001 for both epoetin groups vs placebo). There was no significant difference between the 2 epoetin groups (p value not reported). The mean number of units transfused for each patient was significantly lower in the epoetin groups compared to the placebo group (epoetin 100 units/kg/day, 0.37 ± 0.96; epoetin 300 units/kg/day, 0.58 ± 1.15; placebo, 1.42 ± 1.67; p < 0.01 for both epoetin groups compared to placebo). There was no significant difference between the epoetin groups (p > 0.05).

A meta-analysis of 7 studies (N = 2439) was conducted to evaluate the efficacy and safety of treatment with erythropoietin compared with controls (placebo or no intervention) in patients undergoing total hip or knee arthroplasty (*Voorn et al 2016*). Erythropoietin was shown to reduce exposure to RBC transfusion in both hip (RR, 0.45; 95% CI, 0.33 to 0.61) and knee (RR, 0.38; 95% CI, 0.27 to 0.53) arthroplasty, without differences between indications (p = 0.44), and the mean number of transfused RBC units was decreased in erythropoietin-treated patients (MD, -0.57; 95% CI -0.86 to -0.29) for both indications. There were no differences detected in thromboembolic and vascular AEs (RR, 1.14; 95% CI, 0.71 to 1.84), nor other AEs (RR, 1.01; 95% CI, 0.94 to 1.01) between erythropoietin compared with controls.

A systematic review and meta-analysis of 15 RCTs (N = 2155) was performed to evaluate the hematopoiesis-promoting effect and potential complications of preoperative use of erythropoietin in patients scheduled for total hip or knee arthroplasty (*Zhao et al 2016*). Preoperative use of erythropoietin was associated with lower exposure to allogeneic blood transfusion (OR = 0.41) and higher Hb concentration after surgery (standardized MD, 0.86; p < 0.001). Complications were not generally reported, but there was no significant difference between the group with and without erythropoietin based on given data.

Place in Therapy

CKD

The Kidney Disease Improving Global Outcomes (KDIGO) guidelines suggest that ESAs not be used to maintain Hb concentration > 11.5 g/dL in adults with CKD. In all adult patients, ESAs should not be used to increase Hb concentrations > 13 g/dL (*KDIGO 2012*). Current practice guidelines for anemia of CKD do not specify a preferred agent. The guidelines recommend that 'copy' versions of ESAs should only be those which have been designated true biosimilars. An update to the 2012 guideline is in progress (*KDIGO 2012*).

The National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) reference the 2010 KDIGO practice guidelines for anemia in CKD as current (*National Kidney Foundation Web site*).

In June 2011, the FDA released more conservative recommendations for using the ESAs in patients with anemia of CKD resulting from data showing that using ESAs to target a Hb level of > 11 g/dL increased the risk of cardiovascular events, without providing any additional benefit to patients (*FDA Drug Safety Communication 2011*). For patients with anemia of CKD who are not on dialysis, ESA treatment can be considered when the Hb level is < 10 g/dL, and the dose should be reduced or interrupted when Hb exceeds 10 g/dL. For patients with anemia of CKD currently on dialysis, ESA treatment should be initiated when the Hb level is < 10 g/dL and the dose should be reduced or interrupted when Hb approaches or exceeds 11 g/dL.

The KDOQI US Commentary on the 2012 KDIGO guidelines state that KDOQI endorses the FDA-recommended upper cutoff of 11 g/dL (*Kliger et al 2013*).

The European Renal Best Practice guidelines state that the Hb target range in patients with CKD should be 11 to 12 g/dL, ESAs should not be used to maintain Hb > 11.5 g/dL, and Hb should not exceed 13 g/dL (*Locatelli et al 2009, Locatelli et al 2010, Locatelli et al 2013)*. Continuous erythropoiesis receptor activator (Mircera), a modified recombinant human erythropoietin, has a considerably longer half-life than other ESAs and should be dosed once every 2 weeks for anemia correction and once every 4 weeks for maintenance of Hb levels. The safety and tolerability of continuous erythropoiesis receptor activator are similar to that of other ESAs. A lower Hb target range of 10 to 12 g/dL is reasonable in nondialysis patients with type 2 diabetes. In initiating and maintaining ESA therapy, the potential benefits of reducing blood transfusions and anemia-related symptoms should be balanced against the risks of harm in individual patients (e.g., stroke, vascular access loss, or hypertension). ESAs should be used with great caution, if at all, in CKD patients with active malignancy, in particular when cure is the anticipated outcome, or with a history of stroke or malignancy. The lowest possible ESA dose should be used to reach the Hb target.

Chemotherapy-associated anemia

The National Comprehensive Cancer Network (NCCN) guidelines for the management of cancer and chemotherapy-induced anemia recommends considering ESAs (e.g., epoetin alfa, epoetin alfa-epbx or darbepoetin alfa) for special categories including patients with cancer and moderate to severe CKD, and patients undergoing palliative treatment who have anemia while on myelosuppressive chemotherapy. In patients undergoing palliative treatment, if no other cause of anemia has been identified, RBC transfusion or clinical trial is recommended first; upon the decision to use an ESA, the lowest dose needed to eliminate symptoms and avoid transfusion is recommended. In patients with CKD and a curable solid tumor, ESAs should not be used during chemotherapy. NCCN does not support the use of ESAs in patients with cancer not receiving therapy or receiving non-myelosuppressive therapy due to lack of evidence in these populations (*NCCN 2024*).

The American Society of Clinical Oncology (ASCO)/American Society of Hematology (ASH) recommendations for use of ESAs in patients with cancer state that although ESAs reduce the need for transfusions in anemic patients with cancer receiving chemotherapy, they are associated with increased complications such as higher mortality, increased risk of thromboembolic and cardiovascular events, and reports of increased risk of cancer progression or recurrence. ESAs (including biosimilars) may be offered to patients with chemotherapy-associated anemia whose cancer treatment is not curative in intent with a Hb < 10 g/dL. RBC transfusion is also an option. ESAs may be offered to patients with low-risk myelodysplastic syndrome and low serum erythropoietin levels who are not receiving chemotherapy. Epoetin beta and alfa, darbepoetin, and biosimilar epoetin alfa are considered to be equivalent with respect to effectiveness and safety (*Bohlius et al 2019*).

Perioperative Use of ESA

Literature supports the use of ESAs with or without iron, as ESAs are effective in reducing the number of patients requiring allogeneic blood transfusions and reducing the volume of allogenic blood transfused (*American Society of Anesthesiologists Task Force 2015*) (Category A1-B evidence – supported by a sufficient number of randomized clinical trials to conduct a meta-analysis and supported by membership opinion). Insufficient evidence exists to evaluate the

efficacy of ESA with iron compared to ESA without iron. ESAs with or without iron may be given, when possible, to reduce the need for allogeneic blood transfusions in selected patient populations such as renal insufficiency, ACD, or cases of refusal of transfusion.

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Aranesp is an erythropoiesis-stimulating agent (ESA) indicated for the treatment of anemia due to:

- Chronic Kidney Disease (CKD) in patients on dialysis and patients not on dialysis.
- The effects of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy.

Epogen is an erythropoiesis-stimulating agent (ESA) indicated for:

- Treatment of anemia due to
  - Chronic Kidney Disease (CKD) in patients on dialysis and not on dialysis.
  - Zidovudine in patients with HIV-infection.
  - The effects of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy.
- Reduction of allogeneic RBC transfusions in patients undergoing elective, noncardiac, nonvascular surgery.

Mircera is an erythropoiesis-stimulating agent (ESA) indicated for the treatment of anemia associated with chronic kidney disease (CKD) in:

- adult patients on dialysis and adult patients not on dialysis.
- pediatric patients 3 months to 17 years of age on dialysis or not on dialysis who are converting from another ESA after their hemoglobin level was stabilized with an ESA.

Procrit is an erythropoiesis-stimulating agent (ESA) indicated for:

- Treatment of anemia due to
  - Chronic Kidney Disease (CKD) in patients on dialysis and not on dialysis.
  - Zidovudine in patients with HIV-infection.
  - The effects of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy.
- Reduction of allogeneic RBC transfusions in patients undergoing elective, noncardiac, nonvascular surgery.

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Policy History/Revision Information

Date	Summary of Changes
12/13/2023	Approved by OptumRx P&T Committee
11/21/2024	Annual Review. Updated references. Updated age requirement criteria for Mircera due to updated indication.

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. The insurance reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

OptumRx may also use tools developed by third parties to assist us in administering health benefits. OptumRx Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

Archived Policy Versions (Internal Only)

Effective Date	Policy Number	Policy Title
mm/dd/yyyy – mm/dd/yyyy	######	Title of Policy Hyperlinked to KL or Other Internal Location

Nondiscrimination & Language Access Policy

Discrimination is Against the Law. Aspirus Health Plan, Inc. complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex, (including sex characteristics, including intersex traits; pregnancy or related conditions; sexual orientation, gender identity and sex stereotypes), consistent with the scope of sex discrimination described at 45 CFR § 92.101(a)(2). Aspirus Health Plan, Inc. does not exclude people or treat them less favorably because of race, color, national origin, age, disability, or sex.

Aspirus Health Plan, Inc.:
Provides people with disabilities reasonable modifications and free appropriate auxiliary aids and services to communicate effectively with us, such as:

- Qualified sign language interpreters.
- Written information in other formats (large print, audio, accessible electronic formats, other formats).

Provides free language assistance services to people whose primary language is not English, which may include:

- Qualified interpreters.
- Information written in other languages.

If *you* need reasonable modifications, appropriate auxiliary aids and services, or language assistance services, contact the Nondiscrimination Grievance Coordinator at the address, phone number, fax number, or email address below.

If *you* believe that Aspirus Health Plan, Inc. has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, *you* can file a *grievance* with:

Nondiscrimination Grievance Coordinator
Aspirus Health Plan, Inc.
PO Box 1890
Southampton, PA 18966-9998
Phone: 1-866-631-5404 (TTY: 711)
Fax: 763-847-4010
Email: customerservice@aspirushealthplan.com

You can file a *grievance* in person or by mail, fax, or email. If *you* need help filing a *grievance*, the Nondiscrimination Grievance Coordinator is available to help *you*.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1.800.368.1019, 800.537.7697 (TDD)

Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html. This notice is available at Aspirus Health Plan, Inc.'s website: https://aspirushealthplan.com/webdocs/70021-AHP-NonDiscrim_Lang-Assist-Notice.pdf.

Language Assistance Services

Albanian: KUJDES: Nëse flitni shqip, për ju ka në dispozicion shërbime të asistencës gjuhësore, pa pagesë.Telefononi në 1-800-332-6501 (TTY: 711).

Arabic تنبيه: إذا كنت تتحدث اللغة العربية، فإن خدمات المساعدة اللغوية متاحة لك مجاناً. اتصل بن اعلى رقم الهاتف1-800-332-6501(رقم هاتف الصم والبك : 711)

French: ATTENTION: Si vous parlez français, des services d'aide linguistique vous sont proposés gratuitement. Appelez le 1-800-332-6501 (ATS: 711).

German: ACHTUNG: Wenn Sie Deutsch sprechen, stehen Ihnen kostenlos sprachliche Hilfsdienstleistungen zurVerfügung. Rufnummer: 1-800-332-6501 (TTY: 711).

Hindi: _यान द_: य_द आप ि हंदी बोलते ह_ तो आपके ि लए मु_त म_ भाषा सहायता सेवाएं उपल_ध ह_।1-800-332-6501 (TTY: 711) पर कॉल कर_।

Hmong: LUS CEEV: Yog tias koj hais lus Hmoob, cov kev pab txog lus, muaj kev pab dawb rau koj. Hu rau 1-800-332-6501 (TTY: 711).

Korean: 주의: 한국어를 사용하시는 경우, 언어 지원 서비스를 무료로 이용하실 수 있습니다.1-800-332-6501 (TTY: 711)번으로 전화해 주십시오.

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Vietnamese: CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 1-800-332-6501 (TTY: 711).

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Lao: ໂປດຊາບ: ຖ້າວ່າ ທ່ານເວົ້າພາສາ ລາວ, ການບໍລິການຊ່ວຍເຫຼືອດ້ານພາສາ,ໂດຍບໍ່ເສັງຄ່າ, ແມ່ນມີພ້ອມໃຫ້ທ່ານ. ໂທຣ 1-800-332-6501 (TTY: 711).

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