Erythropoietin Stimulating Agent (ESA)

Guideline Number: MPG103.07
Approval Date: November 10, 2021

Table of Contents
- Policy Summary ......................................................... 1
- Applicable Codes ....................................................... 2
- References ................................................................. 2
- Guideline History/Revision Information ....................... 4
- Purpose .......................................................................... 4
- Terms and Conditions .................................................. 5

Policy Summary

Overview
Erythropoietin is a specialized cytokine that is produced by the kidneys and stimulates the proliferation of red blood cells in the bone marrow. Erythropoietin is released into the blood stream in response to hypoxia. In response to the hypoxia, erythropoietin interacts with the progenitor cells to increase the production of red blood cells. An erythropoietin stimulating agent (ESA) is an analog of erythropoietin. ESAs are biologically engineered hormones produced by recombinant DNA technology. Erythropoietin analogs contain the identical amino acid sequence as naturally occurring erythropoietin and have the same biological effect. A number of chronic conditions, especially chronic renal failure, result in decreased production of or relative resistance to erythropoietin often causing anemia. Supplementation by synthetic drugs with structures identical or similar to naturally occurring erythropoietin has been proven safe and effective in correcting anemia in certain groups of patients. Both erythropoietin and ESAs stimulate the bone marrow to form new red blood cells. They are used to treat anemia by elevating or maintaining the red blood cell level (as demonstrated by the hematocrit and/or hemoglobin levels), therefore decreasing anemia and the need for transfusions.

Guidelines
Section 153b of the Medicare Improvements for Patients and Providers (MIPPA) requires the implementation of End Stage Renal Disease Prospective Payment System (ESRD PPS). It requires that all drugs and biologicals used in the treatment of End Stage Renal Disease (ESRD) be provided and billed by the ESRD facility. When a drug or biological is billed by providers other than the ESRD facility and the drug or biological furnished is designated as a drug or biological that is included in the ESRD PPS (renal dialysis service), the claim will be rejected or denied. In the event that a drug or biological generally used in the treatment of ESRD was furnished to an ESRD beneficiary for reasons other than for the treatment of ESRD, please refer to the Medicare Claims Processing Manual, Publication 100-02, Chapter 8. With the implementation of the ESRD PPS, ESRD-related EPO is included in ESRD PPS payment amount and is not separately payable on Part B claims, as outlined in the manual.

CMS Publication 100-02, Medicare Benefit Policy Manual, Chapter 11, Section 20.3 states: Erythropoiesis stimulating agents (ESAs), such as epoetin alfa and darbepoetin alfa, when furnished to Medicare ESRD patients are always considered to be renal dialysis services and included in the ESRD PPS.
Indications and Limitations
Please see the FDA drug label for the FDA approved indications and dosages. This can be accessed at: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm. Additionally, coverage indications and limitations vary by LCD. Refer to the appropriate LCDs for specific individual state coverage guidelines.

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 guideline 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.

<table>
<thead>
<tr>
<th>HCPCS Code</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>J0881</td>
<td>Injection, darbepoetin alfa, 1 mcg (non-ESRD use) (refer to the Medicare Advantage Policy Guideline titled 'Erythropoiesis Stimulating Agents (ESAs) in Cancer and Related Neoplastic Conditions (NCD 110.21)')</td>
</tr>
<tr>
<td>J0882</td>
<td>Injection, darbepoetin alfa, 1 mcg (for ESRD on dialysis)</td>
</tr>
<tr>
<td>J0885</td>
<td>Injection, epoetin alfa, (for non-ESRD use), 1000 units (refer to the Medicare Advantage Policy Guideline titled 'Erythropoiesis Stimulating Agents (ESAs) in Cancer and Related Neoplastic Conditions (NCD 110.21)')</td>
</tr>
<tr>
<td>J0887</td>
<td>Injection, epoetin beta, 1 microgram, (for ESRD on dialysis)</td>
</tr>
<tr>
<td>J0888</td>
<td>Injection, epoetin beta, 1 microgram, (for non-ESRD use)</td>
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<tr>
<td>J0890</td>
<td>Injection, peginesatide, 0.1 mg (for ESRD on dialysis) (FDA recalled 02/23/2013)</td>
</tr>
<tr>
<td>Q4081</td>
<td>Injection, epoetin alfa, 100 units (for ESRD on dialysis)</td>
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<tr>
<td>Q5105</td>
<td>Injection, epoetin alfa-epbx, biosimilar, (Retacrit) (for ESRD on dialysis), 100 units</td>
</tr>
<tr>
<td>Q5106</td>
<td>Injection, epoetin alfa-epbx, biosimilar, (Retacrit) (for non-ESRD use), 1000 units (refer to the Medicare Advantage Policy Guideline titled 'Erythropoiesis Stimulating Agents (ESAs) in Cancer and Related Neoplastic Conditions (NCD 110.21)')</td>
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<table>
<thead>
<tr>
<th>Modifier</th>
<th>Description</th>
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<tbody>
<tr>
<td>EA</td>
<td>Erythropoietic stimulating agent (ESA) administered to treat anemia due to anticancer chemotherapy</td>
</tr>
<tr>
<td>EB</td>
<td>Erythropoietic stimulating agent (ESA) administered to treat anemia due to anticancer radiotherapy</td>
</tr>
<tr>
<td>EC</td>
<td>Erythropoietic stimulating agent (ESA) administered to treat anemia not due to anticancer radiotherapy or anticancer chemotherapy</td>
</tr>
<tr>
<td>JA</td>
<td>Administered intravenously</td>
</tr>
<tr>
<td>JB</td>
<td>Administered subcutaneously</td>
</tr>
<tr>
<td>JE</td>
<td>Administered via dialysate</td>
</tr>
</tbody>
</table>

References

CMS National Coverage Determinations (NCDs)

NCD 110.21 Erythropoiesis Stimulating Agents (ESAs) in Cancer and Related Neoplastic Conditions
CMS Local Coverage Determinations (LCDs) and Articles

<table>
<thead>
<tr>
<th>LCD</th>
<th>Article</th>
<th>Contractor</th>
<th>Medicare Part A</th>
<th>Medicare Part B</th>
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</thead>
<tbody>
<tr>
<td>L34356 Erythropoiesis Stimulating Agents (ESA)</td>
<td>A56462 Billing and Coding: Erythropoiesis Stimulating Agents (ESA)</td>
<td>CGS</td>
<td>KY, OH</td>
<td>KY, OH</td>
</tr>
<tr>
<td>L36276 Erythropoiesis Stimulating Agents</td>
<td>A57628 Billing and Coding: Erythropoiesis Stimulating Agents</td>
<td>First Coast</td>
<td>FL, PR, VI</td>
<td>FL, PR, VI</td>
</tr>
<tr>
<td>L34633 Erythropoiesis Stimulating Agents</td>
<td>A56795 Billing and Coding: Erythropoiesis Stimulating Agents (ESAs)</td>
<td>WPS</td>
<td>AK, AL, AR, AZ, CA, CO, CT, DE, FL, GA, HI, IA, ID, IL, IN, KS, KY, LA, MA, MD, ME, MI, MO, MS, MT, NC, ND, NE, NH, NJ, NM, NV, OH, OK, OR, PA, RI, SC, SD, TN, TX, UT, VA, VT, WA, WI, WV, WY</td>
<td>IA, KS, MO, NE, IN, MI</td>
</tr>
</tbody>
</table>

CMS Benefit Policy Manual
Chapter 1 Inpatient Hospital Services Covered Under Part A
Chapter 6; § 30 Drugs and Biologicals
Chapter 11 End Stage Renal Disease (ESRD)
Chapter 15; § 50 Drugs and Biologicals

CMS Claims Processing Manual
Chapter 6 SNF Inpatient Part A Billing and SNF Consolidated Billing
Chapter 8 Outpatient ESRD Hospital, Independent Facility, and Physician/Supplier Claims
Chapter 17 Drugs and Biologicals

CMS Transmittals
Transmittal 10566, Change Request 12027, Dated January 14, 2021 (International Classification of Diseases, 10th Revision (ICD-10) and Other Coding Revisions to National Coverage Determination (NCDs)—April 2021)
Transmittal 10920, Change Request 12307, Dated August 10, 2021 (Quarterly Update to the End-Stage Renal Disease Prospective Payment System (ESRD PPS))
Transmittal 2365, Change Request 11244, Dated September 27, 2019 (Discontinuing the Erythropoietin Stimulating Agent (ESA) Monitoring Policy System Edits under the End Stage Renal Dialysis Prospective Payment System (ESRD PPS))

MLN Matters
Article MM10624, Quarterly Healthcare Common Procedure Coding System (HCPCS) Drug/Biological Code Changes – July 2018 Update
Article MM11134, International Classification of Diseases, 10th Revision (ICD-10) and Other Coding Revisions to National Coverage Determination (NCDs), July 1, 2019
Article MM12027, International Classification of Diseases, 10th Revision (ICD-10) and Other Coding Revisions to National Coverage Determination (NCDs)—April 2021
Article MM12307, Quarterly Update to the End-Stage Renal Disease Prospective Payment System (ESRD PPS)—October 4, 2021

UnitedHealthcare Commercial Policy
Erythropoiesis-Stimulating Agents
Others

CMS Medicare Part B ASP Drug Pricing Files
End Stage Renal Disease (ESRD) Prospective Payment System (PPS)
ESRD PPS Consolidated Billing
FDA label for Retacrit (epoetin alfa-epbx) injection
Federal Register: Takeda Pharmaceuticals U.S.A., Inc.; Withdrawal of Approval of a New Drug Application for Omontys (peginesatide) Injection

Medicare Prescription Drug Benefit Manual, Chapter 6, Appendix C - Medicare Part B versus Part D Coverage Issues
Proposed Decision Memo for Erythropoiesis Stimulating Agents (ESAs) for non-renal disease indications (CAG-00383N)
UnitedHealthcare Medicare Advantage Medical Benefit Injectable Policy: Medicare Part B Step Therapy Programs

Guideline History/Revision Information

Revisions to this summary document do not in any way modify the requirement that services be provided and documented in accordance with the Medicare guidelines in effect on the date of service in question.

<table>
<thead>
<tr>
<th>Date</th>
<th>Policy Summary</th>
<th>Summary of Changes</th>
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<tbody>
<tr>
<td>11/10/2021</td>
<td>Added language to indicate: o Section 153b of the Medicare Improvements for Patients and Providers (MIPPA) requires the implementation of End Stage Renal Disease Prospective Payment System (ESRD PPS) ▪ It requires that all drugs and biologicals used in the treatment of End Stage Renal Disease (ESRD) be provided and billed by the ESRD facility ▪ When a drug or biological is billed by providers other than the ESRD facility and the drug or biological furnished is designated as a drug or biological that is included in the ESRD PPS (renal dialysis service), the claim will be rejected or denied ▪ In the event that a drug or biological generally used in the treatment of ESRD was furnished to an ESRD beneficiary for reasons other than for the treatment of ESRD, please refer to the Medicare Claims Processing Manual, Publication 100-02, Chapter 8 ▪ With the implementation of the ESRD PPS, ESRD-related EPO is included in ESRD PPS payment amount and is not separately payable on Part B claims, as outlined in the manual o Centers for Medicare &amp; Medicaid (CMS) Publication 100-02, Medicare Benefit Policy Manual, Chapter 11, Section 20.3 states: Erythropoiesis stimulating agents (ESAs), such as epoetin alfa and darbepoetin alfa, when furnished to Medicare ESRD patients are always considered to be renal dialysis services and included in the ESRD PPS</td>
<td></td>
</tr>
</tbody>
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Applicable Codes

- Revised description for HCPCS codes Q5105 and Q5106

Supporting Information

- Updated References section to reflect the most current information
- Archived previous policy version MPG103.06

Purpose

The Medicare Advantage Policy Guideline documents are generally used to support UnitedHealthcare Medicare Advantage claims processing activities and facilitate providers’ submission of accurate claims for the specified services. The document can be used as a guide to help determine applicable:
- Medicare coding or billing requirements, and/or
- Medical necessity coverage guidelines; including documentation requirements.

UnitedHealthcare follows Medicare guidelines such as NCDs, LCDs, LCAs, and other Medicare manuals for the purposes of determining coverage. It is expected providers retain or have access to appropriate documentation when requested to support
coverage. Please utilize the links in the References section below to view the Medicare source materials used to develop this resource document. This document is not a replacement for the Medicare source materials that outline Medicare coverage requirements. Where there is a conflict between this document and Medicare source materials, the Medicare source materials will apply.

**Terms and Conditions**

The Medicare Advantage Policy Guidelines are applicable to UnitedHealthcare Medicare Advantage Plans offered by UnitedHealthcare and its affiliates.

These Policy Guidelines are provided for informational purposes, and do not constitute medical advice. Treating physicians and healthcare providers are solely responsible for determining what care to provide to their patients. Members should always consult their physician before making any decisions about medical care.

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 member specific benefit plan document identifies which services are covered, which are excluded, and which are subject to limitations. In the event of a conflict, the member specific benefit plan document supersedes the Medicare Advantage Policy Guidelines.

Medicare Advantage Policy Guidelines are developed as needed, are regularly reviewed and updated, and are subject to change. They represent a portion of the resources used to support UnitedHealthcare coverage decision making. UnitedHealthcare may modify these Policy Guidelines at any time by publishing a new version of the policy on this website. Medicare source materials used to develop these guidelines include, but are not limited to, CMS National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), Medicare Benefit Policy Manual, Medicare Claims Processing Manual, Medicare Program Integrity Manual, Medicare Managed Care Manual, etc. The information presented in the Medicare Advantage Policy Guidelines is believed to be accurate and current as of the date of publication and is provided on an "AS IS" basis. Where there is a conflict between this document and Medicare source materials, the Medicare source materials will apply.

You are responsible for submission of accurate claims. Medicare Advantage Policy Guidelines are intended to ensure that coverage decisions are made accurately based on the code or codes that correctly describe the health care services provided. UnitedHealthcare Medicare Advantage Policy Guidelines use Current Procedural Terminology (CPT®), Centers for Medicare and Medicaid Services (CMS), or other coding guidelines. References to CPT® or other sources are for definitional purposes only and do not imply any right to reimbursement or guarantee claims payment.

Medicare Advantage Policy Guidelines are the property of UnitedHealthcare. Unauthorized copying, use, and distribution of this information are strictly prohibited.

*For more information on a specific member's benefit coverage, please call the customer service number on the back of the member ID card or refer to the Administrative Guide.