

Thrombolytic Agents

Guideline Number: MPG308.06
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[↪ Terms and Conditions](#)

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<p>Related Medicare Advantage Reimbursement Policy</p> <ul style="list-style-type: none"> Discarded Drugs and Biologicals Policy, Professional
<p>Related Medicare Advantage Coverage Summary</p> <ul style="list-style-type: none"> Medications/Drugs (Outpatient/Part B)

Policy Summary

[↪ See Purpose](#)

Overview

Thrombosis is the formation of a blood clot (thrombus). It is an important part of the normal hemostatic response that limits hemorrhage caused by microscopic or macroscopic vascular injury. Even when a blood vessel is not injured, blood clots may form in the body under certain conditions. Physiologic thrombosis is counterbalanced by intrinsic antithrombotic properties and fibrinolysis.

The 3 main components of a blood clot are platelets (thrombocytes), thrombin, and fibrin; each of these components is a key therapeutic target. During thrombus formation, circulating prothrombin is activated to the active clotting factor, thrombin, by activated platelets. Fibrinogen is activated to fibrin by the newly activated thrombin. Fibrin is then formed into the fibrin matrix. All this takes place while platelets are being adhered and aggregated.

Fibrin-bound plasminogen will be converted by thrombolytic drugs to plasmin, the rate-limiting step in thrombolysis.

It should be kept in mind that the thrombolysis process works best on recently formed thrombi. Older thrombi have extensive fibrin polymerization that makes them more resistant to thrombolysis; hence, the importance of time for thrombolytic therapy.

Guidelines

As published in [Medicare Program Integrity Manual Chapter 13 §13.5.4](#), in order to be covered, a service shall be reasonable and necessary.

Drugs and biologicals must be determined to meet the statutory definition under the statute [§1861\(t\)\(1\)](#).

[Medicare Benefit Policy Manual - Pub. 100-02, Chapter 15, Section 50](#), describes national policy regarding Medicare guidelines for coverage of drugs and biologicals.

Injection of thrombolytic agents is eligible for payment for the following indications:

- Treatment of acute arterial thrombosis (other than coronary or intracranial)
Treatment Recommendation Guidelines*:

- Acute leg ischemia is one of the most challenging and dangerous conditions in vascular surgical practice and carries a high risk of amputation and death when left untreated. Catheter-directed thrombolysis (CDT) can be considered a complementary and not a competing technology with surgical or percutaneous revascularization, with an acceptably low complication rate.
 - Patients with limb-threatening ischemia are not candidates for local fibrinolysis, which usually takes between 6 and 72 hours to achieve clot lysis. These patients require emergency embolectomy. CDT is reserved for patients with non-life-threatening limb ischemia due to in situ thrombosis of less than 14 days' duration. Consider that patients with thrombosis of more than 30 days' duration are not likely to respond to local fibrinolysis.
 - In patients with acute limb ischemia due to arterial emboli or thrombosis, it is suggested to administer immediate systemic anticoagulation with unfractionated heparin over no anticoagulation; it is suggested to administer reperfusion therapy (surgery or intraarterial thrombolysis) over no reperfusion therapy; it is recommended to perform surgery over intraarterial thrombolysis. In patients undergoing intraarterial thrombolysis, it is suggested to administer recombinant tissue-type plasminogen activator (rt-PA) or urokinase over streptokinase.
- Treatment of acute ischemic stroke
Treatment Recommendation Guidelines* :
 - Intravenous Recombinant Tissue Plasminogen Activator (IV r-tPA) for Acute Ischemic Stroke:
In patients with acute ischemic stroke in whom treatment can be initiated within 3 hours of symptom onset, it is recommended to administer IV r-tPA over no IV r-tPA. In patients with acute ischemic stroke in whom treatment can be initiated within 4.5 but not within 3 hours of symptom onset, it is suggested to administer IV r-tPA over no IV r-tPA. In patients with acute ischemic stroke in whom treatment cannot be initiated within 4.5 hours of symptom onset, recommendations are against IV r-tPA.
 - Intraarterial (IA) Thrombolysis in Acute Ischemic Stroke:
In patients with acute ischemic stroke due to proximal cerebral artery occlusions (i.e., internal carotid artery, middle cerebral artery (MCA), vertebral artery, and basilar artery) who do not meet eligibility criteria for treatment with IV r-tPA, it is suggested to administer IA r-tPA initiated within 6 hours of symptom onset over no IA r-tPA.
 - In patients with acute ischemic stroke it is suggested to administer IV r-tPA over the combination IV/IA r-tPA.
- Treatment of acute pulmonary thromboembolism
Treatment Recommendation Guidelines* :
 - In patients with acute pulmonary embolism (PE) associated with hypotension (e.g., systolic BP < 90 mm Hg) who do not have a high bleeding risk, it is suggested to provide systemically administered thrombolytic therapy over no such therapy.
 - In most patients with acute PE not associated with hypotension, it is recommended against systemically administered thrombolytic therapy.
 - In selected patients with acute PE not associated with hypotension and with a low bleeding risk whose initial clinical presentation, or clinical course after starting anticoagulant therapy, suggests a high risk of developing hypotension, it is suggested to administer thrombolytic therapy.
 - In selected patients with acute PE associated with hypotension in a high bleeding risk patient, (for example, acute post op status of major surgery, recent trauma with surgery, recent ischemic stroke, recent GI bleed) catheter directed therapy with thrombolytics may be used if the appropriate expertise and resources are available.
 - In patients with acute PE, when a thrombolytic agent is used, it is suggested to provide short infusion times (e.g., a 2-hour infusion) over prolonged infusion times (e.g., a 24-hour infusion).
 - In patients with acute PE when a thrombolytic agent is used, it is suggested to provide administration through a peripheral vein over a pulmonary artery catheter unless special circumstances as above are noted.
- Treatment of thrombosed vascular prosthetic devices, implants and grafts
- Treatment of iliofemoral deep vein thrombosis
Treatment Recommendation Guidelines* :
 - In patients with acute proximal deep vein thrombosis (DVT) of the leg, it is suggested to administer anticoagulant therapy alone over systemic thrombolysis.
 - It is believed that systemic thrombolysis should be considered only in patients who meet all of the following criteria:
 - Ilio-femoral DVT, symptoms for < 14 days, good functional status, life expectancy of ≥1 year, and low risk of bleeding. Based on low-quality evidence of greater effectiveness and less bleeding, if resources and expertise are available to

perform CDT, it is considered the preferable approach. Because the balance of risks and benefits with systemic thrombolysis is uncertain, and particularly because of concerns about major bleeding, anticoagulant therapy alone is an acceptable alternative to systemic thrombolysis in all patients with acute DVT who do not have impending venous gangrene.

- Treatment of acute ST segment elevation myocardial infarction (STEMI)

Treatment Recommendation Guidelines*:

- In the absence of contraindications, fibrinolytic therapy should be administered to patients with STEMI at non-percutaneous coronary intervention (PCI)-capable hospitals when the anticipated First Medical Contact (FMC)-to-device time at a PCI-capable hospital exceeds 120 minutes because of unavoidable delays.
- When fibrinolytic therapy is indicated or chosen as the primary reperfusion strategy, it should be administered within 30 minutes of hospital arrival.
- Reperfusion therapy is reasonable for patients with STEMI and symptom onset within the prior 12 to 24 hours who have clinical and/or ECG evidence of ongoing ischemia. Primary PCI is the preferred strategy in this population.
- CLASS I
- In the absence of contraindications, fibrinolytic therapy should be given to patients with STEMI and onset of ischemic symptoms within the previous 12 hours when it is anticipated that primary PCI cannot be performed within 120 minutes of FMC.
- CLASS IIa
- In the absence of contraindications and when PCI is not available, fibrinolytic therapy is reasonable for patients with STEMI if there is clinical and/or ECG evidence of ongoing ischemia within 12 to 24 hours of symptom onset and a large area of myocardium at risk or hemodynamic instability.
- CLASS III: HARM
- Fibrinolytic therapy should not be administered to patients with ST depression except when a true posterior (inferobasal) MI is suspected or when associated with ST elevation in lead aVR.

* Note: The treatment recommendation guidelines are mentioned to serve as references to all providers of these services as to the level of care that is expected and to serve as an educational tool to all those involved in billing, review, and handling these types of services. Medicare realizes that practice guidelines may change or be updated. Future changes or updates to guidelines may result in a change in the coverage criteria including a possible denial of services. We shall make every attempt to keep abreast of these changes. However, we encourage our providers, members, and other stakeholders to notify us of guideline changes.

Medicare will cover thrombolytic treatment via transcatheter, intracoronary, and intracranial infusion when reasonable and necessary per the indications section only in the setting of a hospital, as an inpatient. Thrombolytic treatment via intravenous infusion may be covered in the setting of a hospital, as an inpatient; or in an emergency room; or critical access hospital. There is no limitation on setting for thrombolytic treatment of thrombosed implanted vascular access device or catheter.

Documentation Requirements

All documentation must be maintained in the patient's medical record and made available upon request. Every page of the record must be legible and include appropriate patient identification information (e.g., complete name, dates of service[s]). The documentation must include the legible signature of the physician or non-physician practitioner responsible for and providing the care to the patient. The submitted medical record must support the use of the selected ICD-10-CM code(s). The submitted CPT/HCPCS code must describe the service performed.

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.

HCPSC Code	Description
J0350	Injection, anistreplase, per 30 units (Drug is not available in the US) (Not covered by Medicare in any payment system)
J2993	Injection, reteplase, 18.1 mg
J2995	Injection, streptokinase, per 250,000 IU (Drug is not available in the US)
J2997	Injection, alteplase recombinant, 1 mg
J3101	Injection, tenecteplase, 1 mg
J3364	Injection, urokinase, 5,000 IU vial (Drug is not available in the US)
J3365	Injection, IV, urokinase, 250,000 IU vial (Drug is not available in the US)

Definitions

Off-Label Drug Use: An off-label/unlabeled use of a drug is defined as a use for a non-FDA approved indication, that is, one that is not listed on the drug's official label/prescribing information. Drugs used for indications other than those in the approved labeling may be covered under Medicare if it is determined that the use is medically accepted, taking into consideration the major drug compendia, authoritative medical literatures and/or accepted standards of medical practice. Determinations as to whether medication is reasonable and necessary for an individual patient are made on appeal on the same basis as all other such determinations (i.e., with support from the peer-reviewed literature, with the advice of medical consultants, with reference to accepted standards of medical practice, and in consideration of the medical circumstance of the individual case).

References

CMS Local Coverage Determinations (LCDs) and Articles

LCD	Article	Contractor	Medicare Part A	Medicare Part B
L35428 Thrombolytic Agents	A55237 Billing and Coding: Thrombolytic Agents	Novitas	AR, CO, DC, DE, LA, MD, MS, NJ, NM, OK, PA, TX	AR, CO, DC, DE, LA, MD, MS, NJ, NM, OK, PA, TX

CMS Benefit Policy Manual

[Chapter 15: § 50 Drugs and Biologicals](#)

Other(s)

Social Security Act (Title XVIII):

- [1862\(a\)\(1\)\(A\) Medically Reasonable & Necessary](#)
- [1862\(a\)\(1\)\(D\) Investigational or Experimental](#)
- [1833\(e\) Incomplete Claim](#)
- [1861\(t\) \(1\) Drugs and Biologicals](#)

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.

Date	Summary of Changes
04/01/2021	Template Update <ul style="list-style-type: none"> • Reformatted policy; transferred content to new template
08/12/2020	Related Policies <ul style="list-style-type: none"> • Added reference link to the Medicare Advantage Coverage Summary titled <i>Medications/Drugs (Outpatient/Part B)</i> Policy Summary

Date	Summary of Changes
	<p>Guidelines</p> <ul style="list-style-type: none"> ● Added language to indicate: <ul style="list-style-type: none"> ○ As published in the Medicare Program Integrity Manual Chapter 13 §13.5.4, in order to be covered, a service shall be reasonable and necessary ○ Drugs and biologicals must be determined to meet the statutory definition under the §1861(t)(1) ○ The Medicare Benefit Policy Manual - Pub. 100-02, Chapter 15, Section 50, describes national policy regarding Medicare guidelines for coverage of drugs and biologicals <p>Treatment of Acute Pulmonary Thromboembolism</p> <ul style="list-style-type: none"> ● Updated treatment related guidelines ● Added language to indicate: <ul style="list-style-type: none"> ○ In selected patients with acute PE associated with hypotension in a high bleeding risk patient (for example, acute post op status of major surgery, recent trauma with surgery, recent ischemic stroke, recent GI bleed), catheter directed therapy with thrombolytics may be used if the appropriate expertise and resources are available ○ Patients with acute PE when a thrombolytic agent is used, it is suggested to provide administration through a peripheral vein over a pulmonary artery catheter unless special circumstances are noted <p>Treatment of Acute ST Segment Elevation Myocardial Infarction (STEMI)</p> <ul style="list-style-type: none"> ● Removed language indicating: <ul style="list-style-type: none"> ○ As published in <i>Medicare Program Integrity Manual Chapter 13 §13.5.4</i>, in order to be covered, a service shall be reasonable and necessary ○ UnitedHealthcare shall consider a service to be reasonable and necessary if we determine that the service is: <ul style="list-style-type: none"> ▪ Safe and effective ▪ Not experimental or investigational (exception: routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000, that meet the requirements of the Clinical Trials NCD are considered reasonable and necessary) ▪ Appropriate, including the duration and frequency that is considered appropriate for the service, in terms of whether it is: <ul style="list-style-type: none"> - Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member - Furnished in a setting appropriate to the patient's medical needs and condition - Ordered and furnished by qualified personnel - One that meets, but does not exceed, the patient's medical needs - At least as beneficial as an existing and available medically appropriate alternative <p>Documentation Requirements</p> <ul style="list-style-type: none"> ● Revised language to indicate: <ul style="list-style-type: none"> ○ All documentation must be maintained in the patient's medical record and made available upon request ○ Every page of the record must be legible and include appropriate patient identification information (e.g., complete name, dates of service[s]) ○ The documentation must include the legible signature of the physician or non-physician practitioner responsible for and providing the care to the patient ○ The submitted medical record must support the use of the selected ICD-10-CM code(s) ○ The submitted CPT/HCPCS code must describe the service performed <p>Applicable Codes</p> <ul style="list-style-type: none"> ● Removed: <ul style="list-style-type: none"> ○ Revenue code 0636 ○ Place of Service (POS) codes 04, 12, 13, 14, and 16 ○ ICD-10 diagnosis codes T82.818A, T82.818D, T82.818S, T82.868A, T82.868D, T82.868S, Z45.2, Z51.11, and Z51.12

Date	Summary of Changes
	<p>Supporting Information</p> <ul style="list-style-type: none"> Updated <i>References</i> section to reflect the most current information Archived previous policy version MPG308.05

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](#).