MEDICAL COLLEGE OF WISCONSIN SCHOOL OF PHARMACY STUDENT WRITING CLUB:

Thrombolytics for Pulmonary Embolisms: A Narrative Review

by Sage L. Orlowski, 2025 PharmD Candidate, Soriene N. Ozcan, 2025 PharmD Candidate, Katherine M. Bush, 2024 PharmD Candidate

Abstract

Pulmonary embolism (PE) is a type of venous thromboembolism (VTE) where the pulmonary artery, or its smaller connecting arteries, are blocked, and can lead to significant morbidity and mortality. Thrombolytic therapy can be beneficial in treating pulmonary embolism. First generation thrombolytics include urokinase (Kinlytic®) and streptokinase (Streptase®); second generation thrombolytics include alteplase (Activase®) (tPA); and third generation thrombolytics are tenecteplese (TNKase®) and reteplase (Retavase®). The use of thrombolytics in patients with pulmonary embolisms is progressing rapidly and, in some cases, can be lifesaving, but there are several patient-specific factors and adverse effects that must be considered for each patient case, which may potentially lead to hesitancy when considering thrombolytic agents.

Approximately 60,000-100,000 deaths each year in the United States are caused by pulmonary embolisms.[1] Pulmonary embolism (PE) is a type of venous thromboembolism (VTE) where the pulmonary artery, or its smaller connecting arteries, is blocked.[2] The problematic blockage can be made up of air, fat, tumor, or thrombus. Many cases of PE are a severe development of deep vein thrombosis (DVT) where the pulmonary vein is blocked by a thrombus that detached from another area of the body.[2] There are various sub-types of PE based upon stability, risk, and/or location of the blockage.

Stability can be broken down into massive and sub-massive, with massive having the highest risk of mortality. Massive PE can be defined as PE resulting in a systolic blood pressure of <90 mmHg.[3] Only approximately 50% of patients with massive PE survive over 90 days despite treatment.[3]

Pulmonary embolisms are also classified as high risk, intermediate risk, or low risk. High-risk patients are hemodynamically unstable and have myocardial injury and right ventricular damage.[4] Intermediate-risk patients are hemodynamically stable but symptomatic and may have myocardial injury or right ventricular damage.[4] Treatment is based on which risk level the patient falls into.

Blockage(s) can occur in many different locations in pulmonary vessels. Saddle PE occurs as a PE that straddles a bifurcation, most commonly the main pulmonary trunk bifurcating to the left and right pulmonary arteries.[3,5] Lobar, segmental, and subsegmental PE occur in the branches of the main pulmonary artery, with lobar PE occurring in the larger branches directly bifurcating from the main pulmonary artery, and segmental and subsegmental PE in the increasingly smaller branches.[6] The occlusion of the arteries can cause impaired gas exchange and prevent circulation.[2] Clinical presentation of PE may include hypotension, dyspnea, syncope, hypoxemia, tachycardia, and sudden death. Without prompt detection and treatment, PE can significantly affect morbidity and mortality.

Prophylaxis

As with many diseases, the greatest hope of reducing morbidity and mortality is in preventing PE before it occurs. Since many PEs result from a thrombus detaching and embolizing in a patient with DVT, much of PE prophylaxis is centered on reducing this occurrence. In hospitalized patients with a low risk of thrombosis, the American College of Chest Physicians (CHEST)'s Evidence-Based Clinical Guidelines eighth edition recommends that acutely ill, hospitalized patients with an increased risk of thrombosis be administered anticoagulant thromboprophylaxis such as low-molecular weight heparin (LMWH), low-dose unfractionated heparin (UFH), or fondaparinux.[7] They also recommend that acutely ill or critically ill, hospitalized patients with an increased risk of bleeding or who are actively bleeding and have an increased risk of thrombosis should receive mechanical thromboprophylaxis such as graduated compression stockings or intermittent pneumatic compression as opposed to anticoagulant thromboprophylaxis. Once the risk of bleeding subsides, pharmacological thromboprophylaxis should then be used in place of the mechanical thromboprophylaxis. After the initial anticoagulant prophylaxis, the duration of pharmacological prophylaxis should be extended including when the patient leaves the hospital.

The risk of a DVT, PE, or VTE emergency can increase based on a variety of risk factors including recent surgery, advanced age, estrogen use, severe obesity, and pregnancy. Patients with risk factors should take additional precautions when traveling long distances or flying.

For an initial pulmonary embolism, prophylactic anticoagulation is chosen based on risk factors, in addition to respiratory and hemodynamic support. These risk factors include but are not limited to: age greater than 65, chronic

conditions, cancer, previous stroke, recent falls, recent surgery, and alcohol use.[8] Goals of pulmonary embolism therapy are to prevent the clot from becoming more prominent, prevent recurrent blood clot formation, and prevent long-term complications. Oral anticoagulants are used for prophylaxis in high-risk patients and for long-term management of pulmonary emboli. Commonly used anticoagulants in management of patients with a diagnosed pulmonary embolism are included as oral medications, low molecular heparin injections, fondaparinux, and heparin. An independent analysis of clinical trials in elective surgeries has shown a reduction of 60% to 70% in the incidence of fatal pulmonary embolisms in heparin-treated patients compared to placebo patients.[9]

Treatment

Management of an initial pulmonary embolism diagnosis may include respiratory support, hemodynamic support (including intravenous fluid administration), and use of vasopressors such as norepinephrine or dobutamine.[10] Current pulmonary embolism treatments include thrombolytic therapy, embolectomy, and placing a filter in one of the major blood vessels, such as the vena cava.[11]

In severe cases of life-threatening pulmonary embolisms, thrombolytic therapy may be suggested. Thrombolytic therapy is reserved for patients with severe complications due to pulmonary embolism and with minimal risk of serious bleeding as a side effect of the therapy.[12] Response to thrombolytic therapy is best when there is a short time between the diagnosis of pulmonary embolism and the start of the thrombolytic agents.[13] Thrombolytic agents activate plasminogen to form plasmin, which accelerates the breakdown of the emboli. First generation thrombolytics include urokinase and streptokinase; second generation thrombolytics include alteplase (tPA); and third generation thrombolytics include aretenecteplese and reteplase (Figure 2).

Another pulmonary embolism treatment option is embolectomy. Embolectomy is the removal of pulmonary embolism from the lungs. It may be performed using catheters placed in the blood vessels containing the clot. This procedure can be considered if the patient develops a massive pulmonary embolism within two months of having craniotomy or spinal surgery and for patients with intracranial hemorrhage.[14]

An inferior vena cava filter is a device that blocks the circulation of clots in the bloodstream, especially the movement from the legs to the lungs. It is placed in the inferior vena cava with a catheter inserted into a vein in the groin area and threaded throughout the blood vessels.[15] This treatment can be used for patients who cannot use anticoagulants due to recent surgery, stroke, or significant bleeding in any bodily area. However, when appropriate, an inferior vena cava filter is often used along with other prophylactic and management strategies, such as anticoagulation use, thrombolysis, and embolectomy.[16]

Tissue plasminogen activator (tPA) is a natural fibrinolytic agent found in endothelial cells that demonstrates fibrin affinity and specificity. The goal of thrombolytic therapy is to convert plasminogen into plasmin, via direct or indirect mechanisms, which results in clot dissolution.[16,17] The direct plasminogen activators (urokinase, tPA, reteplase, and tenecteplase) are serine proteases that have a direct action on plasminogen, which catalyzes its activation. On the other hand, indirect plasminogen activators (e.g., streptokinase), lack enzymatic activity on their own, and instead form a 1:1 complex with plasmin or plasminogen. This complex activates the plasminogen molecules present in circulation.[18,19] Adivitiya, Khasa YP offers more detail about the fibrin pathway.[19]

Thrombolytic therapy has been shown to improve oxygenation, perfusion, pulmonary artery pressure, and echocardiographic assessment. These improvements lead to a relief in symptoms, prevention of recurrent PE, and a reduction in mortality.[20] However, these benefits do not necessarily outweigh a patient's risk of bleeding, and, unfortunately, there is not a validated tool that can be used to predict the bleed risk in patients undergoing thrombolytic therapy; only to identify risk factors.[20] As a result, thrombolytic therapy choice depends on many factors, including but not limited to cost, stability, half-life, side effects or tolerability, specificity toward fibrin, and immunogenicity.[18] Consequently, there is a lasting push to develop innovative medications at a lower cost to address these factors.[17]

First-Generation Agents

The first-generation plasminogen activators, namely urokinase and streptokinase, work not only by activating free circulatory plasminogen to plasmin, but also by degrading fibrinogen and other clotting factors. The addition of plasminogen activators results in the degradation of the α2-antiplasmin, which under normal conditions would inhibit free plasmin, resulting in a systemic fibrinolytic state leading to bleeding complications.[18] Although streptokinase is typically preferred over other thrombolytic agents from a cost perspective, it unfortunately has more associated adverse effects, including allergic reactions and hypotension, and is no longer commercially available in the United States. Furthermore, streptokinase has an antigenic structure, meaning it is recognized by the immune system and can trigger an immune response leading to an allergic reaction, and it is not able to be safely re-administered for at least six months.[16]

Alteplase, a second-generation plasminogen activator, on the other hand, is not antigenic, and therefore is infrequently associated with any allergic manifestations.[16] Second-generation plasminogen activators also differ from the first-generation plasminogen activators via targeted thrombolysis opposed to non-specific fibrin degradation. Non-specific fibrin degradation causes systemic fibrinolysis and leads to hemorrhage.[17]

Third-generation plasminogen activators, such as tenecteplase and reteplase, have been engineered to improve some of the functional and structural properties, such as longer half-life, enhanced fibrin specificity, improved safety and efficacy, and resistance to inhibitors.[17]

Tenecteplase and reteplase are both approved for treatment of acute coronary syndromes but have ongoing trials evaluating their use in PE.[18,20]

Fibrin-specific agents require the presence of fibrin for the conversion of plasminogen into plasmin. Some agents, such as alteplase, reteplase, and tenecteplase, can convert plasminogen into plasmin in the absence of fibrin, but on a minimal scale. The fibrin-specific agents have longer half-lives, allowing for bolus administration, and do not hold the risk of allergic reactions commonly associated with first-generation

thrombolytic agents. Non-fibrin specific agents do not require fibrin presence for the conversion of plasminogen into plasmin.[16] Streptokinase, urokinase, and alteplase are the only thrombolytic agents that are FDA-approved for use in PE. Of these agents, alteplase is the only one commercially available in the United States (Figure 1). Fibrin specific thrombolytics are alteplase, reteplase, tenecteplase, and non-fibrin specific thrombolytics are streptokinase, antistreplase, and urokinase (Figure 2).

FIGURE 1. Therapeutic Agents for Thrombolytics

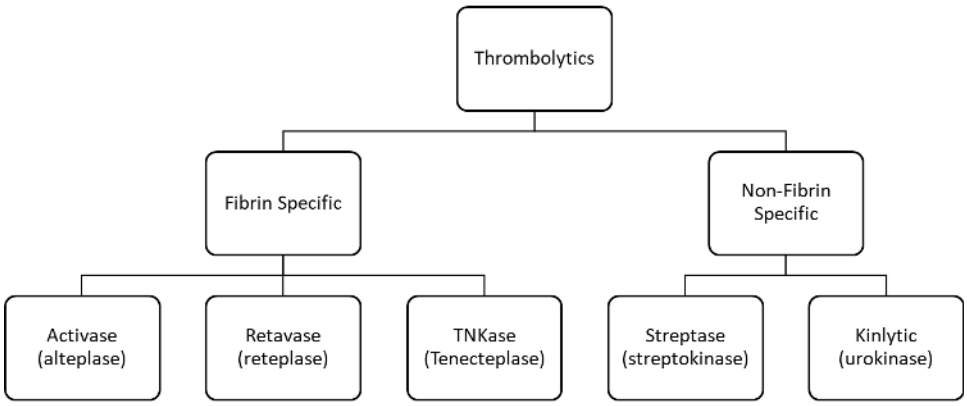
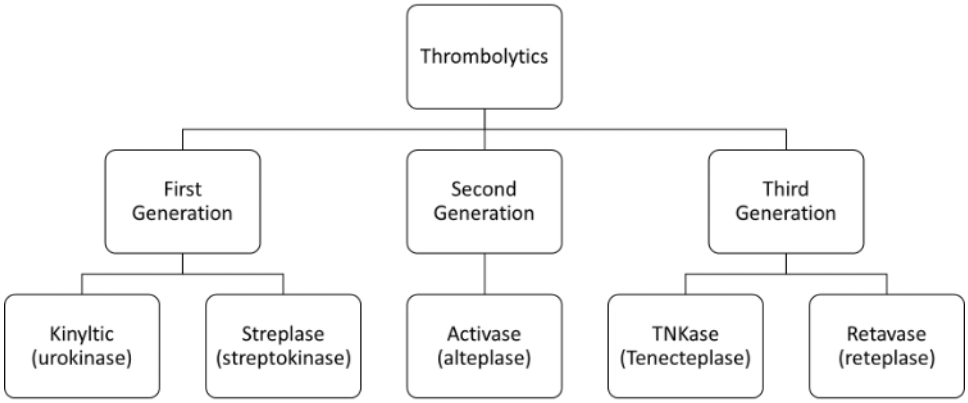


FIGURE 2. Different Generations of Thrombolytics



Alteplase

Alteplase is a tissue plasminogen activator indicated for use in pulmonary embolism. Alteplase is administered using intravenous infusion using a peripheral vein. The dose for acute massive pulmonary embolism is 100 mg administered intravenously for 2 hours once (Table 1). Bolus dosing of alteplase has been investigated in the setting of pulmonary embolism with cardiac arrest, but it is not considered an FDA-approved indication of use and is typically reserved for case-by-case assessment when PE is thought to be the cause of the arrest.[21] Side effects from alteplase are signs of bleeding like blood in vomit or vomit that looks like coffee grounds, skin discoloration, chest pain, severe dizziness, severe headache, vision changes, muscle pain, severe abdominal pain, back pain, nausea, dark urine, vomiting and catheter site pain or irritation. Adverse reactions of alteplase include primarily cardiovascular hemorrhages but are not limited to dermatologic, gastrointestinal, and genitourinary hemorrhages.[22]

Reteplase

Reteplase is a tissue plasminogen activator used off-label for treatment of pulmonary embolisms. Reteplase treatment is initially given as 10 units intravenously over 2 minutes, then followed by a second dose 30 minutes later of 10 units intravenously over 2 minutes (Table 1). Some of the side effects that can occur due to reteplase are vomiting, nausea, abdominal pain, dark urine, muscle pain, vision changes, chest pain, dizziness, severe headache, changes in urine output, skin discoloration, and weakness on one side of the body. Some of the adverse effects from reteplase are bleeding at injection site, and gastrointestinal, oncologic, and hematologic hemorrhage.[23]

Tenecteplase

Tenecteplase is a tissue plasminogen activator and used for pulmonary embolism off-label. Tenecteplase is dosed with weight-based dosing and administered as a bolus dose over five to ten seconds (Table 1). Some side effects with tenecteplase are vomiting, nausea, severe abdominal pain, dark urine, muscle pain, vision changes, chest pain, dizziness, severe headache, changes in urine output, skin discoloration, and weakness in one side of the body. Tenecteplase has possible adverse reactions of hematologic, oncologic, cardiovascular, dermatologic, gastrointestinal, genitourinary, respiratory, and local hemorrhages.[24]

Streptokinase

Streptokinase is a thrombolytic drug that is derived from various streptococci. Streptokinase is a fibrinolytic agent that has been used worldwide due to low cost and good efficacy and safety. Streptokinase is used in treating pulmonary embolism and initially given as 250,000 units intravenously infused over 30 minutes (Table 1).[25] This dose is followed by infusion of a maintenance dose of 100,000 units every hour for 24-72 hours. With this treatment, since thrombolytic activity rapidly fades when infusion has stopped, streptokinase treatment is generally followed by 3-4 hours of intravenous heparin treatment and then oral anticoagulants to prevent re-occlusion. The adverse effects of streptokinase are hemorrhage, rash, fever, nausea, vomiting, and abdominal and back pain.[26,27]

Urokinase

Urokinase is a thrombolytic agent that is produced by human neonatal kidney cells and is found in urine. It converts plasminogen into its active form, plasmin, which results in fibrinolysis. Kinlytic™ (urokinase for injection) is administered

intravenously with a loading dose of 4,400 international units per kilogram and given at the rate of 90 ml per hour over a period of 10 minutes. This loading dose is followed with continuous infusion of 4,400 units per kilogram at the rate of 15 mL for 12 hours (Table 1). The most common adverse reaction from Kinlytic™ (urokinase for injection) is bleeding. In a study, it was found that significant bleeding events requiring transfusion of greater than 2 units of blood were observed during the 14-day study period in 3 of 141 urokinase-treated patients with multiple bleeding events occurring in an individual patient. Most bleeding occurred at sites of external incisions and vascular puncture, with lesser frequency in gastrointestinal, genitourinary, intracranial, retroperitoneal, and intramuscular sites.[28] Other adverse reactions that can occur with Kinlytic™ (urokinase for injection) are myocardial infarction, recurrent pulmonary embolism, hemiplegia, stroke, decreased hematocrit, substernal pain, thrombocytopenia, and diaphoresis.[29,30]

Conclusion

Pulmonary embolisms can significantly affect morbidity and mortality. The use of anticoagulants, thrombolytics, as well as new pharmacological advances can significantly improve patients' chances of survival and quality of life. The use of thrombolytics in patients with pulmonary embolisms is rapidly advancing and, in some cases, can be lifesaving, but there are several patient-specific factors and adverse effects that must be considered with each case, which may potentially lead to hesitancy when considering thrombolytic agents. Adverse side effects of using any thrombolytic agent are similar across the board, which include but are not limited to bleeding and allergic reactions. In thrombolytic agents, streptokinase causes the most allergic reactions; therefore, efficacy may be limited for some patients. Urokinase causes more cases of increased bleeding than other agents. Future generations of thrombolytic agents hope to address many of the adverse effects along with an increase in the efficacy of the agents in the treatment of pulmonary embolisms.

Sage Orlowski and Soriene Ozcan are 2025 Doctor of Pharmacy Candidates at the Medical College of Wisconsin School of Pharmacy in Milwaukee, WI. Katherine Bush is a 2024 Doctor of Pharmacy Candidate at the Medical College of Wisconsin School of Pharmacy in Milwaukee, WI.

PR *This article has been peer-reviewed. The contribution in reviewing is greatly appreciated!*

Acknowledgment: We would like to thank Dr. Zachary Pape, PharmD, BCACP for his mentorship and guidance throughout the review process alongside Dr. Michael Nagy, PharmD, BCACP for his facilitation of the Medical College of Wisconsin: School of Pharmacy Student Writing Club. Without their consistent, unwavering support, this review article would not have been possible.

TABLE 1. Thrombolytic Treatments Used for Pulmonary Embolism

Medication	FDA Approval Status for Pulmonary Embolism	Dosage	How Medication Works	Teaching Points
alteplase	Approved	100 mg intravenously infused over 2 hours	Recombinant plasminogen activator.	Not antigenic therefore it is not associated with any allergic reactions
reteplase	Not Approved	10 units intravenously over 2 minutes, then followed by another10 unit dose over 2 minutes occuring30 minutes after the first dose	Recombinant plasminogen activator, and it catalyzes the cleavage of endogenous plasminogen to generate plasmin.	Can cause hypersensitivity and it can increase the risk of bleeding. Heparin and Retavase are incompatible and cannot be administer at the same time.
tenecteplase	Not Approved	Weight based dosing followed as: • Weight less then 60 kg: 30 mg single intravenous bolus • Weight between 60-70 kg: 35 mg single intravenous bolus • Weight between 70-80 kg: 40 mg single intravenous bolus • Weight between 80-90 kg: 45 mg single intravenous bolus dose • Weight over 90 kg: 50 mg single intravenous bolus	Recombinant plasminogen activator and has higher fibrin specificity with longer half-life with final clearance.	Lacks antigenicity and is more comfortable to administer compared to some other agents.
streptokinase	Approved	250,000 units intravenously over 30 minutes	When it binds to free floating plasminogen, it forms a complex that converts additional plasminogen to active plasmin.	Re-administration of streptokinase within 6 months is not considered safe due to high antigenicity and associated antistreptococcal antibody titer.
urokinase	Approved	Initial dose is 4,400 IU/kg intravenously 90 ml per hour rate for 10 minutes then followed by 4,400 IU/kg intravenously 15 ml per hour for 12 hours.	Physiologic thrombolytic produced by kidney and purified from human urine. Kinlytic directly converts plasminogen into plasmin.	Low antigenicity, and it can allow for more repeated dosing without any allergenic issues.

Disclosures: The authors declare no real or potential conflicts or financial interest in any product or service mentioned in the manuscript, including grants, equipment, medications, employment, gifts, and honoraria.

References

1. Data and statistics on venous thromboembolism. Centers for Disease Control and Prevention. Published June 9, 2022. Accessed January 3, 2023. www.cdc.gov/ncbddd/dvt/data.html.
2. Girard P, Decousus M, Laporte S, et al. Diagnosis of pulmonary embolism in patients with proximal deep vein thrombosis. *Am J Respir Crit Care Med*. 2001;164(6):1033–1037. doi.org/10.1164/ajrccm.164.6.2101045.
3. Ryu JH, Pellikka PA, Froehling DA, et al. Saddle pulmonary embolism diagnosed by CT angiography: frequency, clinical features and outcome. *Respir Med.* 2007;101(7):1537–1542. doi.org/10.1016/j.rmed.2006.12.010.
4. Jimenez D, Bikdeli B, Marshall PS, Tapson V. Aggressive treatment of intermediate-risk patients with acute symptomatic pulmonary embolism. *Clin Chest Med.* 2018;39(3):569-581. doi:10.1016/j.ccm.2018.04.011.
5. Han J, Xiang H, Ridley WE, Ridley LJ. Saddle embolism: pulmonary thromboembolism. *J Med Imaging Radiat Oncol.* 2018;62(Suppl 1):43. doi.org/10.1111/1754-9485.29_12785.
6. Storto ML, Di Credico A, Guido F, Larici AR, Bonomo L. Incidental detection of pulmonary emboli on routine MDCT of the chest. *Am J Roentgenol.* 2005;184(1):264–267. doi.org/10.2214/ajr.184.1.01840264.
7. Kahn SR, Lim W, Dunn AS, et al. Prevention of VTE in nonsurgical patients: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest.* 2012;141(2 Suppl)e195S-e226S. doi:10.1378/chest.11-2296.
8. Skeik N, Westergard E. Recommendations for VTE prophylaxis in medically ill patients. *Ann Vasc Dis.* 2020;13(1):38-44. doi:10.3400/avd.ra.19-00115.
9. Huang CB, Hong CX, Xu TH, et al. Risk factors for pulmonary embolism in ICU patients: a retrospective cohort study from the MIMIC-III database. *Clin Appl Thromb Hemost.* 2022;28:10760296211073925. doi:10.1177/10760296211073925.
10. Sekhri V, Mehta N, Rawat N, Lehrman SG, Aronow WS. Management of massive and nonmassive pulmonary embolism. *Arch Med Sci.* 2012;8(6):957-969. doi:10.5114/aoms.2012.32402.
11. Tarbox AK, Swaroop M. Pulmonary embolism. *Int J Crit Illn Inj Sci.* 2013;3(1):69-72. doi:10.4103/2229-5151.109427.
12. Morrone D, Morrone V. Acute pulmonary embolism: focus on the clinical picture. *Korean Circ J.* 2018;48(5):365-381. doi:10.4070/kcj.2017.0314.
13. Yoo HH, Queluz TH, El Dib R. Outpatient versus inpatient treatment for acute pulmonary embolism. *Cochrane Database Syst Rev.* 2014;(11):CD010019. . doi:10.1002/14651858.CD010019.pub2.
14. Fukuda I, Daitoku K. Surgical embolectomy for acute pulmonary thromboembolism. *Ann Vasc Dis.* 2017;10(2):107-114. doi:10.3400/avd.ra.17-00038.
15. Mismetti P, Laporte S, Pellerin O, et al. Effect of a retrievable inferior vena cava filter plus anticoagulation vs anticoagulation alone on risk of recurrent pulmonary embolism: a randomized clinical trial. *JAMA.* 2015;313(16):1627-1635. doi:10.1001/jama.2015.3780.
16. Isogai T, Yasunaga H, Matsui H, Tanaka H, Horiguchi H, Fushimi K. Effectiveness of inferior vena cava filters on mortality as an adjuvant to antithrombotic therapy. *Am J Med.* 2015;128(3):312.e23-312.e3.12E31. doi:10.1016/j.amjmed.2014.10.034.
17. Ucar EY. Update on thrombolytic therapy in acute pulmonary thromboembolism. *Eurasian J Med.* 2019;51(2):186-190. doi:10.5152/eurasianjmed.2019.19291.
18. Baig MU, Bodle J. *Thrombolytic Therapy*. Updated September 8, 2022. Accessed February 2, 2023. https://www.ncbi.nlm.nih.gov/books/NBK557411/.
19. Adivitiya, Khasa YP. The evolution of recombinant thrombolytics: current status and future directions. *Bioengineered.* 2017;8(4):331-358. doi:10.1080/21655979.2016.1229718.
20. Zuo Z, Yue J, Dong BR, et al. Thrombolytic therapy for pulmonary embolism. *Cochrane Database Syst Rev.* 2021;4(4):CD004437. doi:10.1002/14651858.pub6.
21. Panchal AR, Bartos JA, Cabañas JG, et al. Part 3: adult basic and advanced life support: 2020 american heart association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation.* 2020;142(16_suppl_2):S366-S468. doi:10.1161/CIR.0000000000000916 .
22. Activase (alteplase intravenous). Package insert. Genentech Inc; 1987. https://www.gene.com/download/pdf/activase_prescribing.pdf
23. Retavase (reteplase intravenous). Package insert. Chiesi USA Inc; 1996. https://resources.chiesiusa.com/Retavase/RETAVASE_PI.pdf
24. TKNase (tenecteplase). Package insert. Genentech Inc; 2000. https://www.accessdata.fda.gov/drugsatfda_docs/label/2000/tenegen060200lb.htm#ind
25. Kunamneni A, Abdelghani TT, Ellaiah P. Streptokinase--the drug of choice for thrombolytic therapy. *J Thromb Thrombolysis.* 2007;23(1):9-23. doi:10.1007/s11239-006-9011-x.
26. Streptase (streptokinase). Package insert. CLS Behring Canada, Inc; 2007. https://pdf.hres.ca/dpd_pm/00003639.PDF
27. Shah M, Taylor RT. Low back pain associated with streptokinase. *BMJ.* 1990;301(6762):1219. doi:10.1136/bmj.301.6762.1219-a.
28. McCotter CJ, Chiang KS, Fearrington EL. Intrapulmonary artery infusion of urokinase for treatment of massive pulmonary embolism: a review of 26 patients with and without contraindications to systemic thrombolytic therapy. *Clin Cardiol.* 1999;22(10):661-664. doi:10.1002/clc.4960221014.
29. Kinlytic™ (urokinase for injection). Package insert. Microbix Inc; 2007. https://www.accessdata.fda.gov/drugsatfda_docs/label/2008/021846s101lbl.pdfhttps://www.accessdata.fda.gov/drugsatfda_docs/label/2008/021846s101lbl.pdf
30. Edwards Z, Nagalli S. Streptokinase. In: StatPearls. Treasure Island (FL): StatPearls Publishing. Updated July 4. 2022. Accessed February 2, 2023. https://www.ncbi.nlm.nih.gov/books/NBK553215/