About the NCCN Guidelines for Patients®

Did you know that top cancer centers across the United States work together to improve cancer care? This alliance of leading cancer centers is called the National Comprehensive Cancer Network® (NCCN®).

Cancer care is always changing. NCCN develops evidence-based cancer care recommendations used by health care providers worldwide. These frequently updated recommendations are the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). The NCCN Guidelines for Patients plainly explain these expert recommendations for people with cancer and caregivers.

These NCCN Guidelines for Patients are based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Cancer-Associated Venous Thromboembolic Disease, Version 2.2023 — June 1, 2023.

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Blood clot basics

5  What is a blood clot?
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7  Key points
You may have heard of blood clots. But did you know there’s a strong link between clots and cancer? Read this chapter to learn why people with cancer should be concerned about them.

What is a blood clot?

A blood clot is a gel-like clump of blood. It is made of cells called platelets that stick to body tissue and to each other. The clot is strengthened by a fibrin mesh that holds the sticky platelets together and traps red blood cells.

Normally, blood clots develop to stop bleeding and then dissolve. This is a healthy, protective response of the body. But a blood clot can form inside a blood vessel when there is no bleeding. This type of clot is called a thrombus or thrombi if referring to more than one. A thrombus that breaks free from the vessel wall and travels in the bloodstream is called an embolus.

Both thrombi and emboli can be dangerous. A thrombus may grow large enough to block blood flow. Blocked blood flow caused by a thrombus is called thrombosis, and if caused by an embolus, it’s called an embolism. Blocked blood flow can cause organ damage or failure, heart attack, or a stroke.

Dangerous blood clots are common in people with cancer. They can cause lifelong health problems. They are also a leading cause of death. Lives may be saved if cancer-related blood clots are better understood, prevented, and treated.
Why do many people with cancer get blood clots?

People with cancer usually have multiple risk factors for blood clots. A risk factor is something that increases your chance of developing a disease. People with cancer have the same risk factors for blood clots as people without cancer. They also have risk factors related to cancer.

Cancer itself is a risk factor for blood clots. People with cancer at greatest risk for blood clots have:

- A type of cancer that is linked with sticky blood or slow blood flow
- A cancer that's active and not in remission or cured
- A cancer that has grown or spread to other parts of the body

Many types of cancer treatment also increase the risk for blood clots. Treatment-related risk factors for clots are:

- Major surgery
- Whole-body drug treatment, called systemic therapy, such as chemotherapy, kinase inhibitors, immunotherapy, selective estrogen receptor modulators, and immunomodulating agents
- An implanted device called a central venous access device (also called CVAD or central venous catheter)

Some risk factors for blood clots are made worse by cancer. Infections are a risk factor, and having cancer makes you more likely to get infections. A long period of physical inactivity increases the risk for blood clots. Cancer may make you less active because you feel tired, need bed rest, or are bedridden.
What’s the best treatment for blood clots?

There’s no treatment for blood clots that’s best for everyone with cancer. The best treatment is the treatment that’s right for you. Importantly, your health care should follow best practices. Best practices are based on the latest research and practices at top cancer centers. This book is about the best practices for cancer-related blood clots.

Anticoagulants are anti-clot drugs. They are central to preventing and treating blood clots. Anticoagulants are often called blood thinners, but they do not thin blood. They slow down the body’s ability to form a blood clot.

Not all people with cancer should be on anticoagulants to prevent blood clots. Preventive care is started when there’s an increased risk of clots. Read Chapter 3 to learn who’s at risk and the options for preventive care.

If a clot develops, treatment will be tailored to you. Read Chapter 4 to learn the treatment options for the type of blood clot you have. Some clots are treated right away while others are watched to see if they grow.

Anticoagulants are safe for many people with cancer but have risks. If you start bleeding, your body may have trouble stopping the bleeding. Read Chapter 5 to learn when to contact your care team. Chapter 5 also discusses when you might need a change in treatment.

Key points

- Blood clots are a thickened clump of blood. They can cause lifelong health problems and are sometimes fatal if they block the flow of blood.
- Cancer and its treatment increase the risk of clots. They slow down blood flow or make blood sticky.
- Anticoagulants are drugs that prevent and treat blood clots.

"Your medical team is your greatest asset and friend(s), especially the nurses. They are all highly skilled and sincerely dedicated to help you however they can."

Your medical team is your greatest asset and friend(s), especially the nurses. They are all highly skilled and sincerely dedicated to help you however they can."
2
Spotting blood clots

9 Dangerous blood clots
10 Deep vein thrombosis
10 Superficial vein thrombosis
11 Splanchnic vein thrombosis
12 Pulmonary embolism
12 Key points
This chapter describes different types of blood clots. Learn which blood clots you may be at risk for. Also, learn their symptoms, so you can spot a blood clot early when treatment works best.

**Dangerous blood clots**

A thrombus is an abnormal blood clot inside of a blood vessel. It can develop in either an artery or vein. Arteries transport oxygen-rich blood away from the heart to the whole body. Veins transport blood that lacks oxygen back to the heart. Blood clots in veins have different causes and are treated differently than clots in arteries.

**Venous thromboembolism**

Venous thromboembolism is blood flow blocked by blood clots that started in veins. It is more common than other types of blockages, and there’s more research on how to manage it. Common types of venous thromboembolism are:

- **Deep vein thrombosis** is caused by a blood clot in a vein far beneath the skin.
- **Superficial vein thrombosis** is caused by a blood clot in a vein near the skin.
- **Splanchnic vein thrombosis** is caused by a blood clot in certain veins of the digestive system.
- **Pulmonary embolism** is a blood clot that broke free and got stuck in an artery within a lung.

The types of venous thromboembolism can have vastly different symptoms and prognoses. A prognosis is the likely course and outcome of a disease or condition.

**Deep vein thrombosis**

Deep vein thrombosis is the most common type of blood clot. If not treated, the clot could break free and get stuck in an artery within a lung. This is called a pulmonary embolism. Pulmonary embolisms can be deadly.
outcome of a disease. In the next sections, the risk factors and symptoms of each clot are explained.

Deep vein thrombosis

Deep vein thrombosis can occur in any deep vein but often occurs in the large veins of the legs. It commonly occurs in people with cancer, especially those getting chemotherapy. Treatment received through a catheter in a central vein increases the risk for deep vein thrombosis. This type of catheter is called a central venous access device (also called CVAD or central venous catheter).

A symptom of deep vein thrombosis is ongoing cramps in your calf. Cramping may feel like a charley horse. Another symptom of deep vein thrombosis is swelling in one arm or one leg. Your limb may feel heavy or painful. Instead of a limb, you may have swelling in the face, neck, or the collarbone area if the clot is in these areas.

Symptoms of deep vein thrombosis related to a catheter include swelling in one arm or one leg. You may have swelling near your collarbone or in your neck. The catheter may not be working like it should when there’s a blood clot.

Deep vein thrombosis is serious. Contact your care team right away if you have any of the symptoms.

Superficial vein thrombosis

Superficial vein thrombosis is common in people with cancer but is less likely to be dangerous than other clots. Even so, contact your care team if you have symptoms. Superficial vein thrombosis can grow and involve deep veins.

Also called superficial thrombophlebitis, superficial vein thrombosis may be caused by injections into veins, such as chemotherapy infusion. Other risk factors are surgery, prolonged physical inactivity, and taking estrogen. Having other types of clots increases
the risk for clots in superficial veins. Superficial vein thrombosis can occur at the same time as deep vein thrombosis.

Superficial vein thrombosis causes symptoms more often than other clots. It often occurs in a leg, but you may see symptoms in other places. Your skin that’s over the clot may be red, warm, and swollen. The area may be very tender to the touch. The vein might feel hard.

Splanchnic vein thrombosis

There are several types of splanchnic vein thrombosis. Each one is named after the vein with the blood clot. These veins are in the abdomen, which is below the chest:

- **Hepatic vein thrombosis** occurs in veins that carry blood from the liver to the heart.
- **Portal vein thrombosis** occurs in the vein that carries blood to the liver.

- **Mesenteric vein thrombosis** occurs in veins that carry blood from the intestines to the portal vein.
- **Splenic vein thrombosis** occurs in the vein that carries blood from the spleen to the portal vein.

Splanchnic vein thrombosis is not as common as other types of blood clots. But be aware that the risk is higher in certain situations. The chance of splanchnic vein thrombosis developing is higher after surgery in the abdomen. There’s also an increased risk during estrogen treatment.

There are several diseases linked with splanchnic vein thrombosis. Inflammation of the pancreas and chronic liver disease increase the risk for this clot, and so does a tumor in the abdomen. Your risk for an abdominal clot is high if you have one of these blood diseases—paroxysmal nocturnal hemoglobinuria or myeloproliferative neoplasm.

### Symptoms of clots in the abdomen

Splanchnic vein thrombosis is caused by clots in digestive veins in the abdomen. The abdomen contains many organs including the stomach. Abdominal clots can cause sudden pain, a swollen belly, and nausea and vomiting.
A common symptom of splanchnic vein thrombosis is sudden abdominal pain. The area may feel tender when touched, and your belly may stick out more than normal. If someone tries to touch your abdomen, you may quickly—like a reflex—guard the area.

Other symptoms of splanchnic vein thrombosis make you feel like you have a stomach bug. You may feel like you’re going to throw up. You may vomit or have diarrhea. Some people lose their appetite or have pain when eating. Some people have a fever.

**Pulmonary embolism**

If you have symptoms of a pulmonary embolism, call 911. It is very serious.

Be on the lookout for symptoms if you had a blood clot recently. Pulmonary embolism often starts from deep vein thrombosis in a leg but can start from other types of clots, too.

Common symptoms of a pulmonary embolism are shortness of breath, chest pain, and fainting. Other symptoms include rapid breathing, fast heartbeat, and a new cough that may have bloody mucus. You may feel uneasy or anxious.

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**The 3 S’s of pulmonary embolism symptoms**

- Sudden shortness of breath
- Sharp chest pain
- Short fainting spells

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**Key points**

- It's important for people with cancer to spot a blood clot early. Prompt treatment may prevent lifelong health problems or save your life.
- Deep vein thrombosis occurs in veins far beneath the skin. It may cause a part of your body to swell. Often, one leg or one arm is swollen. Clots in a leg may feel like a charley horse.
- Superficial vein thrombosis occurs in veins near the skin. Your skin that’s over the clot may be red and swollen. The area may feel warm, painful, and hard.
- Splanchnic vein thrombosis occurs in certain veins of the digestive system. A common symptom is sudden abdominal pain. You may also feel like you have a stomach bug.
- Pulmonary embolism occurs in an artery within a lung. Common symptoms of a pulmonary embolism are sudden shortness of breath, sharp chest pain, and fainting.
3 Preventing blood clots

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15 Planning safe care
16 Prevention in the hospital
18 Prevention at home
19 Key points
Some people with cancer are at increased risk for getting blood clots. Because experts know who’s at risk, safe and timely care can be provided to prevent many blood clots. Read this chapter to learn if you should receive preventive care and what type of care is recommended.

Types of preventive care

Preventive care is medicine that is used to prevent the start of a health problem. You may hear it called prophylaxis (sounds like proh-fuh-lak-sis). Preventive care for blood clots is called thromboprophylaxis (throm-bo-proh-fuh-lak-sis).

There are several types of preventive care for blood clots. There are prescription drugs that help prevent blood clots. But there is a device and a sock-like product, too.

Anticoagulants

Anticoagulants are drugs that prevent blood clots. They stop the making of the fibrin mesh that holds the clot together. They work by disabling blood proteins, called clotting factors, that work together to form fibrin. See Guide 1 for a list of anticoagulants used for prevention.

Heparin

Heparin is a substance made by your body and by animals. When injected into the body, it prevents blood clots. Heparin indirectly stops clotting factors by activating a natural anticoagulant in your body called antithrombin.

There are two types of heparin:

- **Unfractionated heparin** stops two clotting factors called Factor Xa and thrombin.
- **Low-molecular-weight heparin** mostly stops Factor Xa.

Unfractionated heparin is sometimes called standard heparin. Dalteparin (Fragmin) and enoxaparin (Lovenox) are low-molecular-weight heparins.

**Indirect factor Xa inhibitors**

Fondaparinux (Arixtra) was made in a lab and is similar to a fragment of heparin. It indirectly stops Factor Xa by activating antithrombin. It has no direct effect on thrombin.

**Direct factor Xa inhibitors**

Direct factor Xa inhibitors attach to and directly block Factor Xa. They include apixaban (Eliquis) and rivaroxaban (Xarelto).

**Intermittent pneumatic compression device**

One type of mechanical prevention is an intermittent pneumatic compression device. It has sleeves that wrap around the legs and squeezes them at times. The squeezing pumps blood out of your legs just like your muscles do when walking. This helps prevent blood clots.

**Graduated compression stockings**

Graduated compression stockings are another type of mechanical prevention. They are like a long sock but squeeze the legs to increase
blood flow in veins. They give the strongest squeeze at the ankle and the weakest squeeze at the knee or thigh. The amount of pressure is measured in millimeters of mercury (mm Hg). Typically, stockings will have either 15 to 20 mm Hg or 20 to 30 mm Hg of pressure.

Planning safe care

Your care team will assess which type of preventive care is right for you. They will consider how well each option works but also the health problems each option could cause. They will not prescribe preventive care that is likely to cause serious harm.

A series of tests will be done to plan preventive care. Since bleeding may occur while on anticoagulation, your team will check for factors that increase risk. These factors include low platelet counts, bleeding disorders, or current bleeding. Read Chapter 5 to learn how to spot abnormal bleeding and how anticoagulants are managed.

Mechanical prevention may not be safe for some people. It should not be used if you had a recent blood clot in a deep vein and are not on anticoagulation. The squeezing of the legs could cause a piece of the clot to break off and travel to your lungs. For some people, having

Guide 1
Anticoagulants that prevent blood clots in people with cancer

<table>
<thead>
<tr>
<th>Generic name</th>
<th>Type of anticoagulant</th>
<th>How it’s received</th>
<th>Prescribed setting</th>
</tr>
</thead>
</table>
| Apixaban       | Direct factor Xa inhibitor     | Tablet                         | • In hospital for surgery
|                |                                |                                | • At home                                   |
| Dalteparin     | Low-molecular-weight heparin   | A shot into the fat under the skin | • In hospital for surgery
|                |                                |                                | • In hospital for other medical care
|                |                                |                                | • At home                                   |
| Enoxaparin     | Low-molecular-weight heparin   | A shot into the fat under the skin | • In hospital for surgery
|                |                                |                                | • In hospital for other medical care
|                |                                |                                | • At home                                   |
| Fondaparinux   | Indirect factor Xa inhibitor   | A shot just under the skin into fat | • In hospital for surgery
|                |                                |                                | • In hospital for other medical care        |
| Unfractionated heparin | Standard heparin | A shot just under the skin into fat | • In hospital for surgery
|                |                                |                                | • In hospital for other medical care        |
| Rivaroxaban    | Direct factor Xa inhibitor     | Tablet                         | • In hospital for surgery
|                |                                |                                | • At home                                   |
a large bruise-like hematoma or an open skin sore makes mechanical prevention unsafe.

Graduated compression stockings should also not be used if blood flow in your arteries is very slow. The stockings could make the problem worse. Another possible reason not to use compression stockings is if you have nerve damage called peripheral neuropathy.

Prevention in the hospital

Being in a hospital can increase the chance of a blood clot. Less physical activity and certain treatments raise the risk. NCCN experts recommend preventive care for people with cancer admitted to the hospital. The exception is people with basal or squamous cell skin cancer because their risk for blood clots is low.

Tests to plan care

Your care team will plan safe preventive care for you based on the tests described next.

Medical history

Your care team will ask about your past and current health and medications. If you took anticoagulants before, your team will want to know about any side effects. Also, be prepared to discuss the health problems of your close blood relatives.

Physical exam

A member of your care team will perform a thorough physical exam of your body. This exam includes checking vital signs, such as heart rate. Your provider will also look over your body and gently press on areas.

Blood and urine tests

To plan preventive care, your team needs to know your level of platelets, clotting ability, and the health of your liver and kidneys.

Platelets in a blood sample are measured with a lab test called a complete blood count. This test also measures other parts of the blood including white and red blood cells.
To assess how well your blood is clotting, coagulation tests on a blood sample will be done. Prothrombin time and activated partial thromboplastin time are two tests that measure how long it takes for your blood to clot.

How well your liver is working is assessed by a group of blood tests called liver function tests. Kidney function tests performed on blood or urine samples reveal the health of your kidneys.

**Risk assessment**
Your care team will assess your chance of getting a blood clot and make decisions based on your level of risk. Your risk is increased when you have cancer and are hospitalized. Your overall health, age, and other factors may further increase your risk.

**Care options**
There are several good options for preventing blood clots in the hospital. You may receive anticoagulants, mechanical care, or both.

**Anticoagulants**
Preventive care with anticoagulants is based on whether you are having surgery or other medical care. It is a low dose of medication compared to what is typically used for treatment of blood clots.

For **surgical hospitalizations**, unfractionated heparin, low-molecular-weight heparin, and fondaparinux are options for many people. These anticoagulants are typically taken for at least 7 to 10 days.

A direct factor Xa inhibitor is an additional option for some people. Apixaban is an option for people having surgery for gynecologic cancer. These cancers include uterine, cervical, and ovarian cancer. Rivaroxaban is an option for people who had laparoscopic surgery for colorectal cancer.

Some surgeries increase the risk of blood clots more than others. Such surgeries include those done in the abdomen or pelvis. Before high-risk surgery, you may receive unfractionated heparin or low-molecular-weight heparin. Additionally, intermittent pneumatic compression may be used.

If you had high-risk surgery for cancer, NCCN experts recommend extended preventive care after being discharged from the hospital. Read the next section, *Prevention at home*, for more information.

For **medical hospitalizations**, blood clots are prevented with unfractionated heparin, low-molecular-weight heparin, or fondaparinux. You'll receive the anticoagulant during your entire hospital stay or for up to 6 to 14 days. The length of treatment depends on your clot risk as assessed by your care team.

If receiving medical care, apixaban and rivaroxaban are not started in the hospital. But either medication may be continued if you were taking it before being admitted. If you have had a side effect called heparin-induced thrombocytopenia, apixaban or rivaroxaban is an option instead of heparin.

**Mechanical care**
When anticoagulants are not an option, mechanical care is used in the hospital. One study found that intermittent pneumatic compression prevented deep vein thrombosis better than graduated compression stockings. People using pneumatic compression also had fewer skin problems. More research is needed to confirm these results.
Prevention at home

Some people with cancer benefit from preventive care of blood clots when at home. NCCN experts have identified two groups at risk for blood clots:

- People discharged from the hospital after a cancer surgery within the abdomen or pelvis
- People at risk for blood clots while receiving systemic therapy

Anticoagulants are used to prevent blood clots at home.

Care options after surgical hospitalization

Blood clots are more likely to occur after cancer surgeries done in the abdomen or pelvis if any of the following describe you:

- You had high-risk surgery, which is a surgery for a gastrointestinal cancer, such as stomach, colon, or rectal cancer
- You’ve had a blood clot before
- You had general anesthesia for more than 2 hours
- You were in the hospital bed for 4 or more days
- You have advanced stage cancer
- You are over 60 years of age

If you’re at risk for blood clots, NCCN experts recommend taking an anticoagulant after being discharged from the hospital. Most likely, your surgeon will be the one to prescribe an anticoagulant before you leave the hospital. You will need to take an anticoagulant every day. Apixaban, dalteparin, and enoxaparin are taken for 4 weeks. Rivaroxaban is taken for 3 weeks after finishing a week of low-molecular-weight heparin in the hospital.

Care options during systemic therapy

Systemic therapy is a whole-body treatment with cancer drugs. It travels in your bloodstream to treat cancer wherever it is in your body. Chemotherapy, immunomodulatory drugs, and endocrine therapy are types of systemic therapy.

A medical oncologist is an expert in systemic therapy. They will prescribe systemic therapy as well as an anticoagulant if needed.

A member of your care team will assess your level of risk for blood clots. There are measures to assess a person’s risk of clots, such as the Khorana score.

The Khorana score is not used to assess risk for people with acute leukemia, brain tumors, multiple myeloma, or a myeloproliferative neoplasm. Information on preventing blood clots among people with multiple myeloma or a myeloproliferative neoplasm can be found at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.
The Khorana score estimates your risk of blood clots based on five items about your health:

- The type of cancer
- The level of platelets in your blood before chemotherapy is started
- The level of a protein called hemoglobin—a marker of your red blood cell level—before chemotherapy is started, or if you are receiving red cell growth factors
- The level of white blood cells, called leukocytes, before chemotherapy is started
- A quick measure of body fat called body mass index

Points from each item are added together for a total score that ranges from 0 to 6. Two points are scored for stomach and pancreatic cancers. One point is scored for lung, gynecologic, bladder, and testicular cancers as well as lymphoma.

Routine preventive care for blood clots is not needed when your score is either 0 or 1. Your care team will check for blood clots at health visits.

When Khorana scores are 2 and higher, NCCN experts recommend that providers consider prescribing an anticoagulant for 6 months or longer if the risk persists. If prescribed, the anticoagulant is taken every day. Your care team will decide the best preventive care for you based on your risk for clots versus your risk for side effects.

Key points

- Some people with cancer are more at risk for blood clots than others. You have an increased risk when hospitalized and after a hospital stay for cancer surgery. Certain people taking cancer drugs, called systemic therapy, also have an increased risk.
- Planning preventive care requires your care team to do a thorough evaluation. They will recommend care that’s safe and works for you.
- Anticoagulants are used for preventive care in the hospital if possible. Additional care with intermittent pneumatic compression may be received if you’re having surgery in the abdomen or pelvis. When anticoagulants are not an option, intermittent pneumatic compression or graduated compression stockings are used in the hospital.
- If you had a high-risk cancer surgery, extended care with anticoagulants is recommended after being discharged from the hospital.
- Your risk for blood clots while on systemic therapy depends on the type of cancer and other factors. If you’re at increased risk, your care team will consider prescribing an anticoagulant.
4

Treating blood clots

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23  Planning safe care
24  Superficial vein thrombosis
25  Deep vein thrombosis
26  Pulmonary embolism
26  Splanchnic vein thrombosis
27  Key points
It is common for people with cancer to have blood clots in veins. These clots may travel to and get stuck in a lung artery. This chapter explains the treatments for these types of clots.

Types of treatment

Anticoagulants are the centerpiece of treatment for acute venous thromboembolism. Venous thromboembolism is blocked blood flow by a blood clot in any vein or in an artery within a lung. It is acute when the onset of symptoms was recent, usually defined as within the past few weeks.

As a treatment, anticoagulants produce good results and are safe for many people with cancer. They are taken as long as there is risk for clots because they also prevent new clots. People who’ve had a clot are more likely to have another one.

Anticoagulants

Anticoagulants stop the making of the fibrin mesh that holds the clot together. They work by disabling blood proteins, called clotting factors, that work together to form fibrin. See Guide 2 for a list of anticoagulants used for treatment.

Guide 2
Anticoagulants that treat blood clots in people with cancer

<table>
<thead>
<tr>
<th>Generic name</th>
<th>Type of anticoagulant</th>
<th>How it’s received</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apixaban</td>
<td>Direct factor Xa inhibitor</td>
<td>Tablet</td>
</tr>
<tr>
<td>Dabigatran</td>
<td>Direct thrombin inhibitor</td>
<td>Capsule</td>
</tr>
<tr>
<td>Dalteparin</td>
<td>Low-molecular-weight heparin</td>
<td>A shot into the fat under the skin</td>
</tr>
<tr>
<td>Enoxaparin</td>
<td>Low-molecular-weight heparin</td>
<td>A shot into the fat under the skin</td>
</tr>
<tr>
<td>Edoxaban</td>
<td>Direct factor Xa inhibitor</td>
<td>Tablet</td>
</tr>
<tr>
<td>Fondaparinux</td>
<td>Indirect factor Xa inhibitor</td>
<td>A shot just under the skin into fat</td>
</tr>
<tr>
<td>Unfractionated heparin</td>
<td>Standard heparin</td>
<td>Slow injection into a vein or a shot just under the skin into fat</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>Direct factor Xa inhibitor</td>
<td>Tablet</td>
</tr>
<tr>
<td>Warfarin</td>
<td>Vitamin K antagonist</td>
<td>Tablet</td>
</tr>
</tbody>
</table>
In Guide 2, you’ll see anticoagulants that are also listed in Chapter 3 for preventive care. A higher dose is typically used for treatment. These anticoagulants include:

- Unfractionated heparin, dalteparin (Fragmin), enoxaparin (Lovenox), and fondaparinux (Arixtra) activate a natural anticoagulant in your body called antithrombin
- Apixaban (Eliquis) and rivaroxaban (Xarelto) directly block Factor Xa

You’ll also see some anticoagulants that are only recommended for treatment:

- Edoxaban (Savaysa) blocks Factor Xa
- Dabigatran (Pradaxa) blocks thrombin
- Warfarin lowers the level of clotting factors by depleting vitamin K

**Treatment used with anticoagulation**

Another type of treatment is sometimes used with anticoagulation. Some clots don’t need additional treatment, and in many cases, more research or training on these other treatments is needed. Recommended options for each type of venous thromboembolism are listed later in this chapter, but here are three examples:

- Medications called thrombolytics dissolve blood clots. They can be slowly injected into a vein and travel throughout the body in the bloodstream. This approach is called systemic thrombolysis. Catheter-directed thrombolytics are injected directly into a clot.
- A procedure called a thrombectomy removes blood clots from the body. It can be performed with a balloon catheter inserted through a cut made in a blood vessel. This approach is called surgical or open thrombectomy. Catheter-directed thrombectomy breaks up or suctions out the clot with a device. This approach has several names including mechanical thrombectomy and percutaneous thrombectomy.
- Pharmacomechanical thrombolysis dissolves and removes clots. Through a catheter, a small amount of a thrombolytic is injected into the clot. Next, the clot fragments are suctioned out from the vein.

**Treatment without anticoagulation**

Anticoagulation may not be an option for you. In this case, clots that don’t pose a great danger will be monitored, and the safety of anticoagulants will be reassessed.

Higher-risk clots may be managed with a removable filter placed in the inferior vena cava (IVC) vein within your abdomen. IVC filters catch clots moving in the bloodstream before they reach the lungs.

A shunt is a small medical tube that is used to manage certain clots in the belly area. Shunts redirect blood flow around a clot by making a new connection between two blood vessels. They can be placed in the body by a catheter. This approach is called transjugular intrahepatic portosystemic shunt or TIPS. Shunts can also be placed during surgery.
Planning safe care

It takes a team of experts to plan cancer care and provide support. When you have a blood clot, your team may include an expert in blood diseases called a hematologist. Other experts that treat blood clots include

- Surgeons, interventional radiologists
- Cardiologists, pulmonologists, vascular medicine specialists
- Internal medicine practitioners

Your care team will assess which treatment of blood clots is right for you. They will consider how well a treatment works but also the health problems it could cause. The main side effect of anticoagulants is bleeding. Read Chapter 5 to learn how to spot abnormal bleeding and how anticoagulants are managed.

Tests are needed to plan your care. Examples of information used for treatment planning are the number of blood platelets and the health of your liver and kidney. Common tests for treating thrombosis are described next.

**Medical history**

Your care team will want to know all about your health. Be prepared to tell them about your past and current health and medications. If you took anticoagulants before, your team will want to know about any side effects. Also, be prepared to discuss the health problems of your close blood relatives.

**Physical exam**

A member of your care team will perform a thorough physical exam of your body. This exam includes checking vital signs, such as heart rate. Your provider will also look over your body and gently press on areas.

**Blood and urine tests**

Platelets in a blood sample are measured with a lab test called a complete blood count. You’re at risk of bleeding if your platelet levels are low. A complete blood count also measures other parts of the blood including white and red blood cells.

To assess how well your blood is clotting, coagulation tests on a blood sample will be done. Prothrombin time and activated partial thromboplastin time are two tests that measure how long it takes for your blood to clot.

How well your liver is working is assessed by a group of blood tests called liver function tests. Kidney function tests performed on blood or urine samples reveal the health of your kidneys.

**Imaging**

Imaging takes pictures of the inside of your body and is used to find diseases. Your care team will use imaging to diagnose a blood clot. Imaging is also used for treatment planning because it shows where the clot is and the size of the clot.

In general, one of two types of imaging is used to see clots. Venous ultrasound uses soundwaves to make images of superficial or deep veins. Computed tomography—often called a CT scan—is used to see clots. It combines many x-rays to make a detailed image. If it’s safe for you, a swallowed or injected contrast should be used to make the images clearer.
A radiologist is a doctor who’s an expert in reading images. This doctor will convey the imaging results to your care team.

Superficial vein thrombosis

Superficial vein thrombosis occurs in veins close to the skin. Often, treatment is not needed because the clot dissolves on its own. But some clots continue to grow. Your care team will monitor the growth of the clot.

**Arm clots**

Superficial vein thrombosis may be caused by a catheter in your arm. In this case, the catheter will be removed if it’s no longer needed. On the other hand, the catheter may remain in place if symptoms quickly resolve or anticoagulation is started.

Anticoagulation is not used at first for superficial arm clots. The goal is to relieve symptoms until the clot naturally dissolves. Symptoms can be reduced with warm compresses, nonsteroidal anti-inflammatory drugs (NSAIDs), and elevating the limb.

Your care team will keep watch for signs that the blood clot is growing. If the clot gets bigger, they will consider prescribing a low-dose anticoagulant. Some people get a higher dose to stop the clot from reaching deep veins.

**Leg clots**

Superficial vein thrombosis in the leg is treated with an anticoagulant. Low-dose treatment is used for clots longer than 5 centimeters or that extend above the knee. It is taken every day for at least 6 weeks. A high dose will be used if the clot is very close to a deep vein at the top of the thigh. A high dose is taken every day for at least 3 months.

**Imaging**

Imaging makes pictures of the insides of the body. It is needed to diagnose blood clots. Ultrasound is often used to find blood clots in limbs (shown).
Instead of starting treatment, leg clots that are unlikely to reach a deep vein may be checked again. A second ultrasound will be done in 7 to 10 days to assess the size of the clot. If it’s larger, your team may prescribe an anticoagulant.

Deep vein thrombosis

Deep vein thrombosis occurs in veins far under the skin. Thrombosis in these veins is treated with an anticoagulant when possible.

Severe clots above the knee may need quicker treatment than anticoagulation. Severe clots may cause major symptoms, lead to limb amputation, or be life-threatening. Your team will consider additional treatment with either pharmacomechanical thrombolysis or mechanical thrombectomy.

Deep vein thrombosis may be related to a central venous access device. Treatment with anticoagulation should continue for 3 months or until the catheter is removed. The catheter will be removed if symptoms persist or it gets infected, damaged, or is no longer needed.

If anticoagulation wasn’t safe at first, your team will keep checking if it is an option now. Clots in the abdomen, pelvis, or upper leg are managed with an IVC filter until they can be safely treated with anticoagulants. Once you’re on an anticoagulant, the filter will be removed.

Untreated clots below the knee are watched using repeated ultrasound. If they grow into the upper leg, treatment consists of either anticoagulation or IVC filter.

Superficial vein thrombosis

Superficial vein thrombosis in an arm may resolve on its own. Symptoms may be relieved by elevating the arm (shown), a warm compress, or ibuprofen.
Pulmonary embolism

A pulmonary embolism is caused by a blood clot that traveled in the bloodstream to an artery in a lung and got stuck. These clots usually start in a deep vein within a leg or arm. A pulmonary embolism is a life-threatening condition at times, but many people survive if promptly treated.

Testing

Common tests of blood clots will be done, but these dangerous lung clots also require special testing. A scan called CT angiography is most often used to see lung clots. Your team will also check your lungs with a chest x-ray.

A lung clot can damage the heart. Your heart function will be assessed with blood tests called troponin and NT-proBNP. You will also have an electrocardiogram (ECG or EKG) to check for an abnormal heartbeat. You may also have an ultrasound of the heart done to check your heart function. This test is called an echocardiogram.

Treatment

If possible, a pulmonary embolism will be treated with an anticoagulant. If you were already on an anticoagulant, the dose may be increased, or a different anticoagulant will be started. After the acute period, you will stay on an anticoagulant. You might return home from the hospital if you’re out of danger. If the embolism worsens, it may be treated with thrombolysis or thrombectomy.

An acute massive pulmonary embolism is severe. It causes the blood pressure to drop and could lead to heart and lung failure. Your care team will consider more treatment in addition to anticoagulation. Before starting anticoagulation, you may receive heart and lung support from a medical device. If your risk for bleeding is low, the clot may be treated with either systemic or catheter-directed thrombolysis. A second option is to remove the clot with a surgical or catheter embolectomy.

If anticoagulation wasn’t safe at first, your team will keep checking if it is an option now. Clots may be managed with an IVC filter until they can be safely treated with anticoagulants.

Splanchnic vein thrombosis

Splanchnic vein thrombosis is caused by a blood clot in veins of the digestive system. Clots in these veins cause symptoms common to many diseases, so more tests may be needed. Your care team will plan testing based on your medical history and physical exam.

A diagnosis of splanchnic vein thrombosis is made with imaging. Treatment is based on which vein the clot is in. It is also based on how long you’ve had signs and symptoms of a clot.

- Acute thrombosis started within the past 8 weeks
- Chronic thrombosis started more than 8 weeks ago

Hepatic vein thrombosis

Hepatic vein thrombosis occurs in veins that carry blood from the liver to the heart. A liver specialist should evaluate anyone with this type of thrombosis. They will review your health records and meet with you.

Acute hepatic vein thrombosis is treated with an anticoagulant when possible. The clot may also be treated with pharmacomechanical thrombectomy, and blood flow redirected with
a shunt. A shunt is also an option for acute thrombosis not treated with anticoagulation.

If you have chronic hepatic vein thrombosis, your care team will decide if an anticoagulant would be helpful. A shunt is also an option.

**Portal, mesenteric, splenic vein thrombosis**

Blood from the digestive system travels through the mesenteric, splenic, and portal veins on its way to the liver. Acute thrombosis in these veins is treated the same as acute hepatic vein thrombosis. Surgery may be needed if the thrombosis caused death of intestinal tissue. You'll meet with a gastroenterologist or surgeon for evaluation.

A gastroenterologist should evaluate anyone with chronic thrombosis. Your care team will decide if an anticoagulant would be helpful. A shunt is another option.

Bleeding is not uncommon when chronic thrombosis is diagnosed. A medication called a beta blocker may be used to reduce the chances of bleeding. Bleeding can also be stopped with a band placed around a blood vessel or with injected medication that scars the vessel.

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**Key points**

- Your care team will do a thorough evaluation to plan safe treatment for you.
- Acute thrombosis in people with cancer is treated with anticoagulation when possible. A possible exception is superficial vein thrombosis in an arm because it may resolve on its own. Anticoagulants are taken as long as there is a risk for blood clots.
- Highly dangerous clots may be quickly dissolved with medication or removed. These clots are also treated with anticoagulation.
- When anticoagulation is not safe, your care team will monitor the growth of clots. They will also reassess the safety of anticoagulation in case it becomes an option. Life-threatening events may be prevented with clot-catching filters or a shunt that redirects blood flow.

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Managing anticoagulants

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Follow-up care

Anticoagulants often work very well in preventing and treating blood clots. For them to work well, you must follow your prescription. Do not stop or skip care. If you’re in the hospital, your team will help you stay on track.

If you’re taking anticoagulants at home, you’ll have regular visits with your care team. Blood tests will also be done on a regular basis. Between visits, contact your team if:

- You have new or worsening symptoms, such as those described in the next section for bleeding
- You are having trouble taking your medicine as prescribed
- Another provider prescribes new medication
- You’re thinking about starting over-the-counter medication, vitamins, or herbals
- You need a medical procedure or surgery

Side effects

Anticoagulants may cause health problems called side effects. Some side effects are unpleasant but bearable. Other side effects may be severe and even life-threatening. Side effects differ among people based on the type of care as well as the person.

Bleeding

The main side effect of anticoagulants is bleeding. Bleeding can be life-threatening, so be on the lookout for it. Signs of abnormal bleeding include:

- The worst headache ever (It’s a symptom of bleeding in the head)
- Sudden mental confusion, weakness on one side of the body, or difficulty talking (These are stroke symptoms)
- Very heavy nosebleeds
- Bloody, black, or tar-like stool (poop)
- Very heavy menstrual periods or vaginal bleeding
- Major weakness, dizziness, shortness of breath, or low blood pressure
- Bleeding from your skin that doesn’t stop after using applying pressure

Heparin-induced thrombocytopenia

Heparin-induced thrombocytopenia is a rare side effect of heparin. Instead of preventing blood clots, heparin may cause your body to make more clots. If you’ve had this dangerous side effect before, heparin will likely not be prescribed for you again.
Changes in treatment

Some people may need a change to their anticoagulant. Here are three reasons for a change.

**Bleeding**

During follow-up care, your care team will monitor your chance of bleeding. Your bleeding risk increases if your platelet count drops to a low level. If abnormal bleeding starts, options include:

- Staying on anticoagulation and receiving transfusions of platelets
- Stopping anticoagulation and having an inferior vena cava (IVC) filter until your platelet count increases
- Taking a lower dose of anticoagulant
- Removing a central venous catheter if it’s causing blood clots in deep veins
- Stopping anticoagulation and monitoring blood clots in lower legs with repeated ultrasound

Some people experience life-threatening bleeding. In this case, the effect of the anticoagulant must be reversed quickly. Medications that reverse effects are referred to as antidotes. Not all anticoagulants have antidotes.

**Medical procedure**

People with cancer often undergo invasive medical procedures like surgery. If you need such a procedure, your care team will decide if a change in your treatment is needed.

Your team will assess the bleeding risk of the procedure plus your risk for dangerous blood clots. Examples of high-risk procedures are heart surgery and brain surgery. Very-low-risk procedures include injections, cavity fillings, and skin biopsies.

If you need a change in treatment, options include:

- Reversing the effect of anticoagulation for emergency surgery
- Pausing anticoagulation
- Temporarily switching to a short-acting anticoagulant, which is called bridging
- Placement of an IVC filter before briefly stopping anticoagulation

**New or worsening blood clots**

Despite being on anticoagulation, the blood clot may grow, or a new clot may form. Be on the lookout for new clots, so changes in treatment may be promptly made. See Chapter 2 for a list of symptoms caused by clots.

If you were on a low dose of anticoagulation, the dose may be increased, or a different anticoagulant will be started.

If you were taking a high dose, your team will consider new causes of blood clots.
You may have developed heparin-induced thrombocytopenia. A tumor may be squeezing a blood vessel, and so a clot formed. An IVC filter may have narrowed a vessel causing a clot to form.

New or worsening clots may be treated with an even higher dose of anticoagulation. Another option is to try a different anticoagulant.

Key points

- To get the best results, keep taking your anticoagulant and don’t skip doses. Contact your care team if you have any changes in symptoms or health care.
- Your care team will regularly check your health with blood tests. Anticoagulants may cause your body to bleed abnormally.
- Learn the symptoms of abnormal bleeding so you can get care right away.
- If bleeding starts, you may get platelet transfusions. If you have a central venous catheter, it may be removed. Your anticoagulation regimen may be altered.
- If you have severe bleeding or need emergency surgery, you may receive a fast-acting antidote for anticoagulation.
- If you need to schedule a procedure that’s likely to cause bleeding, anticoagulation may be paused, and you may get an IVC filter. Another option is to switch to bridging anticoagulation, which is a short-acting dose, until you can safely resume your normal regimen.
- If a blood clot worsens or a new clot forms, the dose of your anticoagulant may be increased or a new anticoagulant may be started.
6 Making treatment decisions

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It's your choice

In shared decision-making, you and your care team share information, discuss the options, and agree on a care plan. It starts with an open and honest conversation between you and your team.

Care decisions are very personal. What is important to you may not be important to someone else.

Some things that may play a role in your decision-making:

- What you want and how that might differ from what others want
- Your religious and spiritual beliefs
- Your feelings about medical care
- Your feelings about pain or side effects
- Cost of treatment, travel to treatment centers, and time away from school or work
- Quality of life and length of life
- How active you are and the activities that are important to you

Think about what you want from cancer care including care for blood clots. Discuss openly the risks and benefits of your options. Share concerns with your doctor.

Questions to ask

Possible questions to ask your cancer care team are listed on the following pages. Feel free to use these or come up with your own. Be clear about your goals for care and find out what to expect from treatment.

Second opinion

It is normal to want to start medical care as soon as possible. While blood clots should not be ignored, there is often time to have another provider review your test results and suggest a care plan. This is called getting a second opinion, and it's a normal part of cancer care. Even doctors get second opinions!

Things you can do to prepare:

- Check with your insurance company about its rules on second opinions. There may be out-of-pocket costs to see providers who are not part of your insurance plan.
- Make plans to have copies of all your records sent to the provider you will see for your second opinion.
Questions about blood clots

1. Am I at increased risk for blood clots?
2. What puts me at risk for blood clots?
3. What can I do to prevent blood clots?
4. What are the symptoms of blood clots?
5. Who should I contact if I notice symptoms of blood clots?
Questions about care options

1. What are my care options for blood clots?
2. Are you suggesting options other than what NCCN recommends? If yes, why?
3. How do my age, sex, overall health, and other factors affect my options?
4. What if I am pregnant, or planning to become pregnant?
5. Will my insurance cover the care you’re recommending? Are there any programs to help pay for care?
6. What are the side effects of each option? Are any serious or life-threatening?
Questions about anticoagulants

1. How long will I have to take an anticoagulant?
2. How is the prescribed anticoagulant taken?
3. Are there any reasons that an anticoagulant should be stopped?
4. Are there any medications I should avoid while taking an anticoagulant?
5. Are there any over-the-counter vitamins or herbals I shouldn’t take?
6. How often will I need to have a follow-up visit?
7. What side effects should I report right away, and who do I contact?
8. Who should I contact with questions or concerns if the office is closed?
Advocate for yourself! Don’t be afraid to ask for a second opinion. Don’t be afraid to ask for help from friends and family, who just want to be told what you need. Move everyday, eat healthy foods, and reduce your stress. Watch funny movies and hug loved ones often. Spend time in nature. Never lose hope!"
Words to know

**abdomen**
The belly area between the chest and pelvis.

**activated partial thromboplastin time**
A measure of the time it takes blood to clot.

**artery**
A tube-shaped vessel that carries blood from the heart to the body.

**anesthesia**
A drug that causes a controlled loss of feeling or awareness.

**anticoagulant**
A drug that stops the making of the fibrin mesh that holds a blood clot together. Also called blood thinner.

**antithrombin**
A blood protein that inhibits blood clotting.

**blood clot**
A thickened mass of blood. Also called a thrombus.

**bridging anticoagulation**
A temporary, short-acting anti-clot medication.

**catheter**
A long and narrow tube-shaped device that is used for medical procedures.

**computed tomography (CT)**
A test that uses x-rays from many angles to make a picture of the insides of the body.

**CVAD**
central venous access device

**deep vein thrombosis**
Blockage of a vein far beneath the skin by a blood clot.

**diagnosis**
The identification of an illness based on tests.

**electrocardiogram (ECG or EKG)**
A test that checks for an abnormal heartbeat.

**embolism**
The blockage of a blood vessel that may be caused by a blood clot.

**embolus**
A blood clot that broke free from its base and traveled in the bloodstream.

**Factor Xa**
A clotting protein.

**fibrin**
The mesh that holds a blood clot together.

**graduated compression stockings**
A sock-like product that prevents blood clots by squeezing the legs.

**heparin-induced thrombocytopenia**
A rare side effect for which symptoms include blood clots.

**inferior vena cava (IVC) filter**
A small device that catches clots moving in the bloodstream.

**intermittent pneumatic compression**
A device that prevents blood clots by applying pressure on the legs.

**Khorana score**
A measure of the risk for blood clots.

**medical history**
A report of all your health events and medications.
Words to know

**NSAIDs**
nonsteroidal anti-inflammatory drugs

**pelvis**
The body area between the hip bones.

**pharmacomechanical thrombolysis**
A procedure that dissolves and removes clots.

**platelet**
A type of blood cell that forms into a blood clot to control bleeding. Also called thrombocyte.

**prognosis**
The likely course and outcome of a disease.

**prophylaxis**
Health care that prevents disease.

**prothrombin time**
A measure of the time it takes blood to clot.

**pulmonary embolism**
Blockage of an artery in a lung by a blood clot.

**shunt**
A small medical tube.

**side effect**
An unhealthy or unpleasant physical or emotional response to treatment.

**splanchnic vein thrombosis**
Blockage of a vein of the digestive system by a blood clot.

**superficial vein thrombosis**
Blockage of a vein near the skin by a blood clot.

**systemic therapy**
A drug used to treat cancer cells throughout the body.

**thrombin**
A clotting protein.

**thrombectomy**
A procedure that removes blood clots from the body.

**thrombolytic**
A drug that dissolves blood clots.

**thromboprophylaxis**
Preventive care for blood clots.

**thrombosis**
The blockage of a blood vessel by a blood clot.

**thrombus**
A blood clot within a blood vessel.
NCCN Contributors

This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Cancer-Associated Venous Thromboembolic Disease, Version 2.2023. It was adapted, reviewed, and published with help from the following people:

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