Targeted Therapy

What is targeted therapy?

As researchers have learned more about the gene changes in cells that cause cancer, they have been able to develop drugs that target these changes. Treatment with these drugs is often called *targeted therapy*.

Targeted therapy drugs, like any drug used to treat cancer, are technically considered "chemotherapy." But targeted therapy drugs do not work in the same ways as standard chemotherapy drugs. They are often able to attack cancer cells while doing less damage to normal cells by going after the cancer cells' inner workings—the programming that sets them apart from normal, healthy cells. These drugs tend to have different (and often less severe) side effects than standard chemotherapy drugs.

Targeted therapies are used to treat many kinds of diseases. Here we will focus on their use to treat cancer. In the past, only a few cancers could be treated with targeted therapy, but now these drugs are used to treat many different types of cancer.

Targeted therapies are a major focus of cancer research today. Many future advances in cancer treatment will probably come from this field.

Here we will explain:

- The different ways that targeted therapy can work
- Some of the types of targeted therapy
- What you can expect if you are being treated with targeted therapy (including some common side effects)

How does targeted therapy work?

Targeted therapy is used to keep cancer from growing and spreading. To become cancer cells, normal cells go through a process called *carcinogenesis* (**car**-sin-oh-**JEN**-eh-sis). Cancer cells may then grow into tumors or reproduce throughout a body system, like blood cancers do. Scientists have learned a lot about the molecules that are part of this process and the signals a cell gets to keep this process going.

Targeted therapy disrupts this process. The drugs target certain parts of the cell and the signals that are needed for a cancer to develop and keep growing. These drugs are often grouped by how they work or what part of the cell they target.

Enzyme inhibitors

Our bodies produce many types of enzymes, which are special proteins that help control many of the things our cells do. When most people think of enzymes, the first ones that come to mind are those that help digest (break down) the food we eat. But some enzymes serve as signals for cancer cells to grow.

Some targeted therapies block (inhibit) enzymes that are signals for cancer cells to grow. These drugs are called *enzyme inhibitors*. Blocking these cell signals can keep the cancer from getting bigger and spreading. So even if the tumor is not getting smaller, its out-of-control growth has been interrupted. This may give regular chemo a better chance to work. Slowing or stopping out-of-control growth may also help people live longer, even without adding other drugs.

Enzyme inhibitors may be called different names based on the enzymes they block:

- Tyrosine kinase inhibitors (**tie**-ruh-seen **kine**-ace)
- mTOR inhibitors
- Proteosome inhibitors (**pro**-tee-us-ohm)
- Growth factor inhibitors
- Signal-transduction inhibitors (trans-**duck**-shun)
- Multi-targeted kinase

A multi-targeted kinase drug blocks many different enzymes. It may also be called a *multikinase inhibitor*.

Apoptosis-inducing drugs

Some targeted therapies change proteins within the cancer cells and cause the cells to die. These are called *apoptosis-inducing drugs*. (*Apoptosis*, pronounced **a**-pop-**TOE**-sis, is the medical word for cell death. These drugs cause or induce cell death.) Many cancer treatments, including radiation and chemo, cause cell changes that lead to apoptosis. But targeted drugs in this group are different, because they are aimed right at the parts of the cell that control whether cells live or die.

Angiogenesis inhibitors

Angiogenesis (**an**-jee-oh-**JEN**-uh-sis) is the process of making new blood vessels. In most cases, this is a normal, healthy process. As the human body grows and develops, it

needs to make new blood vessels to get blood to all of its cells. As adults, we don't have quite the same need for making new blood vessels, but there are times when angiogenesis is still important. New blood vessels, for instance, help the body heal wounds and repair damage.

But in a person with cancer, this same process creates new blood vessels that give a tumor its own blood supply. This blood brings nutrients that allow the cancer to grow and spread. Angiogenesis inhibitors target and stop (or inhibit) this process—they stop the tumors from making new blood vessels. This helps cut off the tumors' blood supply, and without blood, tumors can't grow.

Many of these drugs work by blocking *vascular endothelial* (**vas**-ku-ler **end**-oh-**THEE**-lee-al) *growth factor*, also called VEGF. VEGF is a family of protein growth factors made by some tumors. The VEGF proteins can attach to the VEGF receptors of blood vessel cells. This causes new blood vessels to form around the tumors. Blocking this process prevents angiogenesis, which would form new blood vessels to feed tumors so they could grow.

Types of targeted therapy used today

Today many different types of targeted therapies are used to treat cancer. Looking at examples helps a person understand how these drugs work. A few of the more commonly used targeted therapies are listed here, but this is not a complete list. There are many different targeted therapies in use and new ones are coming out all the time.

There are 2 main types of targeted therapy drugs:

- **Antibody drugs** are man-made versions of immune system proteins (called antibodies) that have been designed to attack certain targets on cancer cells. (The body normally makes antibodies to fight harmful invaders like germs.)
- **Small-molecule drugs** are not antibodies. Since antibodies are large molecules, this other type of drug is called a "small-molecule" targeted therapy drug.

Some targeted therapy drugs

There are many different targeted therapy drugs. Here are a few examples:

Gleevec® (imatinib mesylate)

This is one of the first targeted therapy drugs ever used to treat cancer. It's used to treat gastrointestinal (**gas**-tro-in-**TEST**-uh-nul) stromal tumor (or GIST, a rare cancer of the gastrointestinal tract) and certain kinds of leukemia. Imatinib is a tyrosine kinase inhibitor that targets abnormal proteins, or enzymes, that form on and inside cancer cells and promote uncontrolled growth. Blocking these enzymes inhibits cancer cell growth.

Iressa® (gefitinib)

Gefitinib is used to treat advanced non-small cell lung cancer. This drug targets the epidermal growth factor receptor (EGFR). These receptors are found on the surface of many normal cells, but certain cancer cells have many more of them. EGFR takes in the signal telling the cell to grow and divide. When gefitinib blocks this signal, it can slow or stop cell growth.

Sutent® (sunitinib)

This drug is used to treat advanced kidney cancer and some gastrointestinal stromal tumors, also called GIST. It's considered a multi-targeted kinase inhibitor because it's a type of vascular endothelial (**vas-**ku-lur **en-**doe-**THEE-**lee-uhl) growth factor (VEGF) receptor inhibitor, an angiogenesis inhibitor, and it blocks an enzyme called tyrosine kinase. By doing all of this it slows cancer growth and keeps tumors from making their own blood vessels to help them grow and spread.

Velcade® (bortezomib)

This enzyme inhibitor may be used to treat multiple myeloma that does not respond to other treatments. Bortezomib is a proteasome inhibitor. A proteasome is a complex of enzymes that helps destroy proteins that the cell no longer needs. Some of these proteins help to regulate cell function and growth. Bortezomib stops the proteasome from breaking down these proteins, which in turn causes the cancer cells to die.

Other drugs that may be called targeted therapies

There are other cancer treatments that can be included in the group of drugs called targeted therapies. Some examples of these are:

Monoclonal (**ma-**nuh-**KLO-**nuhl) **antibodies, such as**

- Campath® (alemtuzumab)
- Erbitux® (cetuximab)
- Rituxan® (rituximab)
- Herceptin® (trastuzumab)
- Avastin® (bevacizumab)

Immunomodulating (**im-**yuh-no-**MOD-**you-late-ing) **drugs, such as**

- Thalomid® (thalidomide)
- Revlimid® (lenalidomide)

Cytokines (sy-toe-kines) **such as**

- Interleukins
- Interferons
- Granulocyte-macrophage (**gran**-you-lo-site **mack**-ro-faj) colony-stimulating factor

The prostate cancer vaccine, Provenge® (sipuleucel-T)

The targeted therapies listed above are often grouped as *immunotherapies*, or treatments that work with your immune system to fight cancer. But some of them act more like targeted therapy drugs. For example, bevacizumab acts as an angiogenesis inhibitor, and cetuximab and trastuzumab work like enzyme inhibitors. You can learn more about these drugs in our document called *Immunotherapy*.

What's the goal of targeted therapy treatment?

Depending on the type of cancer and its stage (if and how far it has spread), targeted therapy can be used to:

- Cure the cancer
- Slow the cancer's growth
- Kill cancer cells that may have spread to other parts of the body
- Relieve symptoms caused by cancer

Your doctor will talk to you about the goals of your therapy before you start treatment.

Will targeted therapy drugs be my only treatment for cancer?

Sometimes treatment with a targeted therapy drug will be the only treatment you need. But in most cases, targeted therapy is used along with other treatments such as chemo, surgery, and/or radiation therapy.

Getting targeted therapy treatment

How are targeted therapy drugs given?

The most common way to give these drugs is as a pill (by mouth) or into a vein (intravenous or IV). IV drugs are given in these ways:

- The drug can be given quickly through the catheter right from a syringe over a few minutes. This is called an IV push.

- An IV infusion can last 30 minutes to a few hours. A mixed drug solution flows from a plastic bag through tubing that is attached to the catheter. The flow is often controlled by a machine called an IV pump.
- Continuous infusions are sometimes needed and can last from 1 to 7 days. These are always controlled by electronic IV pumps.

When the drug is given by mouth you are given pills to take at home. If you take a targeted therapy drug by mouth, it's very important to take the exact dose, at the right time, for as long as it has been prescribed. For certain conditions, targeted therapy drugs are taken by mouth for many years.

For more information about any particular targeted drug, you can call us with the drug name or read about in online in our *Guide to Cancer Drugs*. For more general information on medicines that are taken by mouth to treat cancer, please see our document called *Oral Chemotherapy: What You Need to Know*.

Where will I get treated?

The place you get your treatment depends on which drugs you are getting, how the drugs are given, the drug doses, your hospital's policies, your insurance coverage, what you prefer, and what your doctor recommends. Based on these factors, targeted therapy may be given:

- At home
- In your doctor's office
- In a clinic
- In a hospital's outpatient department
- In a hospital

Some of these settings may have private treatment rooms, while others treat many patients together in one large room. It's important to be in a setting that is comfortable for you. Talk to your doctor or nurse ahead of time so that you know what to expect your first day.

How often will I need to get treatment and how long will it last?

How often you get the targeted therapy drug and how long your treatment lasts depend on the kind of cancer you have, the goals of the treatment, the drugs being used, and how your body responds to them. You may get treatments daily, weekly, or monthly. Some drugs are given in on-and-off cycles. The breaks allow your body to build healthy new cells and regain its strength. Other drugs are OK to take every day for many months or even years.

Does targeted therapy hurt?

Getting a targeted therapy drug should not hurt beyond the discomfort of the needle stick needed to put in the catheter for medicines given IV (into a vein). If you feel pain, burning, coolness, or anything unusual while you are getting the medicine, tell your doctor or nurse right away.

What are clinical trials and how do I find them?

Clinical trials are carefully designed research studies that test promising new cancer treatments in human volunteers. Many targeted therapies are being studied in clinical trials, and you may want to talk to your doctor about whether this is an option for you. Patients who take part in research studies are the first to benefit from these treatments. These patients can make an important contribution to medical care because the study results will also help other patients.

In a clinical trial, you get either standard treatment or a new treatment that's thought to be as good as – or maybe better than – the standard treatment. Studies are never done to see if you would recover from cancer without treatment at all. As with any other medical treatment, you decide whether you want to be in the study, and you are free to withdraw from a clinical trial at any time and seek other treatment options.

To learn more about clinical trials:

- Ask for our document on clinical trials called *Clinical Trials: What You Need to Know*, or read it on our website.
- The American Cancer Society also offers a Clinical Trials Matching Service to help you find clinical trials that might be right for you. The service is available by telephone from 7:30 a.m. until 7:00 p.m. CT Monday through Friday at 1-800-303-5691, or you can fill out a screening questionnaire anytime.
- The National Cancer Institute (NCI) can give you a list of clinical trials that may be right for you based on the type and stage of your cancer. Call 1-800-422-6237, or visit the NCI's website at www.cancer.gov.

Can I take other medicines while I am getting targeted therapy?

Some medicines may interfere with your treatment. To be sure that your treatment works as well as it can, tell your doctor or nurse about any and all prescription and non-prescription medicines, vitamins, herbs, and supplements you are taking.

- Make a list of the name of each drug, the dose, how often you take it, the reason you take it, and who prescribed it (if applicable).
- Be sure to include the things you may not think of as medicines, even those you take every now and then. This includes aspirin, herbal and dietary supplements, vitamins,

minerals, and all over-the-counter medicines. Don't forget those you take for fever or aches and pains, drugs for heartburn and other stomach problems, cold and flu remedies, sleeping medicines, allergy symptoms, and other "as needed" drugs.

Your doctor will tell you if you should stop taking any of these medicines before you start treatment. After treatment starts, check with your doctor before taking any new medicines or supplements and before stopping the ones you already take.

How will I know if the drug is working?

Your cancer care team will measure how well your treatments are working with certain tests. These may include physical exams, blood tests, bone marrow biopsies, and imaging tests such as scans and x-rays. Ask your doctor about the test results and what they show about your progress. You may have side effects from treatment, but that doesn't always mean that the treatment is working.

How do I give my permission for this treatment?

As with standard chemotherapy, you will be asked to give your written permission to be treated with a targeted therapy drug. This should be based on your understanding of the drug your doctor is recommending. Know the answers to all of these questions before you sign the consent form.

- Which targeted therapy drug will I be given?
- How will the drug be given to me?
- How often will I need to take this drug?
- How long will my treatments last?
- What is the purpose of this treatment (is it meant to cure, slow cancer growth, help my symptoms)?
- How likely is this treatment to be successful?
- What side effects could I have from these drugs?
- Which side effects should I report to you right away, and which ones can wait a few days?

The specifics of the consent form may vary, but the form usually states that your doctor has explained your condition to you, how the treatment is expected to help you, the risks, and the other options available to you. Your signature on the form means that you have gotten this information, have had the chance to ask questions, and are willing to be treated with this drug. This process is called *informed consent*.

Side effects of targeted therapy drugs

What causes side effects?

Although targeted therapy drugs don't affect the body the same way that standard chemo drugs do, they still cause side effects. Side effects from these drugs depend largely on what the drug targets. Some drugs target substances that are more common on cancer cells, but are also found on healthy cells. So these drugs may affect healthy cells, too, causing some side effects.

When drugs attack more than one target, side effects are more likely. Also, drugs that act as angiogenesis inhibitors affect new blood vessel formation all over the body, not just those near the cancer. This can lead to side effects, as well.

What should I know about side effects?

- Every person doesn't get every side effect. Some people get few, if any.
- The severity of side effects varies greatly from person to person. Be sure to talk to your doctor and nurse about which side effects are most likely with your treatment, how long they might last, how bad they might be, and when you should call the doctor's office about them.
- Although side effects can be unpleasant, they must be measured against the need to fight the cancer.
- Your doctor may give you medicines to prevent some side effects before they happen or to treat certain side effects once they occur.
- Rare and unusual side effects may happen with some of these drugs, and some may be serious. All changes and side effects should be reported to your doctor.
- Many people have no long-term problems from targeted therapy drugs.

How long do side effects last?

Most side effects slowly go away after treatment ends and the healthy cells recover. The time it takes to get over some side effects and regain energy varies from person to person. It depends on many factors, including your overall health and the drugs you were given.

Because many targeted therapy drugs are still quite new, it's hard to say how long you can expect side effects to last. We do know that some of the side effects from standard chemo drugs can last a lifetime, such as when the drug causes long-term damage to the heart, lungs, kidneys, or reproductive organs. We still don't know if targeted therapy drugs cause these kinds of long-term changes.

Patients often become discouraged about how long their treatment lasts or the side effects they have. If you feel this way, talk to your doctor. You may be able to change your medicine or treatment schedule. Your doctor or nurse may be able to suggest ways to reduce problems or discomfort.

What are common side effects?

You are not alone if you have questions about side effects. Before cancer treatment starts, most people worry about whether they will have side effects and, if so, what they will be like. Here's a review of some of the most common side effects caused by targeted therapy drugs. We also share some tips on how to manage them.

Skin problems

Many of the targeted therapy drugs can cause a rash or other skin changes. In fact, more than half the people taking certain drugs have some skin effects. These problems usually develop slowly over days to weeks and are not signs of a drug allergy.

In contrast, allergic reactions to drugs tend to start suddenly, usually within minutes to hours after taking the drug. They may include hives (raised skin welts that often go away within a day or so), and intense itching. An allergic reaction often includes other serious symptoms such as trouble breathing, dizziness, tightness in the throat or chest, or swelling of the lips or tongue. If you have these kinds of symptoms, get emergency help and call your doctor right away.

Why do targeted therapies cause skin changes?

Some targeted therapy drugs target the epidermal growth factor receptor (EGFR) protein, which tells the cancer cells to grow and divide. The problem is that normal skin cells also have a lot of EGFR, and they must grow quickly to maintain the skin's surface layer. Drugs that target or block EGFR often affect skin cells, too. They turn off the signal for skin cells to grow normally and make it harder for them to retain moisture.

Some drugs target other proteins, such as vascular endothelial growth factor (VEGF). These proteins help tumors build and keep a blood supply, but they also seem to be important to the very small blood vessels in the hands and feet. Damage to these tiny blood vessels can cause hand-foot syndrome (described later).

Researchers have noticed that people who are getting radiation therapy at the same time they get targeted drugs often have worse skin problems in the area that receives radiation.

What kind of skin changes can targeted therapies cause?

Changes in how your skin feels: Your skin may start off feeling like it's sunburned, before any redness or rash shows up. Even though it doesn't look different, the sensation can be disturbing. You may notice this change on your face as early as the first week of treatment.

Rash: The most common skin change is a rash. The risk of getting the rash and how bad it is depends on the type of cancer and the type and dose of the targeted therapy drug used to treat it. The rash is mild for most people. It often looks like acne (but with no blackheads) and shows up on the scalp, face, neck, chest, and upper back. In severe cases it can affect other parts of the body.

The rash most often starts as skin redness and swelling and is often worst within the first few weeks of treatment. By about the 4th week of treatment, the skin usually crusts and gets very dry and red. In the weeks after that, round, flat or raised red spots and pimples with pus in the center often appear. The rash can itch, burn, or sting, and may feel tender (painful) when you touch it. It may get better or stay about the same during the rest of treatment, but it should completely go away about a month after treatment is stopped.

The rash can be very distressing and make a person feel self-conscious around others. It might be painful and can lead to infections. Prevention and treatment are discussed later.

Dry skin: The skin can become very dry and scaly and may even crack open. Cracking can happen by itself or come with the rash. Cracking tends to be worse when it happens with the rash.

Itching: Many of the skin changes, like rash or dryness, can cause itching. Steps to prevent and treat skin changes, as discussed later, can help with itching. Some people may need to take medicine by mouth, such as diphenhydramine (Benadryl®), to get relief.

Red, sore cuticles (the areas around the nails): Some targeted therapies cause swollen, red, open, and painful skin sores around the fingernails and toenails. (This can look a lot like an infection or an ingrown nail.) This most often happens to the big toes and thumbs. These sores may become infected. Nails may also become brittle and grow more slowly.

Hand-foot syndrome: Hand-foot syndrome (HFS) has been linked to many cancer treatment drugs, including some targeted therapies. The cause of this syndrome is not known for sure. It may have to do with damage to the tiny blood vessels in the hands and feet, or with the drugs themselves leaking out of the blood vessels and causing tissue damage.

A painful sensitivity of the hands and feet is the earliest symptom of HFS. Then, redness and swelling start in the palms of the hands and the soles of the feet. This redness looks a lot like sunburn and may blister. In severe cases, the blisters can open up and become sores. The affected skin also can become dry, peel, and crack. It may burn, tingle, or feel numb.

HFS can be painful and can affect your ability to walk and do your normal activities. If it becomes severe, pain medicines may be needed. Let your doctor know if you are having HFS symptoms—even if they are mild. Treating HFS early can help keep it from getting worse. Like the other skin changes discussed, it can be treated, and there are things you can do to try to prevent it.

Changes in hair growth: Hair on your head can become thin, dry and brittle, or even curly. Long-term use of targeted therapy may lead to bald patches or complete loss of scalp hair. Facial hair for both men and women may grow faster than usual, including

longer, thicker, curly eyebrows and eyelashes that may need to be trimmed. But in some men, facial hair growth slows down. Eyebrows may thin out as well. These changes usually don't happen right away, but you may notice them later as treatment goes on.

Some people notice sores on the scalp and other hairy areas. Scars caused by these sores may keep your hair from growing back after treatment is finished.

Changes in hair or skin color: Some of these drugs can cause the skin or hair to turn a yellowish color during treatment. In a few people, hair becomes darker. This tends to go away once treatment ends.

Changes in and around the eyes: The eye itself may burn, and become dry or red. In some, the eyelids get tender, swollen, or inflamed, and crusts may be seen in the lashes. In a few people the eyelids may turn inward or outward. Distorted eyelids or prolonged dryness can damage the clear part of the eye (the cornea). Talk with your doctor or nurse about managing these changes to avoid injury, pain, or infection.

Can skin changes be prevented?

You can do some things to help prevent skin changes or at least to try to keep them under control. You should start to do them as soon as targeted therapy treatment begins—before any problems start. Starting good skin care before side effects begin may help to keep the problems to a minimum. Your doctor may ask you to do the following:

- Use a mild soap or body wash and shampoo that do not contain alcohol, perfume, or dye.
- Take baths instead of showers, and try oatmeal bath products to soothe your skin.
- Bathe with cool or lukewarm (instead of hot) water. Avoid hot, humid places.
- Moisturize your skin at least 2 times a day with a thick cream that contains no alcohol, perfume, or dye. Right after you bathe, while your skin is still damp, is the best time to do this.
- Do not use laundry detergents or fabric softeners with strong perfumes.
- Stay out of the sun. Wear hats, long sleeves, and sunscreen if you are outside during the day. Sunlight seems to trigger the rash in some people.
- Use a broad-spectrum sunscreen with SPF of at least 30 and zinc oxide or titanium dioxide at least 1 to 2 hours before going out, if you will be outside during the day. Wear cotton clothes and a hat, too.
- Though the rash may look like acne, acne medicines do not work on it—they can dry it out and make it worse.
- If the soles of your feet are tender, gel shoe inserts may help.
- Wear shoes that fit well and aren't too tight. Thick, soft socks may help if you have shoes that are big enough for the extra bulk.

- Some makeup brands, such as Dermablend®, can cover the rash without making it worse.

One study that looked at using Vitamin K cream twice a day suggested it might reduce the severity of the skin rashes, but this is still being researched. Ask your doctor or nurse if there are other things you can do to help lower the chance of skin problems getting worse.

What should I do if I have skin changes?

It's very important to tell your doctor or nurse right away about any rashes or skin changes you notice. Left untreated, rashes can get worse and lead to infection, which can delay or even cause your doctor to stop treatment. Do not treat your skin with over-the-counter medicines or stop taking your targeted therapy without talking to your doctor first.

Your doctor may give you a skin cream or a medicine to take by mouth to treat the skin changes you have. Use these medicines the way the doctor tells you to and start them right away. Let your health care team know if your skin gets worse, or is not getting better after 2 weeks of treatment.

Be sure to let your doctor or nurse know if:

- You notice a burning feeling, redness, or rash. There are creams you can use to try to keep it from getting worse.
- Your skin is dry, flaking, or cracked. Moisturizing cream may help with this.
- Your skin is itchy. There are creams and gels you can use to ease itching. There are also some medicines you can take by mouth to try to stop the itching.
- The area around your fingernails or toenails becomes sore or red. Creams and soaks can help with this. But you and your health care team will need to watch for changes that could be signs of infection to be sure any infection is treated quickly.
- You have very dry, red, or tender eyes, or if you notice eyelashes growing inward toward the eyeball.
- You get sores on your scalp or other areas with hair. You will want to get them treated to help prevent scars that may block hair growth later.

Try to avoid exposure to sunlight. Even after treatment is over, you may find that you are more sensitive to the sun's rays than before.

Can skin changes be treated?

Because these skin problems are linked to newer drugs, the best ways to handle them are still being studied. But doctors can help you manage them using what's already known about these kinds of changes.

The doctor will need to check your skin fairly often to figure out the problem, the best course of action, and whether treatment is helping. You will probably need extra doctor visits while the problem is being brought under control.

Mild changes: Patients with mild skin changes may not need any treatment. These changes include rashes that are only in a limited area, that are not causing any distress, and are not infected. Heavy skin creams or ointments that contain no alcohol, perfume, or dye can sometimes help with dryness. Be sure to talk with your nurse or doctor before using anything on your skin.

The doctor also may prescribe a mild corticosteroid cream (such as hydrocortisone) or antibiotic gel (such as clindamycin) to put on the rash. Careful cleansing and clean, warm, wet cloths laid over your closed eyes may help if your eyelids are crusty or swollen.

The dose of the targeted therapy drug is usually not changed, and the patient is closely watched to see if the rash gets better or worse.

Moderate changes: These include a rash over a larger area of the body or skin changes causing mild distress from itching or soreness, but with no signs of infection. The skin may be treated with hydrocortisone cream, clindamycin gel, or pimecrolimus (Elidel®) cream. The doctor may also prescribe an antibiotic such as doxycycline or minocycline to be taken by mouth. Drops or ointments may be prescribed to help with eye problems.

The dose of the targeted therapy drug is usually not changed, and the patient is closely watched to see if the rash gets better or worse.

Severe changes: These are bad rashes that cover a lot of skin, cause itching and soreness that affect the patient's quality of life (such as sleep problems or pain), and are likely to get infected. Treatment is much like that used for moderate changes, including a topical cream or gel (hydrocortisone cream, clindamycin gel, or pimecrolimus cream), as well as an antibiotic such as doxycycline or minocycline that is taken by mouth. Along with this, a course of corticosteroid pills, such as methylprednisolone (Medrol®) or prednisone, is often given.

The targeted therapy drug dose is often reduced when a person has severe skin changes. Expect to see your doctor often during this time. If the rash does not get better in 2 weeks, the targeted drug is often stopped until the skin changes improve. It may then be re-started with continued skin care.

A note about steroid skin creams and gels

Steroids that are spread on the skin in the form of creams, ointments, or gels can help many skin problems. They can be used for up to 7 days after the problem has gone away. But it's important to know that using steroid creams for too long can actually cause skin problems, and can make you more likely to get a skin infection. For this reason, steroid creams (even those that don't require a prescription) should not be used more than 14 days in a row unless your doctor tells you to. Many doctors suggest that patients who are given steroids to put on their skin use it in cycles. For instance, you might use it every

day for 14 days, and then stop using it for a 7-day break. This cycle can be repeated as long as you have skin problems, or until your doctor tells you to stop.

Skin rash as a sign that treatment is working

Some people believe that the skin rash may be a sign that the targeted therapy is working (the worse the rash, the better the treatment is working). But long-term follow-up is needed to link the rash to outcomes. People with no rash or with only a mild rash should not assume that the treatment is not working.

The 2 most important things you can do are to take good care of your skin when you start targeted therapy and let your doctor know right away about any skin changes you may have.

High blood pressure

Some targeted therapy drugs can raise your blood pressure. There isn't really anything you can do to prevent this, but your doctor will watch your blood pressure closely if you are on a drug with this side effect. Some people need medicine to bring their blood pressure down to a safe level while being treated with targeted therapy. They should stay on this medicine until their doctor tells them it can be stopped.

Problems with bleeding or clotting

Angiogenesis inhibitors interfere with the formation of new blood vessels. This can lead to problems with bruising and bleeding. Bleeding, such as from the stomach and intestines, can be severe and even cause death. Tell your doctor if you throw up blood or material that looks like coffee grounds, or if you notice blood in your stool. These can be signs of bleeding in the stomach or intestines.

These drugs can also cause clots in the lungs and legs, as well as heart attacks and strokes. Let your doctor know if you have problems with sudden swelling, pain, or tenderness in the arm or leg. If you have chest pain, sudden shortness of breath, vision problems, weakness, seizures, or trouble speaking, get emergency help. These can be symptoms of serious conditions caused by blood clots.

These problems are rare, and there is no way to prevent them. If you have a problem like this, you may need to stop taking the targeted therapy drug.

Problems with wound healing

By blocking the formation of new blood vessels, angiogenesis inhibitors also interfere with wound healing. This can lead to old wounds (cuts) opening up again and new wounds not closing. It can also lead to holes opening up in the stomach or intestine (these are called *perforations*). Tell your doctor right away if you have pain in your belly or vomiting.

Because these drugs interfere with wound healing, they are usually stopped before any planned surgery.

Other side effects

Other less common side effects have also been linked to treatment with targeted therapies. These include:

- Diarrhea
- Nausea and vomiting
- Constipation
- Mouth sores
- Shortness of breath or trouble breathing
- Cough
- Feeling tired all the time (fatigue)
- Headache
- Swelling in your hands and feet
- Low blood cell counts

Keep in mind that these are not all of the side effects that people have had, just some of the more common ones. Some of these drugs also affect the heart and interact with other drugs and even foods. Each drug has different effects. To find out more about the drug you are taking call us or see our online Guide to Cancer Drugs.

Your health care team will watch you closely during treatment and will check you often. Side effects can and should be treated as early as possible. It's important that you tell your health care team about any changes in how you feel or anything you notice that's new or unusual. Tell them right away so they can treat any problems and try to keep them from getting worse.

You can learn more about managing these side effects and cancer treatment in general in our booklet called *Understanding Chemotherapy: A Guide for Patients and Families*.

When to call your doctor

When you are getting cancer treatment, you are likely more in tune with your body than you ever have been in your life. You notice every physical change and imbalance. Do not take any physical symptoms you have lightly.

Some side effects are fleeting and minor, but others may signal serious problems. You should not be the judge. Call your doctor or nurse about any changes you notice. Let them decide if anything needs to be done.

Be sure to tell your doctor right away if you have any of these symptoms during cancer treatment:

- A fever of 100.5°F or greater (taken by mouth)
- Bleeding or unexplained bruising
- A rash or allergic reaction, such as swelling of the mouth or throat, sudden severe itching, trouble breathing or swallowing
- Intense chills
- Pain or soreness at the chemo injection site or catheter site
- Unusual or new kind of pain, including intense headaches
- Shortness of breath or trouble breathing
- Diarrhea that lasts 2-3 days
- Vomiting that lasts more than a day or two
- Bloody stool or blood in your urine
- Any new or unusual problem that you're concerned about

If you're having trouble breathing or swallowing, showing signs of stroke or heart attack, or feeling very dizzy or faint, call 911 for emergency help.

Other questions you may have about targeted therapy

Can I drink alcohol?

Small amounts of alcohol can help you relax and increase your appetite. But alcohol may interact with some drugs so that they don't work as well, or it may make the side effects worse. Be sure to ask your doctor if you can drink beer, wine, or any other alcoholic beverages.

Should I take vitamin or mineral supplements?

There's no single answer to this question, but one thing is clear: No diet or nutritional plan can "cure" cancer. Taking vitamin and mineral supplements or any other

complementary or alternative medicine should never take the place of medical care. You should not take any supplements without talking to your doctor first.

For more information, please call us or visit our website to get our document *Complementary and Alternative Methods and Cancer*.

Do I need to protect my loved ones from exposure to my targeted therapy drug?

Although there are guidelines for protecting those close to you while on standard chemo, little has been written about what's needed while on targeted therapy. Even though these drugs tend to have less severe side effects, anyone taking a targeted therapy drug should avoid exposing their loved ones to the drug unnecessarily. This does not mean that you need to avoid close contact with loved ones while you are on treatment. It means that you should be careful about exposure to the drug itself or any body fluids that could contain the drug. For more information on this, see our document *Understanding Chemotherapy: A Guide for Patients and Families*. If you are taking the drug at home, you should keep your pills away from children and pets. Ask your health care team about precautions you and your family should take.

Will targeted therapy affect my memory and thinking?

Research has shown that cancer treatment can impact the thinking functions of the brain (known as cognitive functioning) for up to 10 years after treatment. Although this is commonly called *chemo brain* or *chemo fog,* it can even occur in people who do not receive drug treatment for their cancer. It isn't clear if targeted therapy drugs given without chemo or radiation can cause chemo brain.

Some of the brain's activities that can be affected by cancer treatment are concentration, memory, comprehension (understanding), and reasoning. The changes that are found in patients are often very subtle, but the people who have these problems are very aware of the changes in their ability to think.

If problems with thinking are interfering with your daily life, there are memory retraining exercises and programs, as well as other treatments that may help you retain or improve your memory and problem-solving abilities. You can also learn strategies that may help you cope with the loss of cognitive function. Ask your doctor if he or she can recommend a health professional who can help. You can learn more in our document called *Chemo Brain*.

What about my sex life?

Some notice little or no change in their sexual desire and energy level. Others find that their sexual interest declines because of the physical and emotional stresses of having cancer and getting treatment.

Cancer and its treatment can affect your desire for sex and may make it harder to enjoy sex. These include emotional changes (see section “Emotions and targeted therapy treatment”) as well as changes that have a more direct effect on your sex life:

- Unrelieved pain
- Worries about changes in how you look (skin rashes, weight changes, hair changes)
- Side effects such as nausea, diarrhea, or sensitive skin
- Surgical changes

A partner’s concerns or fears also can affect the sexual relationship. Some may worry that physical intimacy will harm the person who has cancer. Others may be afraid they might “catch” the cancer or be affected by the drugs.

You and your partner can clear up many of these misunderstandings by talking about sexual concerns with your doctor, nurse, or a counselor. Though you may find it hard to do, talk to a health professional who can give you the information and help you need.

Couples who share their feelings with one another are usually better able to adapt to the realities of cancer. If it’s hard for you to talk to each other about sex or cancer, or both, you may want to talk to a counselor who can help you communicate more openly.

If you were comfortable with and enjoyed sex before starting treatment, chances are you will still find pleasure in physical intimacy during treatment. But you may find that intimacy takes on new meaning. Hugging, touching, holding, and cuddling may become more important, while sexual intercourse may become less important.

If you aren’t in a relationship, or are in a less traditional one, cancer and its treatment can affect your sex life even more. The challenges can involve difficult decisions and be tough to manage.

Whether you’re single or part of a couple, please see our booklets *Sexuality for the Woman With Cancer* and *Sexuality for the Man With Cancer* for more information.

Pregnancy and targeted therapy

It may be possible to get pregnant during treatment, but it should be avoided because targeted therapy drugs may cause birth defects. Doctors advise women of childbearing age – from the teens through the end of menopause – to use birth control throughout treatment. Ask your doctor about what forms of birth control are safe to use - many targeted drugs interact with other drugs so birth control pills may not always be the best choice. Men may also need to use condoms to avoid exposing their partner to the drug or to avoid being exposed by a partner taking targeted therapy.

If a woman is pregnant when her cancer is discovered, it may be possible to delay treatment until after the baby is born. For a woman who needs treatment sooner, the doctor may suggest starting treatment after the 12th week of pregnancy, when the fetus is

beyond the stage of greatest risk. In some cases, termination of the pregnancy may be considered.

Talk to your doctor if you and your partner are considering pregnancy after completing treatment.

Emotions and targeted therapy treatment

What emotional effects can I expect?

Cancer and its treatment can bring major changes to your life. It can affect your overall health, threaten your sense of well-being, disrupt your daily routines, and put a strain on your relationships. It's normal and understandable for you and your family to feel sad, anxious, angry, depressed, and other feelings, such as:

- Guilt and worry over changes in your role and the roles of others in the family
- Fears about the outcome of treatment and the possibility of a shorter life
- Tiredness and lower energy levels
- Anxiety about the family, job, or money

There are ways to cope with these emotional effects, just as there are ways to cope with the physical ones.

Finding support

You can draw support from many sources. Here are some of the most important ones:

Counseling and mental health professionals

Counselors can help you express, understand, and cope with the emotions caused by cancer and cancer treatment. Depending on what you want and need, you might want to talk with a psychiatrist, psychologist, social worker, member of the clergy, or mental health therapist.

Friends and family

Talking with friends or family members may help you feel a lot better. Often, they can comfort and reassure you in ways that no one else can. But you may find that you have to make the first move. Many people do not understand cancer and may withdraw from you because they're afraid of your illness. Others may worry that they will upset you by saying the wrong thing.

You can help relieve others' fears by talking openly with them about your illness, your treatment, your needs, and your feelings. You can correct mistaken ideas and let people know that there's no one "right" thing to say. Once people know they can talk with you honestly, they may be more willing and able to open up.

Support groups

Support groups are made up of people who are going through the same kinds of experiences you are. Many people with cancer find they can share thoughts and feelings with group members more easily than with anyone else. Support groups can also be an important source of practical information about living with cancer.

You can also find support in one-to-one programs that match you with a person like you in age, gender, type of cancer, and so forth. You might talk with this person on the phone or arrange visits.

Where to find information about support programs:

- Your hospital's social work department
- Your local American Cancer Society office, in the "Find support programs and services in your area" section of our website, or by calling us at 1-800-227-2345

Coping tips for everyday life

- Try to keep your treatment goals in mind. This can help you keep going on days when it gets rough.
- Eat well. Your body needs food to rebuild tissues and regain strength.
- Learn as much as you want to know about your disease and its treatment. This can lessen your fear of the unknown and increase your feeling of control.
- Exercise if you can and if your doctor says it's OK. Using your body can help you fight fatigue, build your appetite, and make you feel better about yourself.
- Keep a journal or diary while you're being treated. Recording your activities and thoughts can help you understand the feelings you have as you go through treatment. It may also help highlight questions you need to ask your doctor or nurse. You can use your journal to record side effects. This will help you when you talk about them with your doctor and nurse. Write down the steps you take to cope with side effects and how well those steps work, too. That way, you'll know what worked best for you in case you have the same side effects again.
- Try new hobbies or go back to one you loved before. Learn new skills.
- Take it easy. You may not have as much energy as usual, so try to get as much rest as you can. Let the small stuff slide and only do the things that are most important to you. Get help from friends, neighbors, and family when your energy is low.

Doctors and nurses

If you or your family has questions or worries about your cancer treatment and its effects, talk with members of your health care team. If they are unable to give you the help you need, they can refer you to other health professionals who can help you. If you need

emotional support, they may be able to refer you to local counselors, groups, or networks where you can find support.

Cancer treatment is easier if you get help

No one can do this alone. Even though it can be hard to talk about some things that happen during treatment, don't hesitate to ask for the help you need. Always ask your doctor or nurse any questions you have about your treatment—even questions about things that may seem awkward, like sex or cost. Some people don't want to mention that the medicines prescribed to control side effects aren't working, or that they're having trouble with parts of the treatment plan. You can always start by saying, "This is a hard question for me to ask," or "I don't know how to talk about this," but then go ahead and bring it up anyway.

Open and honest talks between you, your family, and your cancer care team is the best way to understand what is happening to you, your body, and the cancer. You can also learn more about how cancer affects you and your family in the "To learn more" section under "Living with cancer."

Paying for targeted therapy

How do I pay for my treatment?

The cost of targeted therapy varies with the drug used, how it's given, how long and how often it's given, and whether you get treatment at home, in a clinic, office, or hospital. Your cost will also depend on what other treatments are given, such as radiation or standard chemotherapy (chemo) drugs. Many targeted drugs that you take by mouth are very expensive, and can reach costs of thousands of dollars per month. They may be covered under your prescription drug benefit rather than your cancer chemo benefit, so that you may end up paying more out of pocket.

Most health insurance policies, including Medicare (Part B and D), cover at least part of the cost of most kinds of targeted therapy and chemo. But to reduce their costs, companies often don't pay for every drug. Before you start treatment, find out whether your health insurance will pay for your medicines, and how much they will pay for any targeted drug you take by mouth. If it's too costly for you, ask your doctor about getting help from the drug company. To learn more about getting this kind of help, see our document called *Prescription Drug Assistance Programs*.

For more information on how to control your finances so you can better focus your energies on treatment and recovery, see our booklet called *In Treatment: Financial Guidance for Cancer Survivors and Their Families*.

What do I need to know about insurance coverage?

Insurance companies may deny payment for targeted therapy and/or chemo for these reasons:

- They may not be aware of new treatments.
- They may limit the selection of drugs that doctors can use.
- They may restrict payment to the uses first approved by the Food and Drug Administration (FDA).

If you are going to take part in a clinical trial, find out if your insurance will cover any of those costs, too. Health plans that start in 2014 or later are required to cover most of the costs for those in clinical trials for serious health conditions. Still, coverage of clinical trials varies state to state in older "grandfathered" insurance plans, and insurers may deny payment.

If your insurer denies payment for your treatment, don't give up. There are ways to appeal these decisions. You can learn more about health insurance in our documents called *Health Insurance and Financial Assistance for the Cancer Patient* and *Children Diagnosed With Cancer: Financial and Insurance Issues*.

What do I do if my health care claim is not paid?

Before you appeal, you may want to take these steps:

- Ask your customer service representative for a full explanation of why the claim was denied.
- Review your health insurance plan's benefits.
- If your plan is through your or your spouse's employer, contact your health plan administrator at work to find out more about the refusal.
- Contact reimbursement specialist hotlines at the pharmaceutical company that makes the drug for which payment was denied (ask your doctor's office the drug name and which company makes it). People there are specially trained to help with insurance issues that may come up with "their" drugs.
- Tell your health care team if you have been denied payment so that they can contact your insurer and help answer any questions.
- Ask your doctor's office staff to give your insurance company the results of scientific studies showing that a certain drug works for your type of cancer.
- Keep a record of dates, names, and conversations you have about the denial.
- Put off payment until the matter is resolved. Keep the originals of all the letters you get; your cancer care team may be able to help you make copies if you need them.

If this doesn't work, request an internal appeal (or internal review) which is done by the insurance company. Your cancer care team may be able to help with this. You have 6 months (180 days) from receiving your claim denial to file an internal appeal. If it's still denied, you can request an independent external review of the decision.

You can read more about appealing a claim denial in our document called *Health Insurance and Financial Assistance for the Cancer Patient*. You can also contact your hospital's social service office, which may be able to direct you to other sources of help.

And the American Cancer Society can help you, too. Contact us anytime, day or night, for cancer-related information and support. Call us at **1-800-227-2345** or visit www.cancer.org.

To learn more

More information from your American Cancer Society

Here is more information you might find helpful. You also can order free copies of our documents from our toll-free number, 1-800-227-2345, or read them on our website, www.cancer.org.

Communication is key

Talking With Your Doctor (also in Spanish)

Helping Children When a Family Member Has Cancer: Dealing With Treatment (also in Spanish)

Living with cancer

After Diagnosis: A Guide for Patients and Families (also in Spanish)

Pain Control: A Guide for Those with Cancer and Their Loved Ones (also in Spanish)

Caring for the Patient With Cancer at Home: A Guide for Patients and Families (also in Spanish)

Distress in People With Cancer

Nutrition for the Person With Cancer During Treatment: A Guide for Patients and Families (also in Spanish)

Nutrition for Children With Cancer (also available in Spanish)

Fertility and Women With Cancer

Fertility and Men With Cancer

Sexuality for the Man With Cancer (also in Spanish)

Sexuality for the Woman With Cancer (also in Spanish)

Cancer treatment information

Chemo: What It Is, How It Helps

Understanding Chemotherapy: A Guide for Patients and Families (also in Spanish)

Chemotherapy Principles: An In-depth Discussion of the Techniques and Its Role in Cancer Treatment

Oral Chemotherapy: What You Need to Know

Immunotherapy

Understanding Radiation Therapy: A Guide for Patients and Families (also in Spanish)

Understanding Cancer Surgery: A Guide for Patients and Families (also in Spanish)

Clinical Trials: What You Need to Know (also in Spanish)

Complementary and Alternative Methods and Cancer

Cancer treatment side effects

Chemo Brain

Chemotherapy Side Effects Worksheet

Fatigue in People With Cancer

Nausea and Vomiting

Peripheral Neuropathy Caused by Chemotherapy

Along with the above, the American Cancer Society has information about many different cancer treatment drugs and their side effects.

Insurance and money matters

Health Insurance and Financial Assistance for the Cancer Patient (also in Spanish)

In Treatment: Financial Guidance for Cancer Survivors and Their Families (also in Spanish)

Prescription Drug Assistance Programs (also in Spanish)

Children Diagnosed With Cancer: Financial and Insurance Issues

Along with the above, the American Cancer Society has information about many different types of cancer and how they are treated.

National organizations and Web sites*

Along with the American Cancer Society, other sources of information and support include:

National Cancer Institute
Toll-free number: 1-800-4-CANCER 1-800-422-6237
Website: www.cancer.gov

> For up-to-date cancer information, including information for caregivers and family members, and to find a clinical trial that may be right for you

Job Accommodation Network
Toll-free number: 1-800-526-7234
TTY: 1-877-781-9403
Website: www.askjan.org

> A free consulting service of the US Department of Labor that gives information to help you keep your job (and insurance) during cancer treatment. Offers information on your rights under the Americans with Disabilities Act, and how to talk with your employer

**Inclusion on this list does not imply endorsement by the American Cancer Society.*

No matter who you are, we can help. Contact us anytime, day or night, for cancer-related information and support. Call us at **1-800-227-2345** or visit www.cancer.org.

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