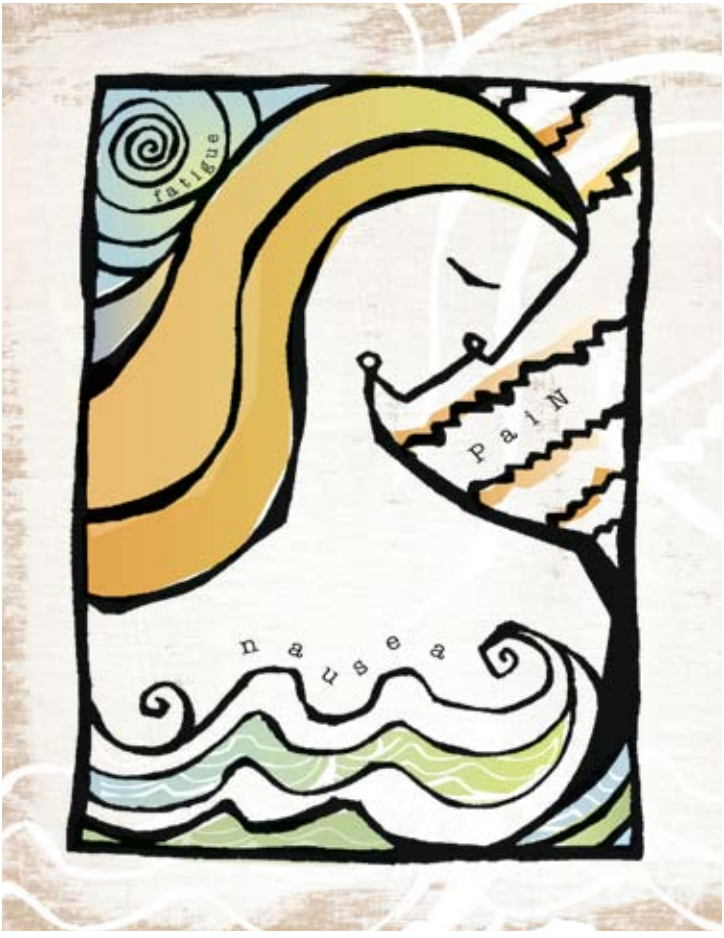
# A Patient's Guide to Side Effects




**Fatigue** ■ Hair **Loss** ■ **Pain** ■ Nausea & **Vomiting** ■ **Anemia**
■ **Neutropenia** ■ **Depression** ■ Oral **Mucositis** ■ **Rash** ■ **and More**

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CANCER UPDATES, RESEARCH & EDUCATION

**Based on science, but filled with humanity, *CURE* makes cancer understandable.**

# A Patient's Guide to Side Effects

**TREATMENT FOR CANCER** may include surgery, chemotherapy, hormone therapy, radiation therapy or a combination, and **each brings with it side effects that may be mild or severe depending on the dose and individual reactions.** In the past, suffering from side effects of treatment was an accepted part of cancer treatment, but today there are many ways to alleviate most side effects.

**THIS POCKET GUIDE has been designed to help you understand side effects** and report to your physician to what degree you are experiencing symptoms and their impact on your quality of life. Remember that you may or may not have a particular side effect depending on your treatment, its duration and your personal response. **No one expects cancer treatment to be easy,** but by working together with your physician, there are ways to manage side effects and maintain a good quality of life.

**For more information about the following and other side effects, visit the American Cancer Society's website at www.cancer.org or the Oncology Nursing Society's website at www.cancersymptoms.org.** It is important to keep a log of any side effects you experience. The American Cancer Society offers downloadable worksheets to track side effects that you can then review with your doctor at your next appointment. Severe side effects should be reported to your doctor or nurse immediately.

# Nausea & Vomiting

**CANCER-RELATED NAUSEA AND VOMITING is divided into the following categories: anticipatory, which occurs before a new chemotherapy cycle; acute, which occurs within a day of chemotherapy; and delayed, which occurs more than one day after treatment.**

## Solutions

Following the body's exposure to certain chemotherapy agents, a chemical signal known as serotonin is released. Serotonin then binds to the serotonin receptors to activate neurons, resulting in nausea and vomiting. Nausea and vomiting can also be caused by radiation therapy directed at the gastrointestinal tract, liver or brain.

Anti-nausea drugs (antiemetics) that inhibit the binding of serotonin to the receptor have become important in the treatment of nausea and vomiting that results from chemotherapy. The difference between the drugs lies in how they are metabolized by the body, their ability to bind to other types of receptors in the body and how long their effects last. Specific drugs include:

- **Aloxi® (palonosetron):** Designed to have a long half-life for more prolonged efficacy.
- **Anzemet® (dolasetron):** Generally given orally or intravenously 30 minutes prior to chemotherapy.
- **Kytril® (granisetron):** Usually given one hour before chemotherapy either orally or intravenously and then every 24 hours for two to three days by mouth.
- **Zofran® (ondansetron):** Given orally or intravenously 30 minutes before chemotherapy. Continued treatment every eight hours for one to two days after chemotherapy. An oral spray version of ondansetron called **Zensana™** may become available as soon as next year.

Many chemotherapy agents cause nausea and vomiting by stimulating proteins in the brain known as NK1 receptors, which trigger the vomiting response. **Emend® (aprepitant)** is an NK1-receptor inhibitor, so the drug is able to block this signal and prevent both acute and delayed chemotherapy-induced nausea and vomiting. Approved in 2003, Emend is used in combination with other antiemetics and was the first therapy approved for the treatment of delayed nausea and vomiting, which is frequently seen with cisplatin therapy.

It is very important to prevent and control nausea and vomiting in patients with cancer. Uncontrolled nausea and vomiting can interfere with the patient's ability to receive cancer treatment and can cause chemical changes in the body, loss of appetite, dehydration and other problems. Here are some tips from the National Cancer Institute for managing nausea and vomiting:

- Eat and drink slowly.
- Drink liquids at least an hour before or after mealtime instead of with your meals. Drink frequently and drink small amounts.
- Try to avoid odors that bother you, such as cooking smells, smoke or perfume.
- Eat a light meal before treatment.

# Hair Loss

**HAIR LOSS occurs when cancer-killing chemotherapy kills rapidly dividing cells, including those being formed in the hair follicles.**

## Solutions

The degree, pattern and timing of chemotherapy-related hair loss vary among patients, as do the changes that may occur during hair regrowth. The phase of cell division affected by a chemotherapy drug, the dose of the drug and the treatment schedule determine whether hair loss is complete or partial or whether it occurs at all.

Some drugs like Adriamycin® (doxorubicin), Taxol® (paclitaxel) and Taxotere® (docetaxel) may cause profound hair loss, whereas Oncovin® (vincristine) and Gemzar® (gemcitabine) usually cause much less hair loss. Some targeted agents, such as Herceptin® (trastuzumab) and Gleevec® (imatinib), are now being used that do not cause hair loss because they are aimed directly at the cancer cells and thus have no adverse effect on hair follicles.

Hair loss sometimes starts with a "tingling feeling" as the first strands come out and can begin as soon as three weeks after the first treatment. Hair on the face (even nasal hair, eyebrows and eyelashes), arms and legs is not immune to the effects of chemotherapy and can be lost at any time during treatment.

Suggestions for hair and scalp care during chemotherapy include the use of soft hairbrushes, mild shampoos and conditioners and low heat while drying the hair. Dying, perming and relaxing the hair should be avoided during treatment. The prescription for dealing cosmetically with hair loss on the scalp is straightforward: Patients should do whatever feels most comfortable, from covering the head with scarves, caps, turbans, hairpieces or wigs to simply leaving it bare. The National Cancer Institute advises the following for patients who choose to cover their heads:

- Get your wig or hairpiece before you lose a lot of hair. That way, you can match your current hair style and color.
- Take your wig to your hairdresser or the shop where it was purchased for styling and cutting to frame your face.
- Some health insurance policies cover the cost of a hairpiece needed because of cancer treatment. It is also a tax-deductible expense. Be sure to check your policy and ask your doctor for a "prescription."
- If your insurance does not cover the cost of a wig, check with the nurse or social work department at your hospital about resources for free wigs in your community.

Hair usually begins growing back at a normal rate within a few weeks after the end of chemotherapy, and using a product like Rogaine® (minoxidil), which is recommended for chronic age-related hair loss, is unlikely to speed up growth in cancer patients undergoing chemotherapy. Strategies to retard, reduce or prevent hair loss caused by some cancer drugs are generally ineffective.

# Anemia

**ANEMIA results when the body has too few red blood cells (RBCs), which carry oxygen to the body's tissues, resulting in symptoms such as fatigue and shortness of breath, symptoms that can greatly impact not only quality of life but cancer treatment as well.**

## Solutions

Anemia occurs in the majority of cancer patients, depending on the type of cancer and treatment. In addition to fatigue and shortness of breath, other signs of anemia include headache, heart palpitations, an increased heart rate and feeling faint when standing or sitting. Additionally, because the brain needs oxygen, cognition may become more difficult.

Anemia can be a direct result of the cancer, the products created as a result of the cancer or from cancer treatment. RBCs, which are manufactured in the bone marrow from stem cells, can be impacted by chemotherapy and radiation therapy, both of which can damage healthy cells, including RBCs. Radiation can also damage bone marrow.

Patients given potent chemotherapy drugs are highly susceptible to anemia as are patients with leukemia, lymphoma or myeloma, because, in addition to a decrease in RBCs because of treatment, leukemia, lymphoma and myeloma can grow in the bone marrow and crowd out healthy RBCs.

In addition to cancer-related treatment, a person may develop anemia because of nutritional deficiencies as a result of digestive problems if they have intestinal or colon cancer or internal bleeding from stomach or colon cancer. Cancer treatments can also suppress the patient's appetite, making proper nutrition difficult. If patients do not get enough iron, folate and vitamin $B_{12}$, their body may not be able to adequately produce RBCs.

Physicians will determine if a patient has anemia by measuring the concentrations of hemoglobin in the blood, RBC volume, or RBC number. Not all cases of anemia in patients are due to cancer. Some patients may be prone to anemia before they are diagnosed with cancer, as is the case with many premenopausal women who have borderline or low iron levels due to menstrual blood loss.

If the cause of anemia is the lack of RBCs or if the patient's RBC count is dangerously low, the patient can receive a transfusion.

More common, though, is treatment with genetically engineered erythropoietin (EPO), a protein produced in the kidneys. The Food and Drug Administration approved **Procrit® (epoetin alfa)** in 1989 for treating anemia in people undergoing dialysis for chronic kidney failure. In 1993, it was approved for cancer-related anemia. Procrit is identical to the body's own EPO, which tells the body to create more RBCs. Another drug, **Aranesp® (darbepoetin alpha)**, also acts like natural EPO and was approved by the FDA in 2002 for patients with chemotherapy-induced anemia.

# Fatigue

**CANCER-RELATED FATIGUE persists and does not resolve in response to rest. Fatigue can be caused by anemia or low thyroid function and is exacerbated by depression and emotional distress.**

## Solutions

Cancer treatments are now more effective and more complex and often entail several different types of therapies. These multimodality treatments improve patient outcomes but also seem to be associated with more severe fatigue. And with patients living longer, doctors and researchers are only now able to see the long-term impact of disease and treatment on their patients—and for some patients that seems to include cancer-related fatigue.

Although not everyone may experience fatigue to an intense degree, approximately 90 percent of patients are affected by cancer-related fatigue at some point during their treatment, and the symptom can continue for months or even years after therapy ends. Both how and when fatigue affects an individual can vary, which makes it harder for doctors and patients to recognize, describe and treat the symptom.

The first thing a patient should do when they begin to feel fatigued is talk to their doctor or nurse because it might be a symptom of anemia (see “Anemia” section). Cancer and its treatments may also affect thyroid function, which can lead to fatigue. Like anemia, doctors can treat this situation by supplementing the patient’s own hormone production with a drug. Once the biological causes, such as anemia and low thyroid function, are ruled out or treated, a symptom management specialist will look for other solutions and may combine treatments.

Exercise has been found to improve cancer-related fatigue. Excessive inactivity can cause fatigue because as you reduce physical activity, you lose muscle mass and become fatigued more easily. Doctors often start patients on a gentle exercise plan like a walking routine. Excessive exercise can compromise the immune system, so cancer patients should not exercise at high intensities.

In addition to exercise, stimulants like **Ritalin® (methylphenidate)**, which is commonly used to treat attention deficit disorder, can be helpful for some patients with cancer-related fatigue. **Provigil® (modafinil)** has also been used to treat cancer-related fatigue.

Below are some tips for coping with fatigue as recommended by the National Cancer Institute:

- Take short naps or breaks, rather than one long rest period.
- Try easier or shorter versions of activities you enjoy.
- Plan your day so you have time to rest.
- Limit the amount of caffeine and alcohol you drink.
- Allow others to do some things for you that you usually do.
- Save your energy for the most important things.

# Pain

**ACUTE PAIN comes on suddenly and lasts for a short time, while chronic pain is continuous and lasts longer than six months.**

## Solutions

Nearly 90 percent of patients will experience cancer-related pain during and/or after treatment, and more than 50 percent of cancer patients will experience chronic pain. Pain can be caused by cancer or its treatment and can occur when tumors press on nerves or organs, but can often be relieved with surgery or anti-cancer therapy.

An array of treatments provides patients with a choice for personalized pain management, which includes relief for long-term and short-term pain and brief, yet severe, flare-ups called breakthrough pain. Chronic pain often requires around-the-clock medication to stay in front of the pain—taking medication to prevent pain rather than waiting to relieve it once it occurs. Long-acting medications that are continuously given or metabolized slowly in the body are best for chronic pain and can be combined with short-acting medication for acute and breakthrough pain.

It may take time to reach a balance of pain relief and manageable side effects by gradually increasing or trying different opioids to discover the best strategy for individual patients. **Morphine** continues to be the gold standard for chronic pain relief, but, as well as other opioids, it has side effects that can include drowsiness, constipation, sleepiness and nausea, which can be relieved with medication.

Pain relief patches, which are applied to the skin for continuous high-dose pain medication over several days, are more convenient than oral medication because of their long half-life and continuous administration of painkiller. A commonly used fentanyl patch called **Duragesic®** delivers high-dose opioids continuously through the skin for up to 72 hours for chronic pain. A generic version of the fentanyl transdermal patch was approved in early 2005. Newer versions of the pain patch include **buprenorphine,** a potent semisynthetic opioid with fewer side effects than morphine.

**Prialt® (ziconotide)**, a recently approved drug modeled after a South Pacific sea snail toxin, is such a potent drug that it is administered directly into the spinal fluid via a surgically implanted pump near the patient's abdomen. Because Prialt halts the pain process by binding to calcium ions instead of opioid receptors, it has different side effects than oral opioids, including dizziness and headaches, and in rare instances, hallucinations, delirium and possible coma.

While the fear of addiction is common, it is usually an unnecessary concern. After prolonged use of pain medication, a patient may go through withdrawal if the drug is not properly titrated off, but physical dependency should not be confused with addiction. Few patients ever become addicted to pain medication.

With the increased awareness of pain as an important issue for cancer patients and survivors, many cancer centers now have pain specialists and palliative care departments for patients.

# Neutropenia

**NEUTROPENIA occurs when there is a shortage of neutrophils, a type of white blood cell that protects against infection.**

## Solutions

Fast-growing neutrophils, which survive only three days in the body, quickly succumb to traditional chemotherapy drugs, and patients face an increased risk of infection, which can become life-threatening if left untreated. Although chemotherapy is the main cause of neutropenia, radiation therapy, especially to the spine and pelvis, can also lead to neutropenia.

Beyond a fever, other symptoms of neutropenia are not specific and include fatigue and body aches, which can be seen with many chemotherapy drugs. Physicians usually detect neutropenia by doing routine blood tests, such as a complete blood count (CBC) to determine the number of white and red cells in a patient's blood. Doctors calculate the number of neutrophils in the blood by looking at the absolute neutrophil count (ANC), which shows the percentage of white blood cells that are neutrophils.

**Neupogen® (filgrastim)** was approved in 1991 and has become the most popular drug to counter neutropenia. Scientists developed it by looking at certain particles in the body that signal white blood cells to grow. By recreating these blood growth factors, or granulocyte colony-stimulating factors (G-CSF), they were able to help patients with neutropenia return to normal white blood cell levels faster. However, Neupogen, given by injection for five to seven days, can be inconvenient for patients. **Neulasta® (pegfilgrastim)**, a newer version of Neupogen approved in 2002, is longer lasting, so doctors only have to give it every 21 days, if necessary.

These drugs do have side effects, namely bone pain in the arms, lower back and joints, but many patients feel the pain is worth it because the drugs prevent treatment delay or having to take a lower dose of chemotherapy. They also improve quality of life by keeping patients out of the hospital and giving them energy to continue with their daily activities. Promising new agents in the pipeline include a molecule called AMD3100, also known as **Mozobil™ (plerixafor),** and **Telintra™ (TLK199)**.

Patients with neutropenia should take special precautions to prevent infection, including:

- Avoid large crowds or people who might have a cold, flu or other type of infection.
- Keep your mouth and gums healthy by brushing regularly with a soft toothbrush, and use alcohol-free, antiseptic mouthwash.
- Apply lotion to keep skin moist and to prevent dry, cracking skin.
- Do not scratch sores or bites; clean, apply antiseptic and bandage any open sores.
- Do not eat raw (uncooked) foods, including meats, seafood and vegetables, or unpeeled fruits.

# Neuropathy

**NEUROPATHY refers to an injury to the peripheral nerves, which are made up of sensory nerves (needed for touch, temperature and pain) and motor nerves (aid in movement and muscle tone). Sensory neuropathy is more common than motor neuropathy and may result in pain as well as numbness and a tingling or loss of sensation. Motor nerve damage results in a disruption of signals to the muscles and can result in symptoms such as muscle weakness, problems with balance and foot drop.**

## Solutions

Neuropathy may occur weeks, months or even years after treatment ends, but patients receiving vinca alkaloids may develop neuropathy during treatment. Gradually, the symptoms may resolve as the nerves slowly heal.

A number of chemotherapy drugs, including cisplatin, Taxol® (paclitaxel), Eloxatin® (oxaliplatin), Oncovin® (vincristine), Thalomid® (thalidomide) and Velcade® (bortezomib), frequently prove toxic to nerves. Patients with nerves damaged by an inherited disorder, diabetes, excessive alcohol use or another condition may be predisposed to developing chemotherapy-induced neuropathy. In the case of diabetes, a high blood sugar level is thought to weaken the ability of nerves to transmit signals, so it is recommended that patients work with their doctor to keep levels as normal as possible.

While researchers are investigating compounds to protect the nerve, drugs for symptom management include anticonvulsants, such as **Neurontin® (gabapentin)**, and antidepressants, including nortriptyline or amitriptyline. The Food and Drug Administration has not approved these drugs for treating neuropathy, but in practice, physicians have found they often bring patients some relief.

With Neurontin, doctors typically start patients off on a low dose and increase the amount of medication as needed to ease the pain. With a physician's order, a compounding pharmacy can prepare a topical cream containing the active ingredient in Neurontin for application to the skin, which produces fewer side effects. Also available topically is **Lidoderm® (lidocaine patch)**, which is applied to intact skin in the area with the most pain.

Another option is **transcutaneous electrical nerve stimulation** (TENS), which helps prevent pain signals from reaching the brain by delivering painless electrical impulses through electrodes positioned on the skin. TENS doesn't work for all types of pain and is generally less effective for chronic pain as opposed to acute pain.

Drug-free methods used alone or in conjunction with medication include **acupuncture, massage** and **herbs. Physical therapy** may strengthen weakened muscles, and an occupational therapist may recommend assistive devices that help with daily activities.

# Depression

**DEPRESSION is feelings of overwhelming sadness or anxiety that do not lessen over time. Symptoms of clinical depression may include weight loss, fatigue and/or sleep disorders.**

## Solutions

While no one would argue against the fact that a cancer diagnosis and its treatment can bring feelings of sorrow, fear and anxiety, the attitude of depression as "just another side effect" has changed to emphasize the importance of separating appropriate sadness and anxiety from clinical depression.

Clearly, a cancer diagnosis will bring with it feelings of distress, but as treatment is planned and initiated, you should begin to see a shift in feelings that leads to adaptation. If your mood does not change and you would classify your feelings as hopelessness and despair, you need to be assessed for clinical depression. Untreated depression can exacerbate other issues, such as sleep disorders and lack of desire to eat.

Studies indicate as many as 30 percent of cancer patients will meet diagnostic criteria for a depressive or anxiety disorder at some point during treatment, compared with around 10 percent of American adults who will experience clinically significant depression in a given year. But help is available in myriad forms, from support groups and psychological counseling to highly effective antidepressant medications, some of which are listed here.

- **Selective Serotonin Reuptake Inhibitors (SSRIs): Prozac® (fluoxetine), Zoloft® (sertraline), Paxil® (paroxetine)**

Levels of neurotransmitters (chemicals used by nerve cells to communicate in the brain) are reduced during depression. Thus, SSRIs target neurotransmitters and work to block the reabsorption (reuptake) of serotonin into the nerve cells, making more of the chemical available in the brain. Side effects can include headache, difficulty sleeping, decreased libido and upset stomach.

- **Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs): Effexor® (venlafaxine)**

These drugs inhibit reabsorption of both serotonin and norepinephrine, thus increasing levels of both chemicals in the brain. Side effects of Effexor can include increased blood pressure, nausea and insomnia.

- **Norepinephrine and Dopamine Reuptake Inhibitors (NDRIs): Wellbutrin XL® (bupropion)**

Dopamine is another neurotransmitter in the brain thought to contribute to depression. Wellbutrin acts by increasing levels of dopamine as well as norepinephrine. Side effects are similar to SNRIs, and patients with a history of seizures or eating disorders should not take NDRIs.

- **Tricyclic Antidepressants: Elavil® (amitriptyline) and Pamelor® (nortriptyline)**

Tricyclic antidepressants have been used for more than four decades and work by increasing the amount of serotonin and norepinephrine in the brain.

# Oral Mucositis

**ORAL MUCOSITIS is the inflammation of the tissue lining the nose and throat. Chemotherapy and radiation attack dividing cancer cells as well as healthy cells lining the mouth and esophagus. This results in diminished or thinning oral mucosa, sloughing of oral mucosa and ulcerations.**

## Solutions

Oral mucositis is experienced by approximately 40 percent of all patients who take standard-dose chemotherapy and up to 75 percent of patients on high-dose chemotherapy. Certain chemotherapy drugs have a much higher incidence, such as 5-FU and methotrexate. Nearly all patients receiving radiation therapy to the head and neck will experience mucositis, appearing a few days to two weeks after the start of therapy and persisting for at least two weeks after radiation therapy is finished. Early intervention and prompt treatment of mucositis may lessen the degree of these symptoms and potential complications.

Eating well and drinking fluids are important to maintain good health and play a role in the healing process, so it is important to take good care of the mouth and throat. Examine the mouth at least once daily and report changes, such as ulcers, pimples, sores, red areas or patches, to your doctor or nurse. Some other things to keep in mind are:

- Keep the mouth clean and moist. Clean the teeth using a soft toothbrush or swab.
- Do not use common mouthwashes. They often contain alcohol, which can irritate the mouth. Instead, rinse the mouth with salt or baking soda solution.

If sores develop inside the mouth, the patient should:

- Avoid foods and juices that are highly acidic (oranges, tomatoes and grapefruits).
- Work with the doctor and nurse to control pain. Pain relievers, such as liquid **Tylenol® (acetaminophen)** with or without codeine, help lower the perception of pain, but have little impact on the oral manifestations of mucositis.

In December 2004, the Food and Drug Administration approved **Kepivance® (palifermin)** for severe oral mucositis in patients with blood cancers undergoing bone marrow transplant. The safety and efficacy of the drug is being investigated in patients with solid tumors, including head and neck cancer.

**Gelclair® (hyaluronate)**, approved in 2002, exerts its pain-relieving effect by forming a protective barrier, hydrating and coating the oral mucosa without numbing or drying. Gelclair can provide pain relief for up to seven hours in mild to moderate mucositis and up to two hours in severe mucositis.

A new agent called **Saforis™ (glutamine)**, which is effective in preventing and treating oral mucositis in cancer patients, was recently granted priority review by the FDA. An approval decision is expected no later than mid-October.

# Rash

**RASH resulting from certain cancer drugs can resemble an acne-like or rosacea-type skin reaction on the face, neck, chest, back and arms.**

## Solutions

Treatments that target the epidermal growth factor receptor (EGFR), such as Tarceva® (erlotinib) and Erbitux® (cetuximab), may cause some patients to develop an acne-like rash that peaks in the second week of treatment and usually subsides by the fourth week of treatment. A rash will completely disappear once treatment ends. Other cancer treatments that cause rash include experimental treatments called Tykerb® (lapatinib) and panitumumab (formerly ABX-EGF).

Since EGFR is expressed in the epidermal layer of the skin, it is believed that these targeted agents inhibit the EGFR in the skin and an inflammatory response occurs, usually causing an acne-like skin reaction. EGFR is also found in the oil-producing sebaceous glands, so drugs that inhibit EGFR can cause a rosacea-like rash, where, in some cases, topical antibiotics may be helpful. Other types of rash that may develop include pruritus (severe itching), dry skin and erythema (reddening, such as with a sunburn).

The appearance of rash is a predictor of treatment efficacy for some EGFR-targeted agents. If a skin rash develops because the drug is inhibiting EGFR in the skin, it may be a sign the drug is inhibiting the receptor in cancer cells. The development of a rash has been suggested as a possible predictor of response and survival in patients receiving certain EGFR inhibitors, including Tarceva and Tykerb. Further research will be needed to confirm an association between rash and true clinical benefit.

Treatment-related rash is typically mild to moderate, but there is the threat of infection. If the rash becomes too severe, the drug dosage is reduced, delayed or stopped completely.

While there are no guidelines to manage rash and no randomized trial data, treatments can include **antibiotics,** both oral and topical, and **topical corticosteroids** if the reaction is severe. An antihistamine, such as **Benadryl® (diphenhydramine)** or **Atarax® (hydroxyzine)**, may lessen itching. Agents being researched to treat EGFR-associated rash include **Elidel® (pimecrolimus)**, an eczema treatment cream.

Although the rash may resemble acne, acne medications and any substance that dries out the skin will not work and may worsen the condition. The rash may also be aggravated by sunlight, so sunscreen and low exposure to direct sunlight is highly advised. It is suggested that patients use emollients to prevent and alleviate dry skin.