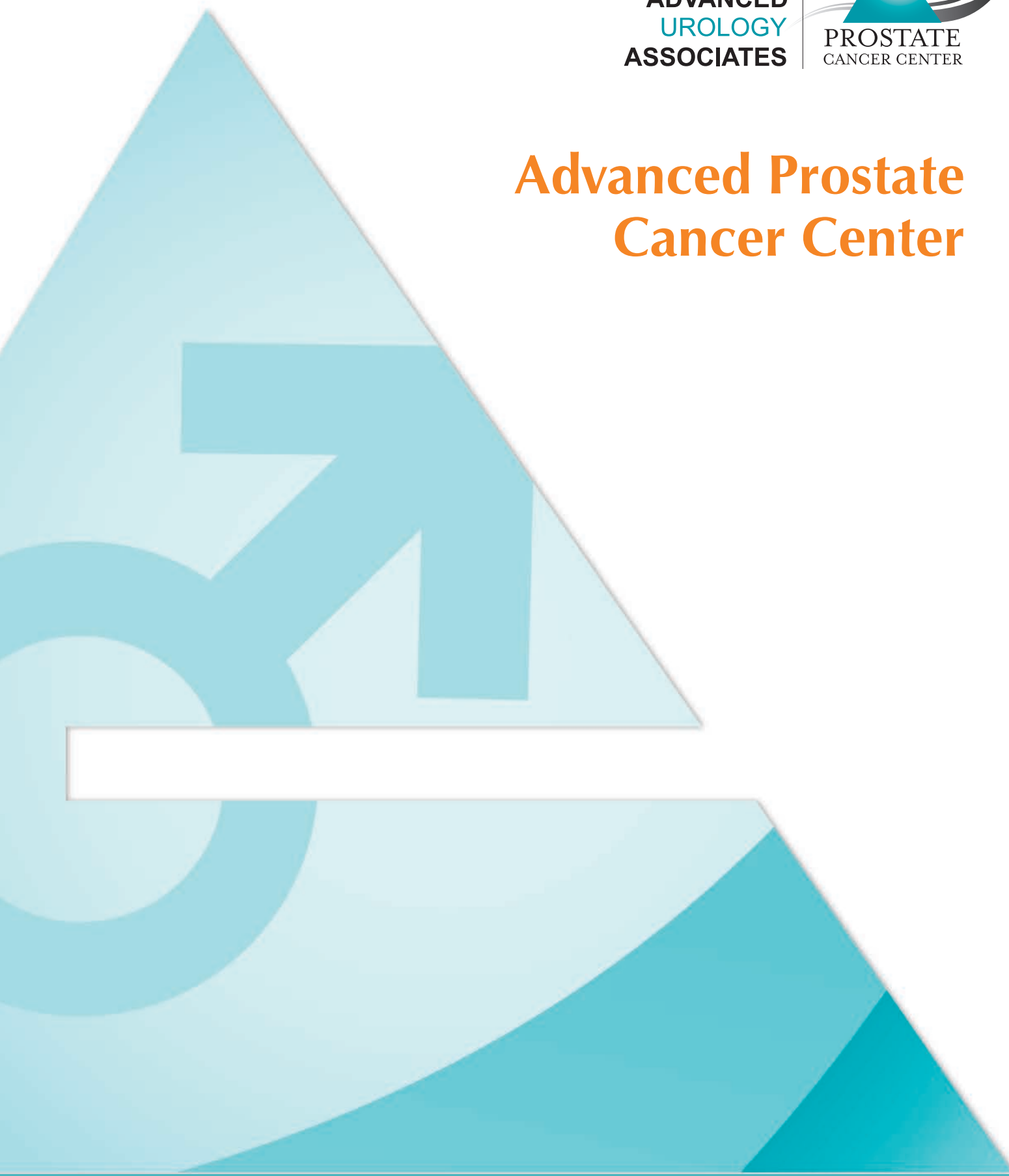


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# Advanced Prostate Cancer Center



# Advanced Prostate Cancer Center

Cancer that spreads outside the prostate gland to the lymph nodes, bones, or other areas is called **metastatic prostate cancer**. Currently, no treatments can cure advanced prostate cancer. However, there are ways to help control its spread and related symptoms.

## Bone Health

Once prostate cancer spreads to the bone, it can potentially become a painful process, but there is hope through treatment. Xgeva is a treatment that stops proteins from signaling bone removal within the skeletal system for use in men with bone metastases from prostate cancer. The body naturally destroys old bone material while making new bone material. The drug slows the process of destroying bone and interrupts skeletal damage to the bones by spreading prostate cancer cells. This inhibits bone loss and fractures and relieves pain from prostate cancer in the bone. Possible side effects of bone treatments include fatigue, diarrhea, nausea, and weakness.

Men should also take Calcium plus vitamin D to help strengthen the bones. The vitamin D helps absorb more of the calcium into the bones.



## Hormonal Treatment/Androgen Deprivation Therapy (ADT)

Male hormones, specifically testosterone, fuel the growth of prostate cancer. By reducing the amount and activity of testosterone, the growth of advanced prostate cancer is slowed. Hormone (endocrine) therapy, known as androgen ablation, androgen deprivation therapy, or androgen suppression therapy, is the first line treatment for aggressive prostate cancer, metastatic prostate cancer and advanced metastatic prostate cancer.

In many patients, endocrine therapy provides temporary relief of symptoms of advanced prostate cancer. Endocrine therapy may reduce tumor size and levels of prostate specific antigen (PSA) in most men.



## Patients will be started on hormone/ADT treatments if:

- The prostate cancer has spread too far to be cured by surgery or radiation, or if the patient is not a candidate to receive these treatments for various medical reasons
- The cancer remains or comes back after initial treatment with surgery or radiation therapy

## Examples of medications used to stop or slow down hormones

- Luteinizing hormone releasing hormone agonists (LHRH agonists) can stop the testicles from making testosterone, including leuprolide (Lupron), leuprolide acetate (Eligard), triptorelin (Trelstar), and goserelin (Zoladex)
- Luteinizing hormone releasing hormone antagonists, such as Firmagon (degarelix)
- Anti-androgens can block the action of androgens (hormones that promote male sex characteristics), such as testosterone. An example is Casodex (bicalutamide).
- Some drugs can prevent the adrenal glands from making androgens, such as ketoconazole.
- Secondary blockers include Xtandi (enzalutamide) ZYTIGA® (abiraterone acetate)

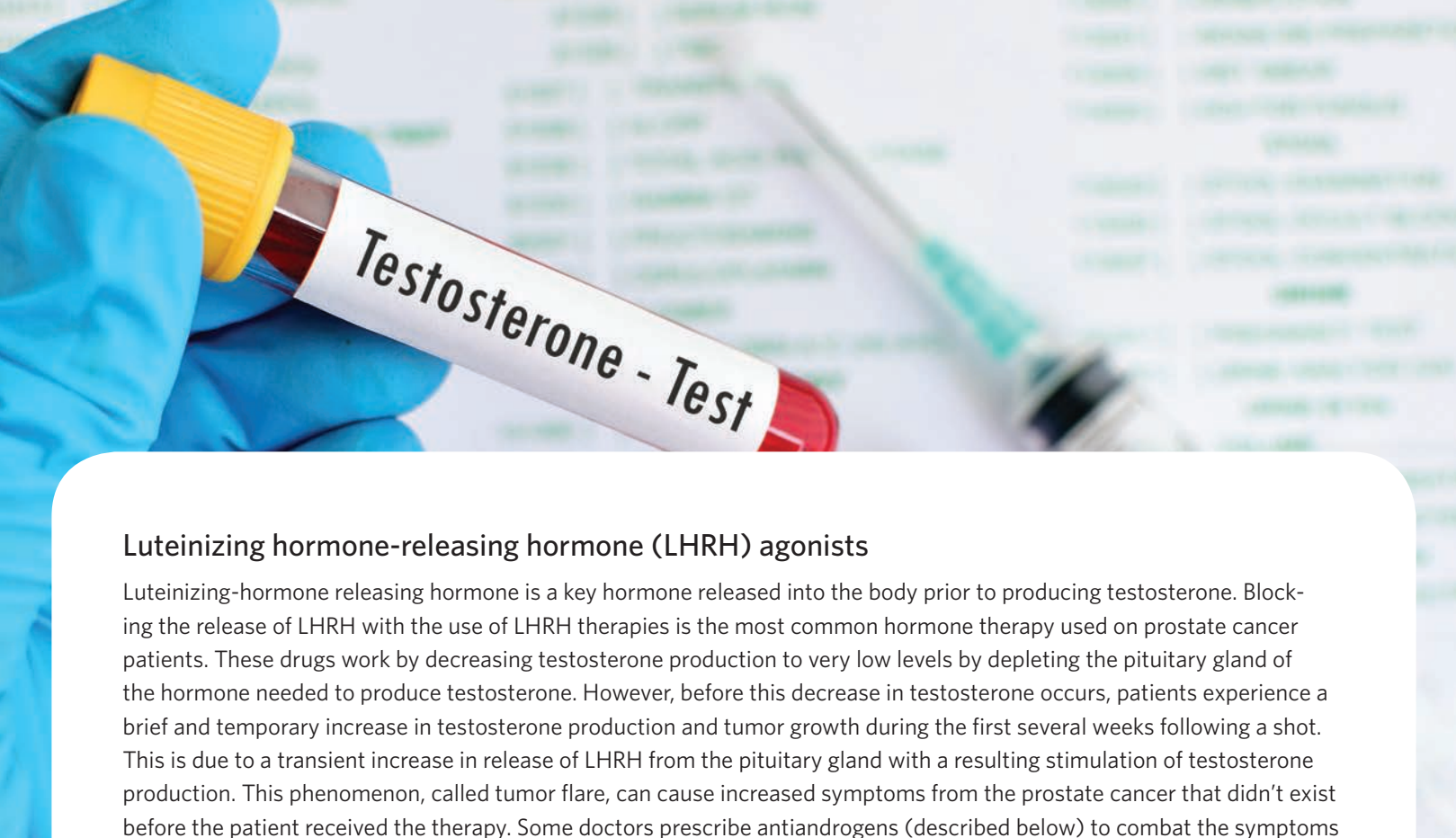
### Orchiectomy

An orchiectomy is a surgical procedure to remove both testicles, the main source of male hormones, such as testosterone, to decrease the amount of hormone being made. This is mostly used after surgical removal of the prostate has failed.

### Hormone-related drugs approved to treat advanced prostate cancer

- luteinizing hormone-releasing hormone (LHRH) analogs
- luteinizing hormone-releasing hormone (LHRH) antagonists
- anti-androgens





### Luteinizing hormone-releasing hormone (LHRH) agonists

Luteinizing-hormone releasing hormone is a key hormone released into the body prior to producing testosterone. Blocking the release of LHRH with the use of LHRH therapies is the most common hormone therapy used on prostate cancer patients. These drugs work by decreasing testosterone production to very low levels by depleting the pituitary gland of the hormone needed to produce testosterone. However, before this decrease in testosterone occurs, patients experience a brief and temporary increase in testosterone production and tumor growth during the first several weeks following a shot. This is due to a transient increase in release of LHRH from the pituitary gland with a resulting stimulation of testosterone production. This phenomenon, called tumor flare, can cause increased symptoms from the prostate cancer that didn't exist before the patient received the therapy. Some doctors prescribe antiandrogens (described below) to combat the symptoms caused by tumor flare.

LHRH agonists are administered as regular shots ranging from once a month to once every six months. The most commonly used LHRH analogs in the U.S. are leuprolide (Eligard, Lupron), histrelin (Vantas), triptorelin (Trelstar), and goserelin (Zoladex). This drug may be used in combination with radiation. They cause side effects similar to those from the surgical orchiectomy. These drugs carry a risk of triggering diabetes, heart disease, osteoporosis, breast pain or enlargement, erectile dysfunction, decrease in libido, diarrhea and/or constipation, increase in belly fat. Before starting one of these drugs, patients should tell their doctor if they have a history of diabetes, heart disease, stroke, heart attack, high blood pressure, high cholesterol, or cigarette smoking.

### Luteinizing hormone-releasing hormone (LHRH) antagonists

This class of drug can block LHRH from stimulating testosterone production without causing a surge of testosterone, eliminating the tumor flare. The drug in this class is called Degarelix (Firmagon). This drug may also be used as combination treatment during radiation. But is also used to treat advanced prostate cancer. It has been shown to decrease the progression of disease, but further trials are needed to look at long-term outcomes. This medicine is given as an injection every 28 days. It is fairly well tolerated with common side effects being local injection site problems, including a lump at the injection site, tenderness, itching, and redness, erectile dysfunction, hot flashes, and bone loss.

### Anti-androgens

The tumor flare or rise in testosterone associated with LHRH drugs can be prevented with anti-androgens such as Casodex (bicalutamide). They can help block the action of testosterone in prostate cancer cells and are used in conjunction with LHRH agonists. Anti-androgens can cause less sexual side effects, but are not as effective as an orchiectomy or LHRH agonists in treating the disease.

### Palliative radiation treatment

Radiation can target specific sites where cancer has metastasized, most commonly the bone. It can be used alone or in combination with hormone therapy or immunotherapy. The radiation can relieve bone pain and can slow the growth of cancer. It can take up to several weeks for pain to lessen.

## Advanced Metastatic Castrate-Resistant Prostate Cancer

Eventually, most patients with advanced prostate cancer stop responding to hormone therapy. The cancer cells become castrate resistant and grow strong enough that hormone therapies have a lessening effect on the cancer. This is known as **castrate-resistant prostate cancer**.

However, there are several other treatment options, including:

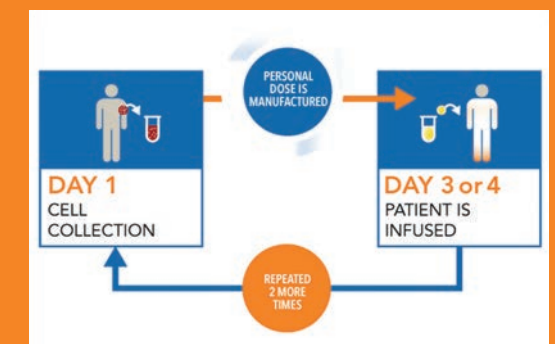
- Immunotherapy-Provenge (sipuleucel-T)
- Secondary or inhibitor/blocker hormone therapy
- Antifungal agent
- Xofigo (radium Ra-223 dichloride)

### PROVENGE® for Advanced Prostate Cancer

Once a patient becomes castrate resistant they may be a candidate to begin Sipuleucel-T (PROVENGE), PROVENGE is a "vaccine" for advanced prostate cancer that helps extend life and is the only FDA approved immunotherapy. Unlike vaccines against infections like measles or mumps, immunotherapy is designed not to prevent, but to treat prostate cancer by using your own immune system to fight the disease. It is designed to activate the immune cells to best identify prostate cancer cells as abnormal cells or invader cells in your body. The immune system has a hard time finding the cancer cells because they look a lot like normal cells to the immune system and cancer cells may give off signals that manipulate the immune system into leaving them alone. Most prostate cancer cells contain phosphates which the immunotherapy recognizes and commands the body to attack.

The PROVENGE process involves extracting white blood cells from your blood, reprogramming them by "training" them in a lab to destroy and fight prostate cancer. The newly "trained" cells are then reinfused back into the body a few days later. Since the original cells are from you, there is little chance of the body rejecting the therapy. This process delivers a treatment designed just for you.

PROVENGE is an immunotherapy treatment for certain patients with advanced prostate cancer that reprograms your body's own ability to fight back.



# immunotherapy

PROVENGE may be used in men who are on hormone therapy and have rising PSA levels, your cancer has spread from the prostate to other places, such as your bones, and if you have few or no prostate cancer symptoms. Since PROVENGE is an immunotherapy that boosts your immune system, it should be used early on in your advanced cancer treatment plan. The National Comprehensive Cancer Network (NCCN) guidelines recommend using Provenge first as it is the only immunotherapy treatment option, making it an approved first line treatment for insurance companies.

When you and your clinician have decided PROVENGE is the next step in your treatment, our office will assist you in completing and signing enrollment forms, including forms for financial assistance programs. These forms get sent to the PROVENGE manufacturing company, Dendreon. Within 24-48 hours, Dendreon will respond back to the clinician's office with information regarding insurance. From there, the office will handle all prior authorizations through the insurance company, which may take up to 3 weeks for determination of coverage. Once approval is obtained, a treatment schedule will be made. Dendreon will then send you a Patient Comfort Kit with items that will support you through the PROVENGE process.

## Treatment Schedule

The schedule is a total of three cell collection dates and three infusion dates. The cell collection is done at ITxM apheresis center, with locations in Orland Park, Rosemont, Chicago, and Rockford. Blood will be drawn from your body and passed through a machine that collects a small portion of your immune cells, along with some platelets and red blood cells. The machine returns the rest of the blood and cells to your body. This process is called leukapheresis and can take 3-4 hours. Your immune cells are then sent to an FDA approved manufacturing facility, two locations in the United States, California and Georgia. Here is the process where the Provenge, a protein molecule, is integrated with your immune cells. The Provenge is then shipped to our office for infusion three days later. It has to be infused within hours of delivery since it has a short shelf life. The infusion appointment will generally take about two hours. This process is repeated two additional times, usually every other week.

## Preparing for Treatment

To prepare for the treatment, you will need to drink more water than usual for 2-3 days before the appointments to stay hydrated. Avoid drinking caffeinated beverages on the day of each cell collection date. Eat a calcium-rich diet, including yogurt, milk, orange juice, bananas, blueberries, and almonds. Wear comfortable clothing and sleeves that can be raised above the elbow to allow for veins to be accessed for the blood collection and infusion. Have a driver the day of the cell collection as you may feel tired after the process. A driver is not necessary on the infusion dates.

### Common Side Effects

The most common side effects include chills, fever, fatigue, back pain, nausea, and headache. There is potential for infusion reactions, but you will be pre-medicated to try and prevent these from occurring.

## Secondary or inhibitor/blocker hormone therapy

Even with hormone injections, cancer may progress to the point where the adrenal glands or prostate cancer cells themselves may produce androgens that fuel the cancer's growth. Stronger treatments need to be added to a regimen of the injected hormone therapies. Hormonal medications that inhibit the synthesis of androgen, include abiraterone acetate (Zytiga), and enzalutamide (Xtandi), both taken orally.

About ten percent of testosterone in the body is created by the adrenal glands and few therapies focus on shutting down this production until it becomes absolutely necessary to rid the body of all testosterone. Zytiga is used with steroids to shut down the adrenal glands while avoiding the adverse effects of chemotherapy. Use of Zytiga is contraindicated with men that have severe liver impairment. Blood pressure and electrolytes (monitored in the blood) need to be controlled before starting on Zytiga. No food two hours before taking Zytiga and one hour after taking this medication.

Xtandi is able to block androgen receptors to slow the production of testosterone without the use of a steroid. Xtandi cannot be used in men with a seizure disorder or with severe renal failure. This medication can be taken with or without food. Blood pressure will be monitored regularly, along with some blood tests, including liver function, kidney, function, and electrolytes. The PSA lab test is the primary way to determine how well the medications are managing the prostate cancer, along with scans.

**Side effects of these therapies include:** breast pain or enlargement, cholesterol level changes, erectile dysfunction and lower libido, diarrhea and / or constipation, increase in belly fat, joint pain, swelling, increased risk of osteoporosis, and cardiovascular events.

## Antifungal agent

Ketoconazole, an antifungal agent, inhibits adrenal and testicular synthesis of testosterone when used at high doses. Response rates in a second line setting are 20%-40% with significant side effects. Doses range from 200mg 3 times a day to 400mg three times a day. The drug must be given with hydrocortisone to prevent adrenal insufficiency.

## Xofigo/Radium Ra-223 dichloride

If several areas of the skeletal system are affected and are causing pain, radiation can be administered in the blood stream by a minute injection in the vein (IV), once a month for a total of six injections. Xofigo is used in men with castrate resistant prostate cancer, metastatic only to the bones. Xofigo contains the radioactive material radium 223. It goes to the areas in the bones that are growing quickly from the bone metastases. It gives off a strong energy, but has a short range that does limited damage to healthy cells around it. It slows progression of the cancer and gives some relief to bone pain for a certain length of time.

Xofigo can be absorbed by other organs, primarily the bone marrow and digestive system, which may result in side effects in those healthy tissues.

**Common side effects include:** nausea, diarrhea, low blood cell counts. Blood counts will be monitored throughout treatment. It is important to stay hydrated.

About **10%** of testosterone in the body is created by the adrenal glands and few therapies focus on shutting down this production until it becomes absolutely necessary.

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