

# A Guide to Hormone Therapy for Prostate Cancer Patients



**Affected by Prostate Cancer?**

**Us  TOO**

**SUPPORT - EDUCATION - ADVOCACY**

[www.ustoo.org](http://www.ustoo.org)



## You are not alone on your journey with prostate cancer.

If you've been diagnosed with prostate cancer or have a family member or friend who is dealing with prostate cancer, you're not alone. Us TOO International Prostate Cancer Education and Support Network was started as a 501(c)(3) not-for-profit organization established in 1990 that serves as a resource of volunteers with peer-to-peer support and educational materials to help men and their families/caregivers make informed decisions about prostate cancer detection, treatment options and related side effects.

### About Prostate Cancer

- Prostate cancer is the most common non-skin cancer in the U.S., affecting one in seven men.
- African American men have the highest incidence of prostate cancer and are 40 percent more likely to develop the disease compared to Caucasian men.
- Men with a family history of prostate cancer are at higher risk for developing prostate cancer.
- Prostate cancer is the second largest cancer killer of men following lung cancer. If detected early, prostate cancer is often treatable.
- Screening for prostate cancer includes a PSA (prostate specific antigen) blood test and a DRE (digital rectal exam). A biopsy is required to diagnose prostate cancer.

- There is confusion over inconsistent messages about the value of PSA testing for prostate cancer. The concern is that this is causing some men to forego testing for early detection resulting in physicians seeing an increase in prostate cancer initially diagnosed at an advanced stage.
- Rather than any "quick fix" for prostate cancer, there are many treatment options and related side effects that each patient needs to evaluate.

#### Our Mission

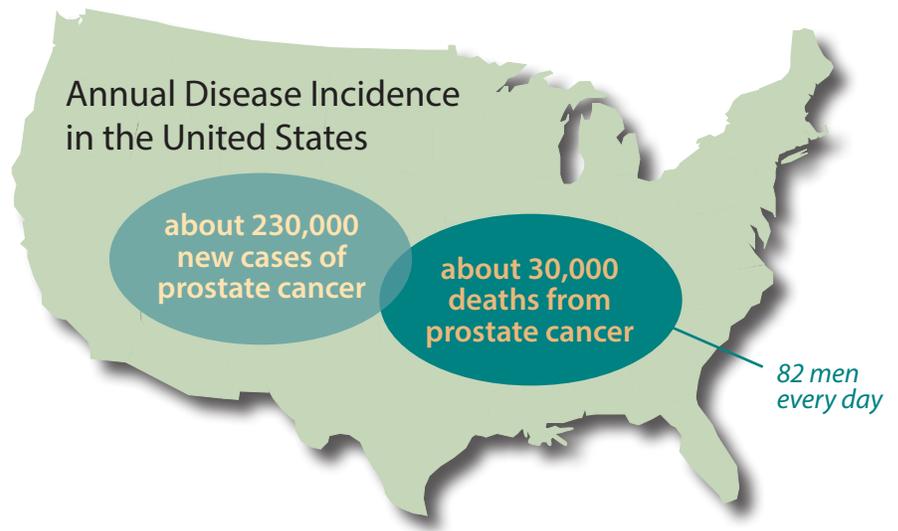
*The mission of Us TOO is to provide hope and improve the lives of those affected by prostate cancer through support, education and advocacy/awareness.*

Affected by Prostate Cancer?



SUPPORT - EDUCATION - ADVOCACY

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There are nearly 3 million men in the U.S. who are living with a prostate cancer diagnosis. This number is estimated to reach 4 million by the year 2024.

## Treatment Options

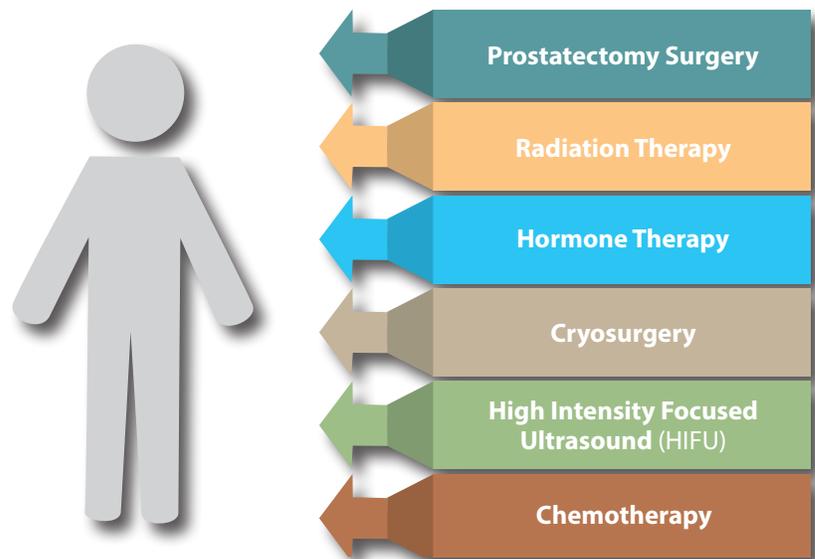
After receiving a diagnosis of prostate cancer, it's important to take the time that's necessary to learn about all available treatment options and their related side effects. If your Gleason score is a 6 or even a 7 (3 + 4), talk with your doctor about active surveillance (watchful waiting); and consider testing the prostate cancer tissue from the biopsy to predict disease aggressiveness.

While we believe that every man has a right to know if he has prostate cancer, no one wants to be under-treated or over-treated. Knowledge is power. Look to the educational resources and support services provided by Us TOO at no charge.

Oftentimes, a combination of treatments will be recommended to treat prostate cancer.

Male hormones are responsible for stimulating prostate cancer growth. Hormone therapy is most often used to treat advancing prostate cancer, but may also be used in early stage

prostate cancer (Stage T2) in combination with radiation therapy, or prior to surgery to reduce the size of the prostate so it's easier to remove.



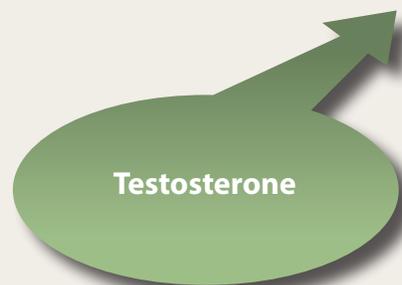
## Hormones and Androgens

Hormones are chemical messengers. They are produced by the body's glands or organs and they cause or control a bodily function. In men, a critical class of hormones called "androgens" has a wide range of functions.

Androgens affect every major tissue in a man's body and are important for building muscle mass, increasing bone formation, and stimulating red blood cell production. Androgens are responsible for many uniquely male features including lower voice, male hair patterns and the male libido, or sexual drive. The two major androgens that fuel prostate cancer are testosterone and dihydrotestosterone (DHT).

### Two Major Androgens Involved in Prostate Cancer

*Produced in the testes and adrenal gland, testosterone and dihydrotestosterone (DHT) are hormones that fuel the growth of prostate cancer.*



**Testosterone is often referred to as "the male sex hormone" and is the "fertilizer" for prostate cancer growth.**



**Created due to the metabolism of testosterone, dihydrotestosterone is five times as potent a growth stimulator of prostate cancer when compared to testosterone.**

# Androgen Deprivation Therapy (ADT)

## Hormone therapy for prostate cancer is known as androgen deprivation therapy (ADT).

Although ADT is often referred to as hormone therapy, it doesn't involve the use of hormones. It includes any treatment that lowers the androgen level to deprive the man's body of testosterone. ADT drugs block the production or absorption of androgen hormones causing the prostate cancer to shrink or grow more slowly. Ideally, testosterone, DHT, and PSA levels drop to practically zero. This point is referred to as 'castrate level' since it replicates the effect of a physical castration (orchiectomy).

If treatment becomes ineffective and the cancer begins to grow despite the absence of androgens, the disease state of the prostate cancer is called **hormone refractory, androgen independent, or castrate resistant**. These names all mean the same thing.

Patients most often treated with ADT include men with:

- Regional spread of prostate cancer
- Early recurrence of prostate cancer after prior treatments such as surgery or radiation
- Metastatic prostate cancer

Androgen deprivation therapy (ADT) can involve the use of a few drugs simultaneously. Various combinations for second-line therapy (*the continuation of ADT after becoming castrate resistant*) may also include the off-label use of ketoconazole, an anti-fungal agent.

Ketoconazole has proven to be effective for treatment of elderly men after at least one androgen suppressive treatment with or without chemotherapy.

## ADT Drug Delivery Options

### Pills or Injections

Provide for concentrated elevations of a drug periodically and can be administered at regular or intermittent intervals.

### Patch

Allows for the delivery of a consistent dosage over a specified period of time that can be adjusted.

### Implant

Delivers consistent dosage for 12 months through a small, flexible cylinder placed under the skin of the upper, inner arm.

Estrogen patches are another alternative means to stop or counter the production of androgens.

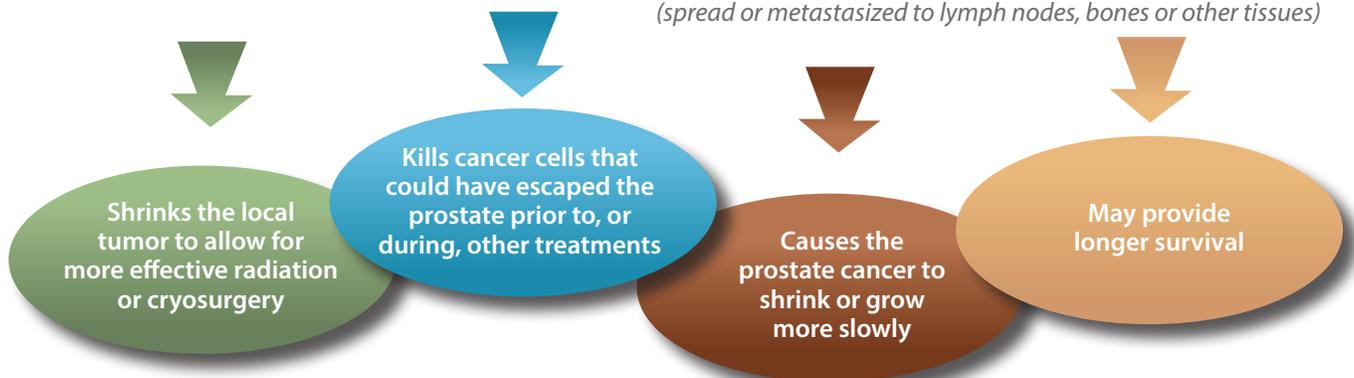
*The goal of androgen deprivation therapy (ADT) is to lower your testosterone to castrate levels with a reading of less than 20 nanograms per deciliter (20 ng/dl). You are not castrate resistant unless your numbers have first dropped to castrate levels. If your doctor told you that you're castrate resistant, question that assessment by looking at past tests to determine if the testosterone was brought down.*

## What Does Androgen Deprivation Therapy (ADT) Do?

For Early-Stage Prostate Cancer:

For Advanced-Stage Prostate Cancer:

(spread or metastasized to lymph nodes, bones or other tissues)



# Overview of Hormone Therapy

## LHRH Therapy

*Injectible luteinizing hormone-releasing hormones cause a drop in the level of testosterone.*

Intramuscular injections of medications are given monthly or alternatively every 84 days, 112 days, or even every six or 12 months. LHRH therapy shuts down the production of luteinizing hormones and causes the testicles to stop producing testosterone. This is often referred to as “medical castration,” or a “medical orchiectomy,” since the effect is the equivalent to the removal of testicles (orchiectomy).

Intermittent androgen deprivation (IAD) involves starting and stopping treatment for periods of time and is often used following a protocol that determines if and when a man can discontinue LHRH therapy and/or antiandrogens, or other anti-prostate cancer agents.

An advantage of LHRH therapy is the elimination of the need for an

orchiectomy for those men preferring not to have surgery. **The key advantage to LHRH therapy is that it is reversible.**

LHRH therapy injections are cumulatively more expensive than a one-time surgical procedure. In most instances, insurance companies, including Medicare, cover the cost of LHRH therapy injections.

## Antiandrogen Therapy

*Antiandrogen drugs block the action of male hormones, including testosterone and androgens released by the adrenal glands.*

Drugs called antiandrogens inhibit the testosterone produced by adrenal androgen by blocking the interaction of the testosterone with cells normally stimulated by testosterone.

Antiandrogens block testosterone contributed by the adrenal glands, as well as any residual testosterone that may not be blocked by LHRH therapy.

Cost and compliance, as well as drug-related side effects, are disadvantages of antiandrogen therapy. Some of these drugs must be taken several times per day and, therefore, some doses may be forgotten.

## Estrogen Therapy

*Administration of estrogen hormones lowers testosterone production resulting in some direct apoptotic (cancer cell death) effects on both androgen-dependent and androgen-independent prostate cancer cells.*

Even though estrogens are able to inhibit androgen production by the testicles,

estrogens such as diethylstilbestrol (DES) are seldom used in the United States

because of cardiovascular side effects such as heart attacks and stroke.

## P450 Enzyme Inhibitors

*Induction of a chemical process to decrease levels of testosterone and adrenal androgens resulting in a direct toxic effect on prostate cancer cells.*

Enzyme inhibitors reduce levels of the androgen called dihydrotestosterone (DHT) to extremely low values. Combining

this treatment with LHRH therapy and antiandrogen therapy is the treatment

of choice for some specialists in prostate cancer management.

## Orchiectomy

*Surgery to remove the testicles, which produce 95 percent of the body's testosterone.*

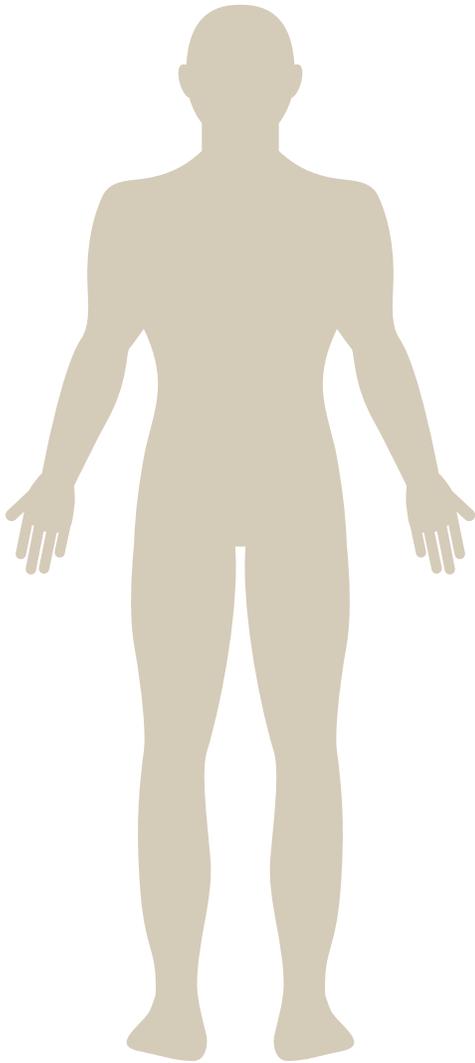
This procedure does not involve the penis. The scrotum remains after both testicles are surgically removed and replaced with silicon testicular prostheses of similar size to the actual testicles. Another surgical option is a sub-capsular orchiectomy

procedure to remove the inside glandular tissue of the testicles without removing the outer shells of the testicles.

An orchiectomy is a one-time minor surgical procedure and eliminates the need

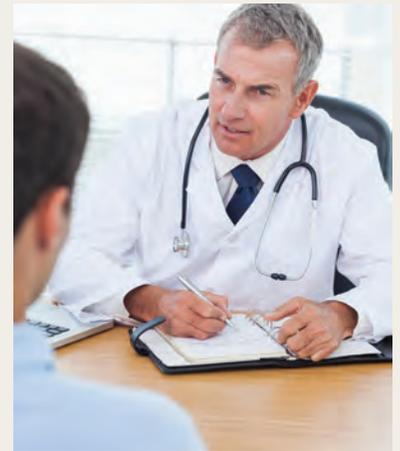
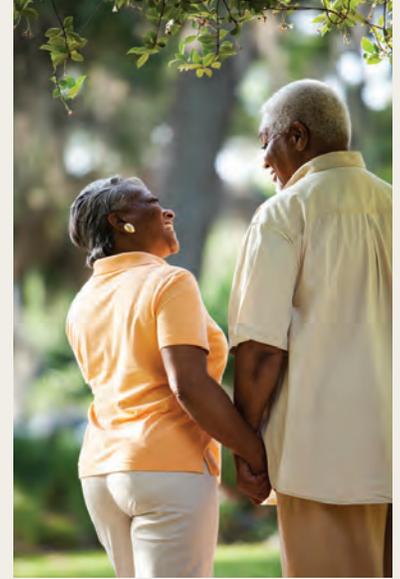
for LHRH therapy injections. However, an orchiectomy is not reversible and has the disadvantage of psychological effects resulting from the removal of a man's testicles.

# Side Effects of Androgen Deprivation Therapy (ADT)



Side effects are different with each treatment option. Talk to your doctor so that you can understand which side effects you might experience, how mild or severe they might be, how long they might last, and what you can do to either prevent them or lessen them.

Although ADT does have side effects, they are non-life threatening. Many patients and their loved ones are able to accept the side effects of ADT in return for a life-prolonging treatment. They recognize the trade-off between some quality of life for quantity of life. Then there are other patients and their loved ones who have a difficult time adjusting to ADT side effects.



SIDE EFFECTS	WHAT THEY MEAN
<p><b>Sexual desire, or libido</b></p>	<ul style="list-style-type: none"> <li>• Most men lose their desire for sexual relations and lose the ability to obtain or maintain an erection.</li> <li>• Your doctor can provide treatments that may restore the ability to have an erection that is satisfactory for sexual intercourse.</li> <li>• Tests are being conducted for lower-dose hormonal therapies (<i>such as antiandrogen pills alone</i>), which may not affect sexual function as much as traditional hormone therapy.</li> <li>• Men do maintain their ability to foster loving and nurturing relationships with their spouses or significant others.</li> </ul>
<p><b>Hot Flashes</b></p>	<ul style="list-style-type: none"> <li>• Most men may experience “hot flashes” periodically.</li> <li>• Your doctor can provide medications to lessen or eliminate these symptoms.</li> <li>• For most men, “hot flashes” are only a minor nuisance.</li> </ul>

SIDE EFFECTS	WHAT THEY MEAN
Change in voice, alteration in hair growth or breast growth	<ul style="list-style-type: none"> <li>• Very rare.</li> <li>• Men should not notice any change in their voice, hair growth or breast growth.</li> <li>• In the past, estrogen pills were used and did cause breast enlargement (<i>gynecomastia</i>) and tenderness.</li> <li>• Low dose hormonal therapy with antiandrogens alone or with other oral drugs can cause breast nipple tenderness or some breast enlargement. To prevent these side effects, options can be discussed with your doctor.</li> </ul>
Anemia	<ul style="list-style-type: none"> <li>• Long term ADT can result in mild anemia. Occasionally, it may be moderate to severe.</li> <li>• Periodic monitoring of the routine blood count (CBC) while on ADT is advised.</li> </ul>
Weight gain	<ul style="list-style-type: none"> <li>• Weight gain is common in men on ADT.</li> <li>• Caloric restriction, attention to carbohydrate intake, and implementing a realistic exercise program can be supportive for men on ADT.</li> </ul>
Decreased muscle mass and strength, and bone loss resulting in osteoporosis	<ul style="list-style-type: none"> <li>• Bone loss is common in men with prostate cancer, even prior to starting ADT.</li> <li>• Low dose or intermittent hormone therapy use may lessen these side effects.</li> <li>• ADT will increase bone loss. Attention should be given to bone health (<i>bone integrity</i>).</li> </ul>
Liver dysfunction	<ul style="list-style-type: none"> <li>• Antiandrogens may also have unique side effects. For example, FDA-approved antiandrogens may cause liver dysfunction.</li> <li>• Liver problems are almost always reversible upon discontinuation of the drug.</li> <li>• Typically, your doctor will monitor your liver with blood tests periodically and will discontinue the antiandrogen if liver abnormalities occur.</li> <li>• Some doctors will prescribe supplements to help protect liver cells from damage. These may include selenium, silymarin, N-acetyl cysteine, curcumin, d-alpha tocopherol succinate and allicin (<i>from garlic</i>).</li> </ul>
Diarrhea	<ul style="list-style-type: none"> <li>• The antiandrogen flutamide may cause diarrhea in approximately seven to 10 percent of men who take it. A lower dose or switching to another antiandrogen may eliminate the problem.</li> </ul>
Delayed adaptation to darkness	<ul style="list-style-type: none"> <li>• Nilutamide may cause a delayed adaptation to darkness, which may affect nighttime driving.</li> </ul>
Lung fibrosis	<ul style="list-style-type: none"> <li>• It may rarely cause lung fibrosis, which is reversible.</li> </ul>
Interactions with alcohol	<ul style="list-style-type: none"> <li>• Although this is not common, antiandrogens can cause interactions with alcohol.</li> </ul>

# Clinical Stages of Prostate Cancer and Androgen Deprivation Therapy (ADT)

## T1

Stage when prostate cancer is believed to be confined within the prostate gland. A tumor cannot be felt by a doctor on a digital rectal examination (DRE).

**Stages T1** and **T2** of prostate cancer are considered confined to the prostate and curable by surgery, radiation, or other local treatment. Androgen deprivation therapy is not traditionally used to treat men with these stages of disease. However, there are exceptions.

In elderly men, or in men with poor overall health who are not candidates for surgery or radiation, ADT can be very effective. For patients with significant tumor volumes, such as clinical **Stage T2b** or **T2c**, ADT is often used for variable periods of time prior to, during, and after radiation treatment or cryosurgery. ADT will shrink the prostate gland and decrease prostate

## T2

Stage when prostate cancer is believed to be confined within the prostate gland and with an abnormality that the doctor feels during a DRE.

cancer volume, which has been shown to provide better overall treatment results in patients treated with radiation.

The use of ADT with men who choose **brachytherapy** results in a decrease in prostate gland size, resulting in the need to place fewer seeds.

ADT also decreases tumor volume, which may allow for a better cell-killing effect by radiation therapy, which is either delivered by permanent seeds or temporarily implanted wires. ADT is usually reserved for men with prostate glands 40 cubic centimeters or larger.

## T3

Stage when prostate cancer has spread outside of the prostate into adjacent local tissues but is believed not to have spread further. Some patients with clinical T1 and T2 are upstaged to T3 or beyond at the time of surgery.

Treatments recommended for **Stage T3** typically included surgery, radiation, or androgen deprivation therapy. A combination treatment of ADT and **external beam radiation** is preferred for most men with clinical **Stage T3** disease.

A popular approach is to start ADT for typically two or three months prior to radiation. ADT therapy is continued during radiation. After radiation, ADT may be continued for two to three months or longer, depending

upon the characteristics of the cancer as determined by a **Gleason grade** and **PSA level**.

The combination of ADT and external beam radiation has improved the outcomes for men with **Stage T3** prostate cancer. Still unknown is the optimal duration of ADT prior to and after radiation therapy. Benefit has been shown after four months, three years, and indefinite use of ADT. It has been suggested that six months of ADT after radiation may be sufficient.

## Stage D

D0, also known as “D-Zero” disease, refers to significantly elevated blood tests such as PSA or acid phosphatase that suggest the cancer has spread despite negative X-ray tests such as CT-scans and bone scans. A rising PSA after surgery or radiation treatment could also be classified as stage D0. Stage D can be further classified. Prostate cancer that has spread or metastasized to lymph nodes (D1) or the bony skeleton or other organs or tissues away from the prostate gland (D2).

**Stage D2** patients with clinical apparent metastatic prostate cancer have traditionally been treated with androgen deprivation therapy. Today there has been a shift using ADT to treat all **Stage D** patients, as well as patients with PSA recurrence. It was suggested that ADT was only palliative for **Stage D2** prostate cancer. It helped symptoms, but did not prolong a man’s survival. However, it’s been shown that starting ADT as soon as a man is diagnosed with this stage does prolong life.

**Stage D1** patients (*lymph node spread only*) have often been treated with surgery, radiation, ADT and combinations of therapy. Over the past years, it has been shown that ADT is necessary for providing the best cancer control for this group of patients. In men who have been treated with a radical prostatectomy or radiation, and who are discovered to have **Stage D1** disease, those who continued on ADT appear to have the best results.

ADT has traditionally been restricted to prostate cancer patients who are without evidence of cancer spread on radiologic tests but who demonstrate an abnormal level of an enzyme in the blood called PAP (Prostatic Acid Phosphatase).

This finding was correlated with the probability that microscopic cancer spread had occurred. Currently, doctors are suspicious about microscopic cancer spread when the prostate specific antigen (PSA) is also elevated in the blood. Different doctors have different threshold values when they consider the PSA test to signify **Stage D0** disease. The **Stage D0** category, like the other **Stage D** categories, may occur when men

are first diagnosed with prostate cancer, or may occur when the cancer recurs after prior treatments such as surgery, radiation, or cryosurgery. A very common current scenario is the man who has a rising PSA, also called PSA recurrence, with negative X-ray tests after prior radiation or surgery. Men in this category are commonly started on ADT.



## Food and Drug Administration (FDA) Approved Hormone Therapy for Prostate Cancer

There may be other drugs used in hormone therapy for prostate cancer that are not listed here.

**Important:** *This drug information is meant to be educational and is not a substitute for medical advice. It may not cover all uses, actions, interactions, side effects, or precautions to be taken while using it. Consult with your health care professional for information about your specific medical condition and the use of each drug.*

GENERIC NAME	UNITED STATES BRAND NAME	USE IN TREATING PROSTATE CANCER
Abiraterone Acetate	Zytiga	Approved for use with prednisone to treat prostate cancer that has metastasized ( <i>spread to other parts of the body</i> ). It is used in patients whose disease has not gotten better with other hormone therapy.
Bicalutamide	Casodex	Approved to treat prostate cancer that has metastasized ( <i>spread to other parts of the body</i> ). It is used with a type of drug called a luteinizing hormone-releasing hormone agonist.
Cabazitaxel	Jevtana	Approved for use with prednisone to treat prostate cancer that has metastasized ( <i>spread to other parts of the body</i> ) in men whose cancer is hormone-refractory ( <i>does not respond to hormone treatment</i> ) and who have already been treated with other chemotherapy.
Degarelix	Firmagon	Approved to treat prostate cancer that is advanced.
Docetaxel	Taxotere	Approved to treat prostate cancer that has metastasized in men whose cancer is hormone-refractory ( <i>does not respond to hormone treatment</i> ).
Enzalutamide	Xtandi	Approved to treat prostate cancer that has metastasized ( <i>spread to other parts of the body</i> ). It is used in patients whose disease is castration resistant ( <i>has not responded to treatments that lower testosterone levels</i> ).
Goserelin Acetate	Zoladex	Approved to treat prostate cancer. It is used with flutamide and radiation therapy in localized prostate cancer and is also used as palliative treatment in advanced prostate cancer.
Histrelin Acetate	Vantas	Approved to treat prostate cancer symptoms using a drug-delivery system placed under the skin to deliver histrelin continuously for 12 months.
Leuprolide Acetate	Eligard Lupron Depot – Ped Lupron Depot – 4 Month Lupron Depot – 3 Month Lupron Depot Lupron Viadur	Approved for palliative treatment of prostate cancer that is advanced.
Mitoxantrone Hydrochloride	N/A	Approved for use with other drugs to treat prostate cancer as palliative treatment in advanced disease that is hormone-refractory ( <i>does not respond to hormone treatment</i> ).

## Affected by prostate cancer? Us TOO...

We're Us TOO International Prostate Cancer Education & Support Network.

**We think we know what you're looking for.**

Us TOO was founded by—and continues to be governed by—people directly affected by prostate cancer. We're a nonprofit established in 1990 that serves as a resource of volunteers with peer-to-peer support and educational materials to help men and their families/caregivers make informed decisions about prostate cancer detection, treatment options and related side effects.

Us TOO develops and delivers valuable resources and services at no charge.

**Visit [www.ustoo.org](http://www.ustoo.org)**

*The information contained in this document is not intended as medical advice, nor is it intended as a substitute for consulting with a physician or healthcare provider. This material is to be used only for educational purposes.*

Access Educational Materials  
& Resources

Call the HelpLine – Talk to  
“Someone who understands”

Find a Support Group

Read the Us TOO  
Hot SHEET Newsletter

Receive News & Emails

Join a Prostate Cancer  
Online Community

### SOURCES:

#### American Cancer Society

[www.cancer.org/cancer/prostatecancer/](http://www.cancer.org/cancer/prostatecancer/)  
1-800-227-2345

#### Androgen Deprivation Therapy

An Essential Guide for Prostate Cancer Patients and Their Loved Ones  
Richard Wassersug, PhD  
Lauren M. Walker, PhD  
John W. Robinson, PhD, R Psych  
2013

#### Judd Moul, M.D.

Duke Urology Clinic  
Durham, North Carolina

#### National Cancer Institute @ The National Institutes of Health

[www.cancer.gov/cancertopics/types/prostate](http://www.cancer.gov/cancertopics/types/prostate)  
1-800-4-cancer (226237)

#### Principles for Managing Advanced Prostate Cancer

Us TOO International Prostate Cancer Education & Support Network  
2011

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**Affected by Prostate Cancer?**

**Us TOO**

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**Us TOO International®  
Prostate Cancer Education  
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