SCHEDULING STATUS:

S4

XTANDI 40 mg

(enzalutamide)

soft gelatine capsules

contains Sugar: Each capsule contains 57,8 mg Sorbitol

Read all of this leaflet carefully before you start taking XTANDI

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- XTANDI has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What XTANDI is and what it is used for
2. What you need to know before you take XTANDI
3. How to take XTANDI
4. Possible side effects
5. How to store XTANDI
6. Contents of the pack and other information

1. WHAT XTANDI IS AND WHAT IT IS USED FOR

The active substance in Xtandi is enzalutamide.

XTANDI is used to treat adult men with prostate cancer:

- That no longer responds to hormone therapy or surgical treatment to lower testosterone.

Or

- That has spread to other parts of the body and responds to a hormone therapy or surgical treatment to lower testosterone.

Or

- Who had prior prostate removal or radiation and have rapidly rising PSA, but cancer has not spread to other parts of the body and responds to a hormone therapy to lower testosterone.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE XTANDI

Do not take XTANDI:

- if you are hypersensitive (allergic) to the active ingredient, enzalutamide or to any of the other ingredients.
- if you have poorly controlled seizures.
- XTANDI is not for use by women.

Warnings and precautions

Talk to your doctor, pharmacist or other healthcare professional before taking XTANDI:

- If you are taking any medicines to prevent blood clots (e.g. warfarin).
- If you use chemotherapy like docetaxel.
- If you have problems with your liver.
- If you have problems with your kidneys.
- If you had or are at risk of having a seizure (fit).

Seizures

XTANDI has been shown to cause seizures.

Some situations in which you may have a higher risk of seizures include:

- If you had earlier episodes of seizures.

- If you drink very large amounts of alcohol either regularly or from time to time.

- If you have had a serious head injury or a history of head trauma.

- If you have had certain kinds of stroke.
- If you have had a brain tumour or metastases of cancer in the brain.
- If you are taking a medicine that can cause seizures or medicines that can increase the susceptibility for having seizures.

If you have a seizure during treatment:
Stop taking XTANDI and do not take any more capsules. See your doctor, pharmacist or other healthcare professional as soon as possible.

Risk of new cancers (second primary malignancies)
There have been reports of new (second) cancers including cancer of the bladder and colon in patients treated with XTANDI.

See your doctor as soon as possible if you notice signs of gastrointestinal bleeding, blood in the urine, or frequently feel an urgent need to urinate when taking XTANDI.

Posterior Reversible Encephalopathy Syndrome (PRES)
There have been reports of PRES, a reversible condition involving the brain, in patients treated with XTANDI. If you have a seizure, worsening headache, confusion, blindness or other vision problems, please contact your doctor as soon as possible.

Please tell your doctor if you have any of the following:
Any heart or blood vessel conditions, including heart rhythm problems (dysrhythmia), or are being treated with medicines for these conditions. The risk of heart rhythm problems may be increased when using XTANDI.

If you are allergic to enzalutamide, this may result in a rash or swelling of the face, tongue, lip or throat. If you are allergic to enzalutamide or any of the other ingredients of this medicine, do not take XTANDI.

Severe skin rash or skin peeling, blistering and/or mouth sores have been reported in association with XTANDI treatment. Seek medical attention immediately if you notice any of these symptoms.

If any of the above applies to you or you are not sure, talk to your doctor, pharmacist or other healthcare professional before taking XTANDI.

Children and adolescents

XTANDI should not be taken by children under 18 years of age.

Other medicines and XTANDI

Always tell your healthcare professional if you are taking any other medicine (this includes complementary or traditional medicines).

Tell your doctor, pharmacist or other healthcare professional if you are taking any of the following medicines. When taken at the same time as XTANDI, these medicines may increase the risk of a seizure:

- Certain medicines used to treat asthma and other respiratory diseases (e.g. aminophylline, theophylline)
- Medicines used to treat certain psychiatric disorders such as depression and schizophrenia (e.g. clozapine, olanzapine, risperidone, ziprasidone, bupropion, lithium, chlorpromazine, mesoridazine, thioridazine, amitriptyline, desipramine, doxepin, imipramine, maprotiline, mirtazapine)
- Certain medicines for the treatment of pain (e.g. pethidine).

Tell your doctor, pharmacist or other healthcare professional if you are taking the following medicines. These medicines may influence the effect of XTANDI, or XTANDI may influence the effect of these medicines.

This includes certain medicines used to:

- Lower cholesterol (e.g. gemfibrozil, atorvastatin, simvastatin)
- Treat pain (e.g. fentanyl, tramadol)
- Treat cancer (e.g. cabazitaxel)
- Treat epilepsy (e.g. carbamazepine, clonazepam, primidone, valproic acid, phenobarbitone, phenytoin)
- Treat certain psychiatric disorders such as severe anxiety or schizophrenia (e.g. diazepam, midazolam, haloperidol)
- Treat sleep disorders (e.g. zolpidem)
- Treat heart conditions or lower blood pressure (e.g. bisoprolol, digoxin, diltiazem, felodipine, nicardipine, nifedipine, propranolol, verapamil)
- Treat serious disease related to inflammation (e.g. dexamethasone, prednisolone)
- Treat HIV infection (e.g. indinavir, ritonavir)
- Treat bacterial infections (e.g. clarithromycin, doxycycline)
- Treat thyroid disorders (e.g. levothyroxine)
- Treat gout (e.g. colchicine)
- Treat stomach disorders (e.g. omeprazole)
- Prevent heart conditions or strokes (e.g. dabigatran etexilate)
- Prevent organ rejection (e.g. tacrolimus)

XTANDI might interfere with some medicines used to treat heart rhythm problems (e.g. quinidine, procainamide, amiodarone and sotalol) or might increase the risk of heart rhythm problems when used with some other medicines [e.g. methadone (used for pain relief and part of drug addiction detoxification), moxifloxacin (an antibiotic), antipsychotics (used for serious mental illnesses)].

Tell your doctor if you are taking any of the medicines listed above. The dose of XTANDI or any other medicines that you are taking may need to be changed.

XTANDI with food and drink

XTANDI can be taken with or without food.

Pregnancy, breastfeeding and fertility

- **XTANDI is not for use in women.** XTANDI may cause harm to the unborn child if it is taken by women who are pregnant, and should not be taken by women who are pregnant, may become pregnant, or who are breastfeeding an infant.
- XTANDI could possibly have an effect on male fertility.
- If you are having sex with a woman who can become pregnant, use a condom and another effective birth control method, during and for 3 months after treatment with XTANDI. If you are having sex with a pregnant woman, use a condom to protect the unborn child.

Driving and using machinery

XTANDI may influence your ability to drive and use machines. Seizures have been reported in patients taking XTANDI.

If you are at higher risk of seizures, talk to your doctor.

Important information about some of the ingredients of XTANDI

XTANDI contains sorbitol (a type of sugar).

3. HOW TO TAKE XTANDI

Do not share medicines prescribed for you with any other person.

Always take XTANDI exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

The usual dose is 160 mg (four soft capsules), taken at the same time once a day.

Swallow the soft capsules whole with water.

Do not chew, dissolve or open soft the capsules before swallowing.

XTANDI can be taken with or without food.

XTANDI should not be handled by persons other than the patient or his caregivers.

Women who are or may become pregnant should not handle damaged or opened XTANDI capsules without wearing protection like gloves.

Your doctor will tell you how long your treatment with XTANDI will last. Do not stop treatment early.
If you have the impression that the effect of XTANDI is too strong or too weak, tell your doctor or pharmacist.

If you take more XTANDI than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

If you forget to take XTANDI

Do not take a double dose to make up for forgotten individual doses.
If you forget to take XTANDI at the usual time, take your usual dose as soon as you remember.
If you forget to take XTANDI for the whole day, take your usual dose the following day.
If you forget to take XTANDI for more than one day, talk to your doctor without delay.

Effects when treatment with XTANDI is stopped

Do not stop taking XTANDI, unless your doctor has advised you to do so.

4. POSSIBLE SIDE EFFECTS

XTANDI can have side effects.
Not all side effects reported for XTANDI are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking XTANDI, please consult your doctor, pharmacist or other healthcare professional for advice.

Seizures

XTANDI can cause seizures. Seizures are more likely if you take more than the recommended dose of XTANDI, if you take certain other medicines, or if you are at higher than usual risk of seizures.

If you have a seizure, see your doctor as soon as possible. Do not take any more XTANDI.

Posterior Reversible Encephalopathy Syndrome (PRES)

There have been reports of PRES (may affect up to 1 in 1 000 people), a rare, reversible condition involving the brain, in patients treated with XTANDI. If you have a seizure, worsening headache, confusion, blindness or other vision problems, please contact your doctor as soon as possible.

Other possible side effects include:

Frequent

Fatigue (tiredness), fall, broken bones, hot flushes, high blood pressure, headache, feeling anxious, dry skin, itching, difficulty remembering, blockage of the arteries in the heart (ischemic heart disease), breast enlargement in men (gynaecomastia), nipple pain, breast tenderness, symptom of restless legs syndrome (an uncontrollable urge to move a part of the body, usually the leg), reduced concentration, forgetfulness, change in sense of taste, difficulty thinking clearly.

Less frequent

Hallucinations, low white blood cell count.

Not known (frequency cannot be estimated from the available data)

Muscle pain, muscle spasms, muscular weakness, back pain, changes in ECG (QT prolongation), upset stomach including feeling sick (nausea), a skin reaction that causes red spots or patches on the skin that may look like a target or “bulls-eye” with a dark red centre

surrounded by paler red rings (erythema multiforme), rash, being sick (vomiting), swelling of the lips, face, tongue and/or throat, reduction in blood platelets (which increases risk of bleeding or bruising), diarrhoea.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor or pharmacist. You can also report side effects to SAHPRA via the “6.04 Adverse Drug Reaction Reporting Form”, found online under SAHPRA’s Publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of XTANDI.

5. HOW TO STORE XTANDI

Store all medicines out of reach of children.

Store at or below 25 °C.

Store in the original container.

Do not use XTANDI after the expiry date which is stated on the cardboard wallet. The expiry date refers to the last day of that month.

Do not take any soft capsule that is leaking, damaged, or shows signs of tampering.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What XTANDI contains

The active substance is enzalutamide.

The other ingredients are:

Capsule Contents:

Butylhydroxyanisole (BHA)(E320), butylhydroxytoluene (BHT)(E321), caprylocaproyl macrogolglycerides.

Capsule Shell:

Gelatin, glycerol, sorbitol sorbitan solution, titanium dioxide (E171).

Black Printing Ink containing:

Macrogol 400, iron oxide black (E172), polyvinyl acetate phthalate, propylene glycol.

What XTANDI looks like and contents of the pack

XTANDI capsules are white to off-white, oblong soft capsules, printed with “ENZ” in black ink.

XTANDI is presented as PVC/PCTFE/Al laminate blister trays containing 28 capsules in 7 blister wells. Each blister well contains 4 capsules (1 daily dose). These blister trays are glued into cardboard wallets to form an inseparable unit. Four wallet/blister trays are packaged as a 112 capsule carton. This provides four weeks’ supply.

HOLDER OF CERTIFICATE OF REGISTRATION

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