Package leaflet: Information for the patient

Nolvadex® D

tamoxifen citrate

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

Nolvadex D will be referred to as Nolvadex throughout this leaflet.

What is in this leaflet:

1. What Nolvadex is and what it is used for

What Nolvadex is

The name of your medicine is Nolvadex. Nolvadex contains a medicine called tamoxifen citrate, which belongs to a group of medicines called 'anti-oestrogens'.

What Nolvadex is used for

- Nolvadex is used to treat breast cancer.

How Nolvadex works

Oestrogen is a natural substance in your body known as a 'sex hormone'. Some breast cancers need oestrogen to grow and Nolvadex works by blocking the effects of oestrogen**.**

2. What you need to know before you take Nolvadex

Do not take Nolvadex:

- If you are pregnant or think you might be pregnant (see the section on 'Pregnancy' below).
- If you are allergic to tamoxifen or any of the other ingredients of this medicine (listed in section 6).

Do not take Nolvadex if any of the above apply to you. If you are not sure, talk to your doctor or pharmacist before taking Nolvadex.

Warnings and precautions

Talk to your doctor or pharmacist before taking Nolvadex.

Menstruation is suppressed in a proportion of premenopausal women receiving Nolvadex for the treatment of breast cancer.

An increased incidence of endometrial changes including hyperplasia, polyps, cancer and uterine sarcoma (mostly malignant mixed Mullerian tumours), has been reported in association with Nolvadex treatment. The underlying mechanism is unknown but may be related to the oestrogen-like effect of Nolvadex. Any patient receiving or having previously received Nolvadex, who report abnormal gynaecological symptoms, especially vaginal bleeding, or who presents with menstrual irregularities, vaginal discharge and symptoms such as pelvic pain or pressure should be promptly investigated.

In delayed breast reconstruction operation (weeks to years after the primary breast operation when your own tissue is moved to shape a new breast), Nolvadex may increase the risk of the formation of blood clots in the small vessels of the tissue flap which may lead to complications.

If you have a history of hereditary angioedema as Nolvadex may cause or worsen symptoms of hereditary angioedema. If you experience symptoms such as swelling of the face, lips, tongue and/or throat with difficulty in swallowing or breathing, contact a doctor immediately.

<u>Venous thromboembolism (VTE)</u>

- A 2–3-fold increase in the risk for VTE has been demonstrated in healthy tamoxifen-treated women (see Possible side effects).

- Prescribers should obtain careful histories with respect to the patient's personal and family history of VTE. If suggestive of a prothrombotic risk, patients should be screened for thrombophilic factors. Patients who test positive should be counselled regarding their thrombotic risk. The decision to use tamoxifen in these patients should be based on the overall risk to the patient. In selected patients, the use of tamoxifen with prophylactic anticoagulation may be justified (see Other medicines and Nolvadex).

- The risk of VTE is further increased by severe obesity, increasing age and all other risk factors for VTE. The risks and benefits should be carefully considered for *all* patients before treatment with tamoxifen. This risk is also increased by concomitant chemotherapy (see Other medicines and Nolvadex)). Long-term anticoagulant prophylaxis may be justified for some patients who have multiple risk factors for VTE.

- Surgery and immobility: Tamoxifen treatment should only be stopped if the risk of tamoxifen-induced thrombosis clearly outweighs the risks associated with interrupting treatment. All patients should receive appropriate thrombosis prophylactic measures and should include graduated compression stockings for the period of hospitalisation, early ambulation, if possible, and anticoagulant treatment.

- If any patient presents with VTE, tamoxifen should be stopped immediately, and appropriate anti-thrombosis measures initiated. The decision to re-start tamoxifen should be made with respect to the overall risk for the patient. In selected patients, the continued use of tamoxifen with prophylactic anticoagulation may be justified.

- All patients should be advised to contact their doctors immediately if they become aware of any symptoms of VTE.

In an uncontrolled trial in 28 girls aged 2–10 years with McCune Albright Syndrome (MAS), who received 20 mg once a day for up to 12 months duration, mean uterine volume increased after 6 months of treatment and doubled at the end of the one-year study. While this finding is in line with the pharmacodynamic properties of tamoxifen, a causal relationship has not been established.

Children
This medicine is not for use in children.

Other medicines and Nolvadex
Tell your doctor or pharmacist if you are taking, have recently taken, or might take any other medicines. This is because Nolvadex can affect the way some other medicines work and some medicines can have an effect on Nolvadex.

In particular, tell your doctor or pharmacist if you are taking any other medicines:

- Antidepressants (e.g. paroxetine, fluoxetine).
- Blood thinning medicines such as warfarin. These are known as 'anti-coagulants'
- Rifampicin which is used for tuberculosis (TB).
- Medicines known as 'aromatase inhibitors' that are used to treat breast cancer. These include anastrozole, letrozole and exemestane.
- Cytotoxic agents

Contraception

Women who can become pregnant should use adequate non-hormonal contraception (e.g., barrier contraception) during treatment with Nolvadex and for an additional nine months after stopping treatment.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Pregnancy

- Do not take Nolvadex if you are pregnant. This is because it may affect your unborn baby.
- Avoid becoming pregnant and breast feeding whilst taking Nolvadex and for nine months after stopping treatment.
- As you should not become pregnant when taking Nolvadex, please see your doctor for advice on what contraceptive precautions you should take, as some may be affected by Nolvadex.

- You should see your doctor immediately if you think you may have become pregnant after starting to take Nolvadex.

Breast-feeding

Talk to your doctor before taking Nolvadex if you are breast-feeding.

Driving and using machines

Nolvadex is not likely to affect your ability to drive or use any tools or machines. However, tiredness has been reported with the use of Nolvadex and caution should be observed when driving or operating machinery while such symptoms persist.

Nolvadex tablets contain lactose, titanium dioxide and sodium

- Nolvadex tablets contain lactose, which is a type of sugar. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.
- Nolvadex tablets contain titanium dioxide. This may cause a problem in a small number of people who are sensitive to this ingredient.
- This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

3. How to take Nolvadex

Always take Nolvadex exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Breast cancer treatment
The recommended dose for breast cancer is 20 mg daily.

If you take more Nolvadex than you should
If you take more Nolvadex than you should, talk to a doctor or pharmacist straight away.

If you forget to take Nolvadex

- If you forget to take a dose, take it as soon as you remember. However, if it is nearly time for the next dose skip the missed dose.
- Do not take a double dose (two doses at the same time) to make up for a forgotten dose.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Side effects can be classified as either due to the pharmacological action of the drug, eg Hot flushes, vaginal bleeding, vaginal discharge, pruritus vulvae and tumour flare or as more general side effects, e.g. gastrointestinal intolerance, headache, light-headedness and occasionally, fluid retention and alopecia.

When side effects are severe, it may be possible to control them by a simple reduction of dosage (to not less than 20 mg/day) without loss of control of the disease. If side effects do not respond to this measure, it may be necessary to stop the treatment.

Skin rashes (including rare reports of erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, cutaneous vasculitis, and bullous pemphigoid) and commonly hypersensitivity reactions, including angioedema have been reported.

Cases of exacerbation of angioedema have been reported in patients with hereditary angioedema receiving Nolvadex.

Uncommonly patients with bony metastases have developed hypercalcaemia on initiation of therapy.

Falls in platelet count, usually to 80,000 to 90,000 per cu mm but occasionally lower, have been reported in patients taking tamoxifen for breast cancer.

Cases of visual disturbances including rare reports of corneal changes and common reports of retinopathy have been described in patients receiving Nolvadex. Cataracts have been reported commonly in association with the administration of Nolvadex.

Cases of optic neuropathy and optic neuritis have been reported in patients receiving tamoxifen and, in a small number of cases, blindness has occurred.

Sensory disturbances (including paraesthesia and dsygeusia) have been reported commonly in patients receiving Nolvadex.

Uterine fibroids, endometriosis and other endometrial changes including hyperplasia and polyps have been reported.

Cystic ovarian swellings have rarely been observed in women receiving Nolvadex. Vaginal polyps have rarely been observed in women receiving Nolvadex.

Leucopenia has been observed following the administration of Nolvadex, sometimes in association with anaemia and/or thrombocytopenia. Neutropenia has been reported on rare occasions; this can sometimes be severe and rarely cases of agranulocytosis have been reported.

There is evidence of ischaemic cerebrovascular events and thromboembolic events, including deep vein thrombosis, microvascular thrombosis, and pulmonary embolism, occurring commonly during Nolvadex therapy When Nolvadex is used in combination with cytotoxic agents, there is an increased risk of thromboembolic events occurring.

Leg cramps and myalgia have been reported commonly in patients receiving Nolvadex.

Uncommonly, cases of interstitial pneumonitis have been reported.

Nolvadex has been associated with changes in liver enzyme levels and with a spectrum of more severe liver abnormalities which in some cases were fatal, including fatty liver, cholestasis and hepatitis, liver failure, cirrhosis, and hepatocellular injury (including hepatic necrosis).

Commonly, elevation of serum triglyceride levels, in some cases with pancreatitis, may be associated with the use of Nolvadex.

Uncommonly incidences of endometrial cancer and rare incidences of uterine sarcoma (mostly malignant mixed Mullerian tumours) has been associated with Nolvadex treatment.

Cutaneous lupus erythematosus has been observed very-rarely in patients receiving Nolvadex.

Porphyria cutanea tarda has been observed very-rarely in patients receiving Nolvadex.

Fatigue has been reported very commonly in patients taking Nolvadex.

Radiation Recall has been observed very rarely in patients receiving Nolvadex.

Depression has been reported with frequency very common in association with the use of Nolvadex.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

5. How to store Nolvadex

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the carton. The expiry date refers to the last day of that month.
- Do not store above 30^{o}C. Store your tablets in the original package. Keep the blister strip in the carton. This will protect your medicine from light and moisture.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Nolvadex Contains

The active substance is tamoxifen.

Each Nolvadex D 20 mg tablet contains Tamoxifen Citrate Ph. Eur. 30.4 mg equivalent to 20 mg Tamoxifen.

The other ingredients are croscarmellose sodium, gelatin, lactose, macrogol, magnesium stearate, maize starch, hypromellose and titanium dioxide.

What Nolvadex looks like and contents of the pack

Nolvadex D 20 mg tablets are white to off-white, octagonal, biconvex, film-coated tablets, intagliated with NOLVADEX D on one face and plain on the reverse. They come in packs of 30 or 250 tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

The Marketing Authorisations for Nolvadex and Nolvadex D are held by AstraZeneca UK Limited, Silk Road Business Park, Macclesfield, Cheshire, SK10 2NA, UK.

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