Package Leaflet: Information for the user

Flutexin® 250

active ingredient: flutamide 250 mg per tablet

Dear patient, Read all of this leaflet carefully before you start taking this medicine.
- 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. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- 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.

In this leaflet:

1. What *Flutexin 250* is and what it is used for

Flutexin 250 is an agent which reduces the effect of special male sexual hormones (non-steroidal antiandrogen).

Indications
For the treatment of patients with advanced prostatic tumour in which suppression of the effects of the male sexual hormone (testosterone) is indicated:
- initial therapy in combination with LH-RH analogon or in connection with orchiectomy (complete blockade of male sexual hormones) as well as in patients already treated with an LH-RH analogon or who have already had a surgical ablation of the testes (removal of male gonads)
- for the treatment of patients who did not respond to other endocrine therapeutic forms (concerning inner gland secretion) or who do not tolerate another endocrine therapy, which is necessarily indicated.

2. Before you take *Flutexin 250*

When must you not take *Flutexin 250*
Flutexin 250 must not be taken in case of hypersensitivity to the active substance flutamide or to any of the other ingredients.

Take special care with *Flutexin 250*
The following describes when you may take *Flutexin 250* only under certain conditions and only with special caution. Please ask your doctor regarding this. This also applies if this data was relevant for you once before.

In cases of impaired liver function, treatment with *Flutexin 250* should be based on careful assessment of the benefits versus the risks in the isolated case in longer-term treatment.
You should not begin treatment with *Flutexin 250* if serum transaminase values are two or three times higher than normal values. If laboratory diagnostic findings give evidence of liver damage or jaundice, which do not have their origin in liver metastases, which have been secured with tissue examinations, *Flutexin 250* has to be discontinued. In patients with clinical evidence for jaundice or serum transaminase values exceeding normal values two- or threefold, *Flutexin 250* should also be discontinued.

Flutexin 250 should be taken with caution in patients with impaired kidney function.

If hypersensitivity reactions occur, *Flutexin 250* must be discontinued immediately.

Flutexin 250 can lead to elevated testosterone and estradiol levels and thus to fluid retention, so that this medicine should be used with caution in the presence of a cardiovascular disease.

Possible impairments of the liver function are generally reversible after discontinuation of *Flutexin 250*. As a particularly severe course of the liver dysfunction has been reported in single cases, which was in temporal connection with the treatment, regular monitoring of the liver values is indicated by the treating doctor in monthly intervals during the first 4 months, then at regular intervals, and immediately if first symptoms or signs of impaired liver function occur (e.g. itching, dark urine, persistent underweight or emaciation, jaundice, pain in the right upper abdomen or unspecific "flu-like symptoms").

In the case of long-term therapy in patients without medicinal or surgical castration, the sperm counts are to be determined at regular intervals.

Amber-coloured or green-yellow discoloration of the urine can occur. However, you might not feel worried about this, since it is a normal reaction towards the intake of *Flutexin 250*.

Flutamide is only intended for use in male patients. During treatment with *Flutexin 250*, contraceptive measures should be taken and reliably restrained.

Taking other medicines
Please take into account that this data also applies to medicinal products used in the recent past.

The effect of certain medicines inhibiting blood coagulation (oral anticoagulants) can be enhanced. A new dose determination of the anticoagulants through the attending doctor may therefore be required.

Pregnancy and lactation
Flutexin 250 is only intended for use in male patients.

What must you heed when driving, operating machinery as well as when working in unsafe posture?
Possible side effects like drowsiness and confusion can impair the ability to drive and use machines.

Important information about some of the ingredients of *Flutexin 250*
This medicinal product contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking *Flutexin 250*.

Advice to diabetics: 1 tablet contains 0.03 BE (bread exchange units).

3. How to take *Flutexin 250*

Always take *Flutexin250* exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

If not otherwise prescribed by the doctor, the usual dose is
Take one tablet of *Flutexin 250* 3 times daily (corresponding to 750 mg flutamide daily).

Comment on adjunction
When initiating therapy with LH-RH analogons, the tumour-flare phenomenon can be reduced in terms of frequency and intensity (transient activation of the tumour disease) by an initiation of *Flutexin 250* therapy.
Hence it is recommended to start therapy with the daily intake of one tablet of *Flutexin 250* three times daily at least 3 days before the first administration of LH-RH analogons and then to keep this dosage.

Method of use
Take the tablets without chewing preferably after meals with some liquid.

Duration of treatment
The duration of treatment is determined by the attending doctor. It depends on the mode, severity and the progress of the disease.
Please speak with your doctor if you have the impression that the effect of *Flutexin 250* is too strong or too weak.

If you take more *Flutexin 250* than you should
Severe intoxications have not been described so far. Please consult your doctor if an overdose is suspected so that he/she can decide on the further procedure.

If you forget to take *Flutexin 250*
Do not take more tablets the next time, but continue treatment with the dose prescribed.

If you stop taking *Flutexin 250*
Talk to your doctor in any case before interrupting or prematurely finishing treatment with *Flutexin* 250 - e.g. due to the occurrence of side effects.

4. Possible side effects

Like all medicines, *Flutexin 250* can cause side effects, although not everybody gets them.

The following frequency data is the basis for the evaluation of side effects:

Very common	more than 1 in 10 treated patients
Common	less than 1 in 10, but more than 1 in 100 treated patients
Uncommon	less than 1 in 100, but more than 1 in 1,000 treated patients
Rare	less than 1 in 1,000, but more than 1 in 10,000 treated patients
Very rare	less than 1 in 10,000 treated patients
not known	cannot be estimated from the available data

Monotherapy
The most frequent side effects observed in clinical trials with *Flutexin 250* monotherapy are increased mammary gland tissue (gynaecomastia) and/or breast pain, sometimes accompanied by secretion of milk (galactorrhoea). Micronodular changes in the body of breast can occasionally occur.

Initially, *Flutexin 250* monotherapy may lead to a reversible increase in serum testosterone (male sexual hormone).

Furthermore, skin reddening with warming or changes of the type of hairiness can occur.

Occasionally, diarrhoea, nausea, vomiting, increased appetite, sleeplessness, tiredness, transient abnormal liver function and inflammation of the liver (hepatitis) have been reported.

Rarely, the following side effects occur: decreased libido, indigestion, loss of appetite (anorexia), ulcer-like pain, heartburn, constipation, accumulation of liquid in tissue (oedema), haematoma over a large area (ecchymosis), shingles (herpes zoster), itching (pruritus), lupus-like syndrome, headache, hot flushes, dizziness, weakness, indisposition, blurred vision, thirst, breast pain, anxiety, depression, lymphostasis (lymphatic oedema), loss of hair of head and muscular cramps.

Cardiovascular disorders rarely occur.

A diminished production of sperms has rarely been described.

Adjunction
The side effects most frequently observed in clinical studies with combination therapy of flutamide with LH-RH agonists were hot flushes, diminished libido, disturbance in fertility (impotence), diarrhoea, nausea and vomiting. With the exception of diarrhoea, these side effects are known from monotherapy with LH-RH agonists in comparable frequency.
Enlargement of breast glandular tissue (gynaecomastia) frequently occurring with flutamide monotherapy was significantly reduced in adjunction.

Uncommonly, hepatitis (inflammation of the liver) occurred.

Rarely, the following occurred: anaemia, diminished number of white blood counts (leukopenia), reduction in blood platelets (thrombopenia), unspecific gastrointestinal disorders, loss of appetite (anorexia), and rash, neuromuscular symptoms, jaundice (icterus), urinary tract disorders (urogenital tract symptoms), high blood pressure, accumulation of liquid in tissue (oedema) and side effects in the central nervous system (somnolence, depression, confusion, anxiety, nervousness).

Very rarely, symptoms of the respiratory tract such as dyspnoea have occurred.

In addition, the following further side effects of flutamide have been reported: special forms of anaemia (haemolytic anaemia, megalocytic anaemia, methaemoglobinaemia, sulfhaemoglobinemia), thromboembolism, photosensitisation reactions (sensitivity to light with the occurrence of cutaneous disorders due to the influence of light) including inflammatory reddening of the skin (erythema), ulcerations, formation of blisters and extensive blistered detachment of the upper layer of the skin (epidermal necrolysis).

In addition, jaundice (cholestatic jaundice) and, in particular in patients with liver metastasis, liver-related brain disease (encephalopathy) and death of liver cells (liver cell necrosis) have been observed. Usually these side effects subsided after discontinuation of therapy. However, isolated cases of liver damage with lethal outcome have been reported in connection with the intake of flutamide.

Secondary malignancy: In 2 cases during treatment with flutamide, male mamma tumours have been observed. In one of these cases, a patient with benign prostatic hypertrophy, a breast node deteriorated, which had already been detected 3 to 5 months before the beginning of treatment. After operative removal it had been identified as small differentiated ductal carcinoma. In the other case, the patient suffered from advanced prostatic carcinoma in which beside gynaecomastia, one node was noticed about 6 months after the beginning of flutamide monotherapy. Nine months after initiation of therapy, the node was removed and identified as moderately differentiated, invasive, ductal tumour. However, no metastases have occurred.

The reported abnormal laboratory diagnostic values were composed of liver function values, increased blood urea and - rarely- increased serum creatinine values.

If you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

Countermeasures
Generally, the intensity of these side effects did neither require dose reduction nor discontinuation of therapy.

Increase in breast glandular tissue, breast pain with or without milk flow and micronodular changes in the body of breast completely subside if treatment is discontinued or the dose reduced.

Loss of appetite, nausea, vomiting, tiredness, discoloration of the urine, complaints in the gastrointestinal tract and jaundice may be signs of a severe liver damage. Inform your attending doctor immediately if you experience such complaints.

5. How to store *Flutexin 250*

Keep out of the reach and sight of children.

Do not use *Flutexin 250* after the expiry date which is stated on the label and the carton. The expiry date refers to the last day of that month.

6. Further information

What *Flutexin 250* contains
One tablet contains 250 mg flutamide.

The other ingredients are:
microcrystalline cellulose, lactose monohydrate, magnesium stearate (Ph.Eur.), maize starch, sodium dodecyl sulphate, colloidal silicon dioxide

Pharmaceutical form and contents
Flutexin 250 is a yellowish, round, biconvex tablet with one-sided score notch and is available in packs containing 84 and 100 tablets.

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Last update of information
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Keep out of the reach and sight of children!

1 A Pharma GmbH wishes a speedy recovery!

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