PATIENT LEAFLET IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

Flutine® 20

Capsules

Composition:

Each capsule contains:

Fluoxetine (as hydrochloride) 20 mg

For information about inactive ingredients: see section 6 – "Additional information".

Read the entire leaflet carefully before using the medicine. This leaflet contains concise information about the medicine. If you have additional questions, refer to the doctor or the pharmacist.

This medicine has been prescribed for treatment of your illness. Do not pass it on to others. It may harm them even if it seems to you that their medical condition is similar.

Antidepressant and anti-anxiety medicines increase the risk for suicidal behavior and thoughts in children, adolescents and young adults up to the age of 25. When beginning treatment with the medicine, patients of all ages and their relatives should pay attention to behavioral changes such as: worsening of depression, suicidal thoughts, aggression and the like.
If such changes occur, refer to the doctor immediately.

1. WHAT IS THE MEDICINE INTENDED FOR?

Flutine 20 is intended for adults treatment of:
- Major depressive episodes.
- Obsessive-compulsive disorder (OCD).
- Binge eating (bulimia nervosa): Fluoxetine is indicated as a complement of psychotherapy for the reduction of binge-eating and purging activity.

In children and adolescents aged 8 years and above, Flutine 20 is intended for treatment of moderate to severe major depressive episode, if depression is unresponsive to psychological therapy after 4-6 sessions. Antidepressant medication should be offered to a child or young person with moderate to severe depression **only** in combination with a concurrent psychological therapy.

Therapeutic class: Flutine 20 belongs to the group of antidepressants of the selective serotonin reuptake inhibitors (SSRI) class.

How does this medicine work?

Everyone has a substance called serotonin in their brain. People who suffer from depression, obsessive-compulsive disorder or bulimia nervosa have lower levels of serotonin in comparison with other people. The way that Flutine 20 and other SSRI preparations work is not fully understood, but they may help by increasing the level of serotonin in the brain. Treating these disorders is important in order to help you improve your condition. If the disorder is not treated, it may not go away and may become more severe and harder to treat. You may need to be treated for a few weeks or months to ensure your symptoms have passed.

2. BEFORE USING THE MEDICINE

Do not use the medicine if you:

- Are sensitive (allergic) to fluoxetine or to any of the other ingredients this medicine contains (see section 6 – "Additional information"). **If you develop a rash or other allergic reactions (such as itching, swelling of the lips or face or shortness of breath), stop taking the capsules without delay and refer to the doctor immediately.**
- Are taking other medicines known as irreversible nonselective monoamine oxidase inhibitors (MAOIs) (such as iproniazid which is used for the treatment of depression), since serious and even fatal reactions may occur. Treatment with Flutine 20 should only be started two weeks after discontinuation of treatment with irreversible nonselective MAOI.
  Do not take any irreversible nonselective MAOI for at least 5 weeks after you stop taking Flutine 20. If Flutine 20 has been prescribed for a long period and/or at a high dosage, the doctor should consider a longer interval.
- Are taking metoprolol (for treatment of heart failure), as there is an increased risk of your heart rate becoming too slow.

Special warnings regarding the use of the medicine

Before treatment with Flutine 20, tell the doctor if any of the following conditions applies to you:
- Heart problems.
- Appearance of fever, muscle stiffness or tremor, changes in your mental state such as confusion, restlessness or extreme agitation. You may suffer from "serotonin syndrome" or "neuroleptic malignant syndrome". Even though this syndrome occurs rarely, it may lead to conditions that may be life-threatening. **Refer to the doctor immediately** as the treatment with Flutine 20 may need to be discontinued.
- Current or previous mania. If you suffer from a manic episode, refer to the doctor immediately as the treatment with Flutine 20 may need to be discontinued.
- History of bleeding disorders or appearance of bruises or abnormal bleeding, or if you are pregnant (see "Pregnancy" section).
- Ongoing treatment with medicines that thin the blood (see "Drug interactions" section).
- Epilepsy or seizures. If you suffer from a seizure or notice an increase in seizure frequency, refer to the doctor immediately. The treatment with Flutine 20 may need to be discontinued.
- Ongoing treatment with ECT (electroconvulsive therapy (electric shock)).
- Ongoing treatment with tamoxifen (used for the treatment of breast cancer) (see "Drug interactions" section).
- You start to feel restless and cannot sit or stand still (akathisia). Increasing the dosage of Flutine 20 can make this worse.
- Diabetes (the doctor may need to adjust the dosage of insulin or other antidiabetic treatment).
- Liver problems (the doctor may need to adjust your dosage).
- Slow resting heart rate and/or if you know that you may suffer from salt depletion as a result of prolonged and severe diarrhea and vomiting, or as a result of using diuretics.
- Ongoing treatment with diuretics, especially if you are elderly.
- Glaucoma (increased intra-ocular pressure).

Thoughts of suicide and worsening of your depression or anxiety disorder

If you suffer from depression and/or an anxiety disorder, you may sometimes have thoughts of self-harm or suicide. These may be increased when first starting treatment with antidepressants, since these medicines take time to start working, usually two weeks but sometimes a longer period of time. Thoughts of self-harm or suicide may be more likely to appear:
- If you have suffered in the past from thoughts of self-harm or suicide.
- If you are a young adult. Information from clinical trials has shown increased risk of suicidal behavior in adults aged less than 25 years with psychiatric disorders who were treated with an antidepressant.

If you suffer from thoughts of self-harm or suicide at any time, **refer to the doctor or to a hospital without delay. You may find it helpful to tell a relative or close friend** that you suffer from depression or an anxiety disorder and ask them to read this leaflet. You can ask them to let you know if they think your depression or anxiety is getting worse or if they are worried about changes in your behavior.

Children and adolescents aged 8 to 18

Patients under the age of 18 are at an increased risk of suffering from side effects such as suicide attempt, suicidal thoughts and hostility (especially aggression, oppositional behavior and anger) while taking medicines of this type. In children and adolescents from age 8 to 18, Flutine 20 should only be used for treatment of moderate to severe major depressive episodes (in combination with psychological therapy) and this medicine should not be used for treatment of other conditions.

In addition, there is only limited information about the long term safety of Flutine 20 regarding growth, maturation and mental, emotional and behavioral development in this age group. Despite this, if you are under the age of 18, your doctor may prescribe you Flutine 20 for treatment of moderate to severe major depressive episodes, in combination with psychological therapy, since he has decided it is in your best interest. If you are under the age of 18 and your doctor prescribed you Flutine 20 and you want to discuss it, please go back to your doctor. If you are under the age of 18, inform your doctor if any of the symptoms listed above develop or worsen while taking Flutine 20.

Do not use Flutine 20 in children under the age of 8.

Sexual dysfunction

Medicines such as Flutine 20 (that belong to the SSRI group) may cause symptoms of sexual dysfunction (see section 4). In certain cases, these symptoms have continued after stopping the treatment.

Drug interactions:

If you are taking, or have recently taken, other medicines including non-prescription medicines and nutritional supplements, tell the doctor or the pharmacist.

Do not take Flutine 20 with:
- Certain preparations from the group of **irreversible nonselective monoamine oxidase inhibitors (MAOIs)**, some of which are used to treat depression. Do not use irreversible nonselective MAOIs with Flutine 20 as serious and even fatal reactions (serotonin syndrome) may occur (see "Do not use this medicine" section). Treatment with Flutine 20 should only be started two weeks after discontinuation of treatment with an irreversible nonselective MAOI (such as tranylcypromine). **Do not take** any irreversible nonselective monoamine oxidase inhibitor for at least 5 weeks after you stop taking Flutine 20. If Flutine 20 has been prescribed for a long period and/or at a high dosage, the doctor may need to consider a longer interval than 5 weeks.
- **Metoprolol** when used for treatment of heart failure. There is an increased risk of your heart rate becoming too slow.

Flutine 20 may affect the way the following medicines work (interaction):
- **Tamoxifen** (used for the treatment of breast cancer). Since Flutine 20 may change the levels of this medicine in the blood, which may lead to a possible decrease in the effect of tamoxifen, the doctor may need to consider prescribing a different antidepressant treatment.
- **Monoamine oxidase inhibitors A (MAOI-A)** including moclobemide, linezolid (an antibiotic) and methylthioninium chloride (also called methylene blue, a medicine used for the treatment of methemoglobinemia resulting from exposure to a medicine or to a chemical substance) – due to the risk of serious and even fatal reactions (serotonin syndrome). Treatment with fluoxetine can be started the day after stopping treatment with reversible MAOIs, but the doctor may want to monitor you carefully and use a lower dose of the MAOI-A medicine.
- **Mequitazine** (for treatment of allergies). Since taking this medicine with Flutine 20 may increase the risk for changes in the electrical activity of the heart.
- **Phenytoin** (for treatment of epilepsy). Since Flutine 20 may change the levels of the medicine in the blood, the doctor may need to start treatment with phenytoin more carefully and perform periodic check-ups when given with Flutine 20.
- **Lithium**, **selegiline**, **Hypericum**, **tramadol** (an analgesic), **triptans** (for treatment of migraine) and **tryptophan** - there is an increased risk for mild serotonin syndrome when these medicines are taken with Flutine 20. The doctor may perform more frequent periodic check-ups.
- Medicines that may affect heart rhythm, such as **class IA and III antiarrhythmic medicines, antipsychotic medicines** (such as phenothiazine derivatives, pimozide, haloperidol), **tricyclic antidepressants,** certain **antimicrobial preparations** (such as sparfloxacin, moxifloxacin, intravenous erythromycin, pentamidine), **anti-malaria treatment**, especially halofantrine or certain **antihistamines** (astemizole, mizolastine), since taking one or more of these medicines with Flutine 20 may increase the risk for changes in the electrical activity of the heart.
- **Anticoagulants** (such as warfarin), **non-steroidal anti-inflammatory drugs – NSAID** (such as ibuprofen, diclofenac), **aspirin and other medicines that can thin the blood** (including clozapine which is used for the treatment of certain mental disorders). Flutine 20 may change the effect of these medicines on the blood. If you start or discontinue treatment with Flutine 20 while you are taking warfarin, the doctor may need to perform certain tests, adjust the anticoagulant dosage and examine you more frequently.
- **Cyproheptadine** (for treatment of allergies), since it may decrease the effect of Flutine 20.
- **Medicines that decrease the levels of sodium in the blood** (including medicines that increase urination, desmopressin, carbamazepine and oxcarbazepine), since these medicines may increase the risk of sodium levels in the blood becoming too low while taking Flutine 20.
- **Antidepressants** such as tricyclic antidepressants, other selective serotonin reuptake inhibitors (SSRIs) or bupropion, **mefloquine** or **chloroquine** (used for the treatment of malaria), **tramadol** (used for treatment of severe pain) or **antipsychotic medicines** such as phenothiazines or butyrophenones, since Flutine 20 may increase the risk of seizures while taking these medicines.
- **Flecainide**, **propafenone**, **nebivolol** or **encainide** (for treatment of cardiac problems), **carbamazepine** (for treatment of epilepsy), **atomoxetine** or **tricyclic antidepressants** (e.g., **imipramine**, **desipramine** and **amitriptyline**) or **risperidone** (for treatment of schizophrenia); since Flutine 20 may change the levels of these medicines in the blood, the doctor may need to decrease their dosage when administered with Flutine 20.

Use of the medicine and food

Flutine 20 can be taken with or without food.

Use of the medicine and alcohol consumption

Avoid alcohol while taking this medicine.

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding, think you might be pregnant or are planning to become pregnant, refer to the doctor or pharmacist for consultation before taking this medicine.

Pregnancy

Talk to the doctor as soon as possible if you are pregnant, may be pregnant or are planning to become pregnant.

Certain studies have described an increased risk of congenital malformations affecting the heart in infants whose mothers took fluoxetine during the first months of pregnancy. In the general population, about 1 out of 100 babies is born with a heart defect. This frequency increased to about 2 out of 100 babies in mothers who took fluoxetine.

When taken during pregnancy, particularly in the last 3 months of pregnancy, medicines such as fluoxetine may increase the risk of a serious medical condition in infants, called persistent pulmonary hypertension of the newborn (PPHN), which causes fast breathing and a bluish appearance of the baby. These symptoms usually appear during the first 24 hours after the birth. If this occurs in your baby, you should refer to the midwife and/or doctor immediately. If you take Flutine 20 near the end of the pregnancy, there is an increased risk of heavy vaginal bleeding immediately after birth, especially if you have previously suffered from bleeding disorders. The doctor or midwife should be aware that you are taking Flutine 20, so they can advise you.

It is advisable not to use this treatment during pregnancy, unless the potential benefit outweighs the potential risk. Therefore, you and your doctor may decide on gradually stopping the treatment with Flutine 20 during or before pregnancy. However, depending on your circumstances, the doctor may suggest that it is advisable for you to keep taking Flutine 20.

Caution should be exercised when used during pregnancy, especially during the late stages of pregnancy or just before giving birth, since the following effects have been reported in newborns: restlessness, tremor, muscle weakness, persistent crying and suckling or sleeping difficulties.

Breastfeeding

Fluoxetine is excreted into breastmilk and may cause side effects in infants. You should only breastfeed if it is absolutely necessary. If breastfeeding is continued, the doctor may prescribe you a lower dosage of the medicine.

Fertility

Fluoxetine has been shown to reduce the quality of sperm in animal studies. Theoretically, this could affect fertility, however impact on human fertility has not been observed yet.

Driving and operating machinery

Psychotropic medicines, such as Flutine 20, may affect your judgment or coordination. Do not drive or operate machinery until you know how Flutine 20 affects you.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the medicine according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and how to use the medicine.

The dosage and treatment regimen will be determined only by the doctor. The generally accepted dosage is:
- **Major depressive episodes –** the accepted dosage is 20 mg (one capsule) per day.
  The doctor may change the dosage as necessary within 3-4 weeks of starting treatment. If needed, the dosage may be gradually increased up to a maximum of 60 mg (3 capsules) per day. The dosage should be increased cautiously, in order to guarantee that you are taking the lowest effective dosage. You may not feel an improvement immediately after starting treatment with the medicine. It usually takes several weeks from the start of treatment until there is an improvement in the symptoms of depression. Patients suffering from depression should be treated for at least 6 months.
- **Binge eating (bulimia nervosa) –** the accepted dosage is 60 mg (3 capsules) per day.
- **Obsessive-compulsive disorder (OCD) –** the accepted dosage is 20 mg (one capsule) per day.
  The doctor may change the dosage as necessary after two weeks of treatment. If needed, the dosage may be gradually increased up to a maximum of 60 mg (3 capsules) per day. If there is no improvement within 10 weeks, the doctor will consider changing treatment.

Use in children and adolescents aged 8-18 who suffer from depression – treatment should be started and be supervised by a specialist. The starting dosage is 10 mg of fluoxetine (as hydrochloride) per day, which is given as an oral solution (marketed by a different company). After 1-2 weeks, the doctor may increase the dosage to 20 mg per day. The dosage should be increased cautiously in order to guarantee that you are taking the lowest effective dosage. Low-weight children may need lower dosages. If there is a satisfactory reaction to the treatment, the doctor will review the need to continue treatment for more than 6 months. If there is no improvement within 9 weeks, the doctor will reassess your treatment.

Elderly patients – the dosage should be increased with extreme caution. The daily dosage is usually up to 40 mg (2 capsules) per day, the maximum dosage is 60 mg (3 capsules) per day.

Liver function impairment – if you suffer from liver function impairment or are using other medicines that can affect Flutine 20, the doctor may decide on a lower dosage or instruct you to take one capsule of the medicine every other day.

Do not exceed the recommended dose.

Do not chew! Swallow the medicine with water.

No information is available regarding the use of the capsule content through a nasogastric tube.

If you took a higher dosage or if a child accidentally swallowed this medicine, refer immediately to a doctor or to the nearest hospital emergency room and bring the package of the medicine with you.

Overdose symptoms include: nausea, vomiting, convulsions, heart problems (such as irregular heart rate and cardiac arrest), lung problems and change in mental condition ranging from agitation to coma.

If you forgot to take this medicine at the required time
- Take the next dose on the following day, at the usual time. Do not take a double dose in order to compensate for the dose that you forgot to take.
- Taking your medicine at the same time each day may help you remember to take it regularly.

Follow the treatment as recommended by the doctor.

If you stop taking the medicine
- **Do not stop** taking Flutine 20 without consulting the doctor first, even when you start to feel better. It is important to continue taking your medicine.
- Make sure to avoid a situation in which you run out of the medicine.

If you stop taking the medicine, you may notice the following effects (withdrawal effects): dizziness, tingling sensation such as pins and needles, sleep disturbances (dreams that seem very realistic, nightmares, inability to sleep), feeling restless or agitated, abnormal tiredness or weakness, feeling of anxiety, nausea or vomiting, tremor, headaches. Most people find that the symptoms associated with discontinuing Flutine 20 are mild and go away within a few weeks. If you suffer from symptoms when discontinuing treatment, refer to the doctor. When discontinuing treatment with Flutine 20, the doctor will help you to reduce the dosage slowly over one or two weeks – this should help decrease the chance of withdrawal effects.

Do not take medicines in the dark! Check the label and the dose every time you take the medicine. Wear glasses if you need them.

If you have any other questions regarding use of the medicine, consult the doctor or the pharmacist.

4. SIDE EFFECTS

As with any medicine, using Flutine 20 may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not experience any of them.
- If you suffer from thoughts of self-harm or suicide at any time, **refer to the doctor or to a hospital without delay** (see section 2).
- If you develop a rash or an allergic reaction such as itching, swelling of the lips/tongue or wheezing/shortness of breath, **stop taking the capsules without delay and inform the doctor immediately**.
- If you feel restless and cannot sit or stand still, you may suffer from akathisia; increasing the dosage of Flutine 20 may worsen your feeling. If you feel as described above, **refer to the doctor.**
- **Inform the doctor immediately** if skin redness appears or if you develop another skin reaction, if blisters develop on the skin or if the skin starts to peel. This effect is very rare.

Very common side effects (effects that occur in more than 1 out of 10 users):

• Insomnia, headache, diarrhea, nausea and fatigue.

Some patients have suffered from the following effects:
- A combination of symptoms (known as "serotonin syndrome") including unexplained fever with increased breathing rate or heart rate, sweating, muscle stiffness or tremor, confusion, extreme agitation or sleepiness (in rare cases only).
- Feeling of weakness, drowsiness or confusion, especially in the elderly and in (elderly) people who take diuretics.
- Prolonged and painful erection.
- Restlessness and extreme agitation.
- Heart problems, such as rapid or irregular heartbeat, fainting, collapsing or dizziness when standing up, which may indicate abnormal functioning of the heart rate.

If you suffer from any of the side effects listed above, you should inform the doctor immediately.

Additional side effects:

Common side effects (side effects that occur in 1 out of 10 users):

• Lack of hunger sensation, weight loss • agitation, anxiety • restlessness, impaired concentration • a tense feeling • decreased libido or sexual function problems (usually difficulty maintaining an erection for sexual activity) • sleeping problems, unusual dreams, tiredness or somnolence • dizziness • changes in the sense of taste • uncontrollable shaking movements • blurred vision • rapid and irregular heartbeat sensations • flushing • yawning • digestive difficulties, vomiting • dry mouth • rash, hives, itch • excessive sweating • joint pain • more frequent urination • unexplained vaginal bleeding • shaking or chills sensation

Uncommon side effects (side effects that occur in 1 out of 100 users):

• Feeling detached from yourself • strange thinking • abnormally elated mood • sexual dysfunction, including orgasm problems, which occasionally persist after discontinuing treatment • thoughts of self-harm or suicide • teeth grinding • muscle spasms, involuntary movements or problems with balance or coordination • memory disorders • enlarged (dilated) pupils • ringing in the ears • low blood pressure • shortness of breath • nosebleeds • difficulty swallowing • hair loss • increased tendency to bruising • unexplained bruising or bleeding • cold sweat • difficulty urinating • feeling hot or cold • abnormal liver function test results

Rare side effects (side effects that occur in 1 out of 1,000 users):

• Low levels of salt in the blood • decreased number of platelets in the blood, which increases the risk of bleeding or bruising • reduced white blood cell count • untypical wild behavior • hallucinations • agitation • panic attacks • confusion • stuttering • aggressiveness • convulsions • vasculitis (inflammation of the blood vessels) • rapid swelling of the tissues around the neck, face, mouth and/or throat • pain in the esophagus • hepatitis • lung problems • sensitivity to sunlight • muscle pain • problems passing urine • milk production

Side effect with unknown frequency (cannot be estimated from the available data):

Heavy vaginal bleeding shortly after birth (postpartum hemorrhage), see "Pregnancy" in section 2 for further information.

Bone fractures – an increased risk of bone fractures has been observed in patients taking medicines of this type.

Most of these side effects are expected to go away with continued treatment.

In children and adolescents (8-18 years): in addition to the possible side effects listed above, Flutine 20 may slow growth or possibly delay sexual maturation. Suicide-related behaviors (suicide attempt and suicidal thoughts), hostility, mania and nose bleeding have also been commonly reported in children.

If a side effect occurs, if one of the side effects worsens, or if you suffer from a side effect not mentioned in this leaflet, consult your doctor.

Reporting side effects

Side effects may be reported to the Ministry of Health by clicking on the link "Report side effects due to medicinal treatment" found on the Ministry of Health website homepage (www.health.gov.il), which will direct you to the online form for reporting side effects, or by clicking on the following link: https://sideeffects.health.gov.il

5. HOW TO STORE THE MEDICINE?
- Avoid poisoning! This medicine and any other medicine must be kept in a closed place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting without an explicit instruction from the doctor.
- Do not use the medicine after the expiry date (exp. date) appearing on the package. The expiry date refers to the last day of that month.
- **Store at a temperature below 25°C.**
- Do not discard medicines via wastewater or household waste. Ask the pharmacist how to dispose of medicines you no longer use. These measures will help protect the environment.

6. ADDITIONAL INFORMATION

In addition to the active ingredient, the medicine also contains:

Pregelatinized starch, simethicone emulsion, colloidal silicon dioxide

What does the medicine look like and what are the contents of the package:

A turquoise capsule containing white-yellowish powder. The body of the capsule is imprinted with "Flutine" and with "20" below it. The cap of the capsule is imprinted with "TEVA". The package contains 30 capsules.

Name and address of the license holder and manufacturer:

Teva Israel Ltd., 124 Dvora HaNevi'a, Tel Aviv 6944020.

The leaflet was revised in November 2023 in accordance with the Ministry of Health guidelines.

Registration number of the medicine in the national drug registry of the Ministry of Health: 062.52.27648

teva