

Patient Information Leaflet (PIL)

Salipax™ capsules, hard Fluoxetine

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.

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1. SERIOUS SIDE EFFECTS

WARNING–SUICIDALITY AND ANTIDEPRESSANT DRUGS

Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of Major Depressive Disorder (MDD) and other psychiatric disorders. Anyone considering the use of fluoxetine or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. Fluoxetine is approved for use in pediatric patients with MDD and Obsessive Compulsive Disorder (OCD).

2. WHAT SALIPAX IS AND WHAT IT IS USED FOR

Salipax contain the active substance fluoxetine which is one of a group of medicines called selective serotonin re-uptake inhibitors (SSRI) antidepressants.

This medicine is used to treat the following conditions:

Adults:

- Major depressive episodes
- Obsessive-compulsive disorder
- Bulimia nervosa: Salipax is used alongside psychotherapy for the reduction of binge-eating and purging

Children and adolescents aged 8 years and above:

• Moderate to severe major depressive disorder, if the depression does not respond to psychological therapy after 4-6 sessions. Salipax should be offered to a child or young person with moderate to severe major depressive disorder **only** in combination with psychological therapy.

How Salipax works

Everyone has a substance called serotonin in their brain. People who are depressed or have obsessive-compulsive disorder or bulimia nervosa have lower levels of serotonin than others. It is not fully understood how Salipax and other SSRIs work but they may help by increasing the level of serotonin in the brain.

Treating these conditions is important to help you get better. If it's not treated, your condition may not go away and may become more serious and more difficult to treat.

You may need to be treated for a few weeks or months to ensure that you are free from symptoms.

3. BEFORE YOU USE SALIPAX

Do not take Salipax if you are:

- allergic to fluoxetine or any of the other ingredients of this medicine (listed in section 6). **If you develop a rash or other allergic reactions (like itching, swollen lips or face or shortness of breath), stop taking the capsules straight away and contact your doctor immediately.**
- taking other medicines known as irreversible, non-selective monoamine oxidase inhibitors (MAOIs), since serious or even fatal reactions can occur (e.g. iproniazid used to treat depression).

Treatment with Salipax should only be started at least 2 weeks after discontinuation of an irreversible, non-selective MAOI.

Do not take any irreversible, non-selective MAOIs for at least 5 weeks after you stop taking Salipax.

If Salipax has been prescribed for a long period and/or at a high dose, a longer interval needs to be considered by your doctor.

- taking metoprolol (to treat heart failure) since there is an increased risk of your heart beat becoming too slow.

Warnings and precautions

Talk to your doctor or pharmacist before taking Salipax if any of the following applies to you:

- heart problems;
- appearance of fever, muscle stiffness or tremor, changes in your mental state like confusion, irritability and extreme agitation; you may suffer from the so-called "serotonin syndrome" or "neuroleptic malignant syndrome". Although this syndrome occurs rarely it may result in potentially life threatening conditions; **contact your doctor immediately**, since Salipax might need to be discontinued;
- mania now or in the past; if you have a manic episode, contact your doctor immediately because Salipax might need to be discontinued;
- history of bleeding disorders or appearance of bruises or unusual bleeding;
- ongoing treatment with medicines that thin the blood (see "Other medicines and Salipax");
- epilepsy or fits. If you have a fit (seizures) or experience an increase in seizure frequency, contact your doctor immediately; Salipax might need to be discontinued;

- ongoing ECT (electro-convulsive therapy);
- ongoing treatment with tamoxifen (used to treat breast cancer) (see “Other medicines and Salipax”);
- starting to feel restless and cannot sit or stand still (akathisia). Increasing your dose of Salipax may make this worse;
- diabetes (your doctor may need to adjust your dose of insulin or other antidiabetic treatment);
- liver problems (your doctor may need to adjust your dosage);
- low resting heart-rate and/or if you know that you may have salt depletion as a result of prolonged severe diarrhoea and vomiting (being sick) or usage of diuretics (water tablets);
- ongoing treatment with diuretics (water tablets), especially if you are elderly;
- glaucoma (increased pressure in the eye).

Thoughts of suicide and worsening of your depression or anxiety disorder.

If you are depressed and/or have anxiety disorders you can sometimes have thoughts of harming or killing yourself. These may be increased when first starting antidepressants, since these medicines all take time to work, usually about two weeks but sometimes longer.

You may be more likely to think like this:

- If you have previously had thoughts about killing or harming yourself.
- If you are a young adult. Information from clinical trials has shown an increased risk of suicidal behaviour in adults aged less than 25 years with psychiatric conditions who were treated with an antidepressant.

If you have thoughts of harming or killing yourself at any time, **contact your doctor or go to a hospital straight away.**

You may find it helpful to tell a relative or close friend that you are depressed or have an anxiety disorder, and ask them to read this leaflet. You might ask them to tell you if they think your depression or anxiety is getting worse, or if they are worried about changes in your behaviour.

Children and adolescents aged 8 to 18 years:

Patients under 18 have an increased risk of side effects such as suicide attempt, suicidal thoughts and hostility (predominantly aggression, oppositional behaviour and anger) when they take this class of medicines. Salipax should only be used in children and adolescents aged 8 to 18 years for the treatment of moderate to severe major depressive episodes (in combination with psychological therapy) and it should not be used to treat other conditions.

Additionally, only limited information concerning the long-term safety of Salipax on growth, puberty, mental, emotional and behavioural development in this age group is available. Despite this, and if you are a patient under 18, your doctor may prescribe Salipax for moderate to severe major depressive episodes, in combination with psychological therapy, because he/she decides that this is in your best interests. If your doctor has prescribed Salipax for a patient under 18 and you want to discuss this, please go back to your doctor. You should inform your doctor if any of the symptoms listed above develop or worsen when patients under 18 are taking Salipax.

Salipax should not be used in the treatment of children under the age of 8 years.

Sexual dysfunction

Medicines like Salipax (so called SSRIs) may cause symptoms of sexual dysfunction (see section 4). In some cases, these symptoms have continued after stopping treatment.

Other medicines and Salipax

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Do not take Salipax with:

- Certain **irreversible, non-selective monoamine oxidase inhibitors (MAOIs)**, some used to treat depression. Irreversible, nonselective MAOIs must not be used with Salipax as serious or even fatal reactions (serotonin syndrome) can occur (see section “*Do not take Salipax*”). Treatment with Salipax should only be started at least 2 weeks after discontinuation of an irreversible, non-selective MAOI (for instance tranylcypromine). **Do not** take any irreversible, non-selective MAOIs for at least 5 weeks after you stop taking Salipax. If Salipax has been prescribed for a long period and/or at a high dose, a longer interval than 5 weeks may need to be considered by your doctor.
- **metoprolol** when used for heart failure; there is an increased risk of your heart beat becoming too slow.

Salipax may affect the way the following medicines work (interaction):

- **tamoxifen** (used to treat breast cancer); because Salipax may change the blood levels of this drug, resulting in the possibility of a reduction in the effect of tamoxifen, your doctor may need to consider prescribing a different antidepressant treatment.
- **monoamine oxidase inhibitors A (MAOI-A)** including moclobemide, linezolid (an antibiotic) and methylthionium chloride (also called methylene blue, used for the treatment of medicinal or chemical product induced methemoglobinemia): due to the risk of serious or even fatal reactions (called serotonin syndrome).
Treatment with fluoxetine can be started the day after stopping treatment with reversible MAOIs but the doctor may wish to monitor you carefully and use a lower dose of the MAOI-A drug.
- **mequitazine** (for allergies); because taking this drug with Salipax may increase the risk of changes in the electrical activity of the heart.
- **phenytoin** (for epilepsy); because Salipax may influence the blood levels of this drug, your doctor may need to introduce phenytoin more carefully and carry out check-ups when given with Salipax.
- **lithium, selegiline, St. John’s Wort, tramadol** (a painkiller), **triptans** (for migraine) and **tryptophan**; there is an increased risk of mild serotonin syndrome when these drugs are taken with Salipax. Your doctor will carry out more frequent check-ups.
- medicines that may affect the heart’s rhythm, e.g. **Class IA and III antiarrhythmics, antipsychotics** (e.g. phenothiazine derivatives, pimozide, haloperidol), **tricyclic antidepressants**, certain **antimicrobial agents** (e.g. sparfloxacin, moxifloxacin, erythromycin IV, pentamidine), **anti-malaria treatment** particularly halofantrine or certain **antihistamines** (astemizole, mizolastine), because taking one or more of these drugs with Salipax may increase the risk of changes in the electrical activity of the heart.
- **Anti-coagulants** (such as warfarin), **NSAID** (such as ibuprofen, diclofenac), **aspirin** and **other medicines which can thin the blood** (including clozapine, used to treat certain mental disorders). Salipax may alter the effect of these medicines on the blood. If Salipax treatment is started or stopped when you are taking warfarin, your doctor will need to perform certain tests, adjust your dose and check on you more frequently.

- **cyproheptadine** (for allergies); because it may reduce the effect of Salipax.
- **drugs that lower sodium levels in the blood** (including, drug that causes increase in urination, desmopressin, carbamazepine and oxcarbazepine); because these drugs may increase the risk of sodium levels in the blood becoming too low when taken with Salipax.
- **anti-depressants** such as tricyclic anti-depressants, other selective serotonin reuptake inhibitors (SSRIs) or bupropion, **mefloquine** or **chloroquine** (used to treat malaria), **tramadol** (used to treat severe pain) or **anti-psychotics** such as phenothiazines or butyrophenones; because Salipax may increase the risk of seizures when taken with these medicines.
- **flecainide, propafenone, nebivolol** or **encainide** (for heart problems), **carbamazepine** (for epilepsy), **atomoxetine** or **tricyclic antidepressants** (for example **imipramine, desipramine** and **amitriptyline**) or **risperidone** (for schizophrenia); because Salipax may possibly change the blood levels of these medicines, your doctor may need to lower their dose when administered with Salipax.

Salipax with food, drink and alcohol

- You can take Salipax with or without food, whatever you prefer.
- You should avoid alcohol while you are taking this medicine.

Pregnancy, breast-feeding and fertility

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

Talk to your doctor as soon as possible if you're pregnant, if you might be pregnant, or if you're planning to become pregnant.

In babies whose mothers took fluoxetine during the first few months of pregnancy, there have been some studies describing an increased risk of birth defects affecting the heart. In the general population, about 1 in 100 babies are born with a heart defect.

This increased to about 2 in 100 babies in mothers who took fluoxetine.

When taken during pregnancy, particularly in the last 3 months of pregnancy, medicines like fluoxetine may increase the risk of a serious condition in babies, called persistent pulmonary hypertension of the newborn (PPHN), making the baby breathe faster and appear bluish. These symptoms usually begin during the first 24 hours after the baby is born.

If this happens to your baby you should contact your midwife and/or doctor immediately.

It is preferable not to use this treatment during pregnancy unless the potential benefit outweighs the potential risk. Thus, you and your doctor may decide to gradually stop taking Salipax while you are pregnant or before being pregnant. However, depending on your circumstances, your doctor may suggest that it is better for you to keep taking Salipax.

Caution should be exercised when used during pregnancy, especially during late pregnancy or just before giving birth since the following effects have been reported in new born children: irritability, tremor, muscle weakness, persistent crying, and difficulty in sucking or in sleeping.

Breast-feeding

Fluoxetine is excreted in breast milk and can cause side effects in babies. You should only breast-feed if it is clearly necessary. If breast-feeding is continued, your doctor may prescribe a lower dose of fluoxetine.

Fertility

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

Driving and using machines

Psychotropic drugs such as Salipax may affect your judgment or co-ordination. Do not drive or use machinery until you know how Salipax affects you.

4. HOW TO TAKE SALIPAX HARD CAPSULES

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure. Do not take more capsules than your doctor tells you. Swallow the capsules with a drink of water. Do not chew the capsules.

Adults:

The recommended dose is:

- **Depression:** The recommended dose is 1 capsule (20 mg) daily. Your doctor will review and adjust your dosage if necessary within 3 to 4 weeks of the start of treatment. If required, the dosage can be gradually increased up to a maximum of 3 capsules (60 mg) daily. The dose should be increased carefully to ensure that you receive the lowest effective dose. You may not feel better immediately when you first start taking your medicine for depression. This is usual because an improvement in depressive symptoms may not occur until after the first few weeks. Patients with depression should be treated for at least 6 months.
- **Bulimia nervosa:** The recommended dose is 3 capsules (60 mg) daily.
- **Obsessive-compulsive disorder:** The recommended dose is 1 capsule (20 mg) daily. Your doctor will review and adjust your dosage if necessary after 2 weeks of treatment. If required, the dosage can be gradually increased up to a maximum of 3 capsules (60 mg) daily. If no improvement is noted within 10 weeks, your doctor will reconsider your treatment.

Use in children and adolescents aged 8 to 18 years with depression:

Treatment should be started and be supervised by a specialist. The starting dose is 10 mg/day. After 1 to 2 weeks, your doctor may increase the dose to 20 mg/day. The dose should be increased carefully to ensure that you receive the lowest effective dose.

Lower weight children may need lower doses. If there is a satisfactory response to treatment, your doctor will review the need for continuing treatment beyond 6 months. If you have not improved within 9 weeks, your doctor will reassess your treatment.

Elderly:

Your doctor will increase the dose with more caution and the daily dose should generally not exceed 2 capsules (40 mg). The maximum dose is 3 capsules (60 mg) daily.

Liver impairment:

If you have a liver problem or are using other medication that might affect Salipax, your doctor may decide to prescribe a lower dose or tell you to use Salipax every other day.

If you take more Salipax than you should

- If you take too many capsules, go to your nearest hospital emergency department (or casualty) or tell your doctor straight away.
- Take the pack of Salipax with you if you can.

Symptoms of overdose include: nausea, vomiting, seizures, heart problems (like irregular heart beat and cardiac arrest), lung problems and change in mental condition ranging from agitation to coma.

If you forget to take Salipax

- If you miss a dose, do not worry. Take your next dose the next day at the usual time. Do not take a double dose to make up for a forgotten dose.
- Taking your medicine at the same time each day may help you to remember to take it regularly.

If you stop taking Salipax

- **Do not** stop taking Salipax without asking your doctor first, even when you start to feel better. It is important that you keep taking your medicine.
- Make sure you do not run out of capsules.

You may notice the following effects (withdrawal effects) when you stop taking Salipax: dizziness; tingling feelings like pins and needles; sleep disturbances (vivid dreams, nightmares, inability to sleep); feeling restless or agitated; unusual tiredness or weakness; feeling anxious; nausea/vomiting (feeling sick or being sick); tremor (shakiness); headaches.

Most people find that any symptoms on stopping Salipax are mild and disappear within a few weeks.

If you experience symptoms when you stop treatment, contact your doctor.

When stopping Salipax, your doctor will help you to reduce your dose slowly over one or two weeks –this should help reduce the chance of withdrawal effects.

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

5. POSSIBLE SIDE EFFECTS

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

- If you have thoughts of harming or killing yourself at any time, **contact your doctor or go to a hospital straight away** (see Section 2).
- If you get a rash or allergic reaction such as itching, swollen lips/tongue or wheezing/shortness of breath, **stop taking the capsules straight away and tell your doctor immediately.**
- If you feel restless and cannot sit or stand still, you may have akathisia; increasing your dose of Salipax may make you feel worse. If you feel like this, **contact your doctor.**
- **Tell your doctor immediately** if your skin starts to turn red or you develop a varied skin reaction or your skin starts to blister or peel. This is very rare.

The most frequent side effects (very common side effects that may affect more than 1 user in 10) are insomnia, headache, diarrhoea, feeling sick (nausea) and fatigue.

Some patients have had:

- a combination of symptoms (known as “serotonin syndrome”) including unexplained fever with faster breathing or heart rate, sweating, muscle stiffness or tremor, confusion, extreme agitation or sleepiness (only rarely);
- feelings of weakness, drowsiness or confusion mostly in elderly people and in (elderly) people taking diuretics (water tablets);
- prolonged and painful erection;
- irritability and extreme agitation;
- heart problems, such as fast or irregular heart rate, fainting, collapsing or dizziness upon standing which may indicate abnormal functioning of the heart rate.

If you have any of the above side effects, you should tell your doctor immediately.

The following side effects have also been reported in patients taking Salipax:

Common (may affect up to 1 in 10 people)

- not feeling hungry, weight loss
- nervousness, anxiety
- restlessness, poor concentration
- feeling tense
- decreased sex drive or sexual problems (including difficulty maintaining an erection for sexual activity)
- sleep problems, unusual dreams, tiredness or sleepiness
- dizziness
- change in taste
- uncontrollable shaking movements
- blurred vision
- rapid and irregular heartbeat sensations
- flushing
- yawning
- indigestion, vomiting
- dry mouth
- rash, urticaria, itching
- excessive sweating
- joint pain
- passing urine more frequently
- unexplained vaginal bleeding
- feeling shaky or chills

Uncommon (may affect up to 1 in 100 people)

- feeling detached from yourself
- strange thinking
- abnormally high mood
- sexual problems, including orgasm problems, occasionally persisting after treatment discontinuation
- thoughts of suicide or harming yourself
- teeth grinding
- muscle twitching, involuntary movements or problems with balance or co-ordination
- memory impairment
- enlarged (dilated) pupils
- ringing in the ears
- low blood pressure
- shortness of breath
- nose bleeds
- difficulty swallowing
- hair loss
- increased tendency to bruising
- unexplained bruising or bleeding
- cold sweat
- difficulty passing urine
- feeling hot or cold

- abnormal liver test results

Rare (may affect up to 1 in 1,000 people)

- low levels of salt in the blood
- reduction in blood platelets, which increases risk of bleeding or bruising
- reduction in white blood cell count
- untypical wild behaviour
- hallucinations
- agitation
- panic attacks
- confusion
- stuttering
- aggression
- fits
- vasculitis (inflammation of a blood vessel)
- rapid swelling of the tissues around the neck, face, mouth and/or throat
- pain in the tube that takes food or water to your stomach
- hepatitis
- lung problems
- sensitivity to sunlight
- muscle pain
- problems urinating
- producing breast milk

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

Most of these side effects are likely to disappear with continued treatment.

In children and adolescents (8-18 years) – In addition to the possible side effects listed above, Salipax may slow growth or possibly delay sexual maturity. Suicide-related behaviours (suicide attempt and suicidal thoughts), hostility, mania, and nose bleeds were also commonly reported in children.

6. HOW TO STORE SALIPAX

Keep out of reach of children.

Do not store above 30°C. Store in the original package in order to protect from light.

Do not use this medicine after the expiry date which is stated on the carton after “EXP.” The expiry date refers to the last day of that month.

7. FURTHER INFORMATION

a. What Salipax contains

1 capsule of Salipax capsule contains fluoxetine hydrochloride, equivalent to 20 mg fluoxetine, the colorants quinoline yellow (E 104) and indigo carmine (E 132), and other excipients.

b. What Salipax look like and contents of the pack

Capsule, hard.

Hard gelatin capsule with a light green opaque cap imprinted «FL» and an ivory opaque body, imprinted «MP» and containing a white powder mixture.

The capsules are packed in PVC/PE/PVDC-Aluminium blisters.

Packs of 10 and 30 capsules.

Not all pack sizes may be marketed.

c. Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:

Acino Pharma AG,

Birsweg 2, 4253 Liesberg, Switzerland

Manufacturer/Batch releaser:

Acino Pharma AG,

Birsweg 2, 4253 Liesberg, Switzerland

This leaflet was last revised in June 2019

To report any side effect (s):

- **Saudi Arabia:**

- The National Pharmacovigilance and Drug Safety Center (NPC):

- Fax: +966-11-205-7662
- Call NPC at 8002490000 (free phone)
- SFDA call center: 19999
- E-mail: npc.drug@sfda.gov.sa
- Website: www.sfda.gov.sa/npc

- **Acino Pharma Scientific Office:**

- **Phone:** +966-11-4631459
- **E-mail:** pv@acino.swiss

- **Other GCC states**

Please contact the relevant competent authority

This is a Medicament

- Medicament is a product which affects your health and its consumption contrary to instructions is dangerous for you.

- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.

- The doctor and the pharmacist are the experts in medicines, their benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.
- Keep all medicaments out of reach of children.

Council of Arab Health Ministers
and Union of Arab Pharmacists