

**PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986**  
The medicine is dispensed with a doctor's prescription only

## Esto 10, Esto 15, Esto 20

### Film-coated tablets

#### Composition:

**Esto 10:** Each film-coated tablet contains: Escitalopram (as oxalate) 10 mg

**Esto 15:** Each film-coated tablet contains: Escitalopram (as oxalate) 15 mg

**Esto 20:** Each film-coated tablet contains: Escitalopram (as oxalate) 20 mg

For a list of inactive and allergenic ingredients in the preparation, see section 6: "Further information" and section 2: "Before using the medicine".

**Read this leaflet carefully in its entirety before using the medicine.** This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist. This medicine has been prescribed to treat you. Do not pass it on to others. It may harm them even if it seems to you that their medical condition is similar. **The medicine is not generally intended for use in children and adolescents below the age of 18.**

Antidepressants and anti-anxiety medicines increase the risk of suicidal behavior and thoughts in children, adolescents and young adults up to the age of 25. Upon commencement of treatment, patients of all ages and their relatives should monitor behavioral changes such as: worsened depression, suicidal thoughts, aggressiveness and the like. If such changes occur, refer to a doctor immediately.

#### 1. WHAT IS THE MEDICINE INTENDED FOR?

**Esto** is an antidepressant from the selective serotonin reuptake inhibitors (SSRI) group. The medicines belonging to this group act on the serotonin system in the brain by increasing serotonin levels. **Esto** is used to treat the following conditions: depression, panic disorders, generalized anxiety, social anxiety, obsessive-compulsive disorder. It may take a few weeks until you start to feel better. Continue taking the medicine even if it takes time until your feeling improves.

Talk to the doctor if you do not experience an improvement or if you feel worse.

#### 2. BEFORE USING THE MEDICINE

**Do not use the medicine if:**

- You are sensitive (allergic) to the active ingredient or to any of the other ingredients contained in the medicine (see section 6: "Further information").
- You are taking other medicines from the non-selective, irreversible monoamine oxidase inhibitors (MAOI) group, such as: phenelzine, iproniazid, isocarboxazid, nialamide, tranylcypromine. Wait 14 days after taking these medicines and commencing use of **Esto**, or wait 7 days after taking **Esto** and commencing treatment with these medicines. In addition, do not concomitantly take **Esto** with reversible MAO-AI-type monoamine oxidase inhibitors (such as moclobemide, for the treatment of depression), or the non-selective and reversible MAOI linezolid (an antibiotic), or irreversible monoamine oxidase B (MAOB) inhibitors (e.g., selegiline, for the treatment of Parkinson's). The combination of these medicines increases the risk of serotonin syndrome (see "**Drug Interactions**" section).

- You are suffering from heart rhythm disorders (tested by ECG, a heart function test), or from a congenital defect in the electrical activity of the heart.
- You are taking medicines that treat heart rhythm disorders or medicines that may have an effect on the heart rhythm (see "**Drug Interactions**" section).
- You are taking the medicine pimozide.

#### Special warnings regarding use of the medicine

**Before treatment with Esto, tell the doctor if:**

- You are pregnant or breastfeeding (see "Pregnancy, breastfeeding and fertility" section).
- You have, or have had in the past, epilepsy. Stop treatment with **Esto** if you have an epileptic seizure for the first time or if the frequency of seizures increases (see section 4: "Side effects").
- You are suffering, or have suffered in the past, from impaired liver or kidney function. The doctor may want to adjust the dosage of the medicine.
- You have diabetes. Treatment with **Esto** may influence your sugar level balance. The dosage of insulin and/or other diabetic medicine may have to be adjusted.
- You have reduced blood sodium levels.
- You have a tendency to easily bleed or bruise, or if you are pregnant (see "Pregnancy, breastfeeding and fertility" in this section).
- You are being treated with electroconvulsive therapy (ECT).
- You are suffering, or have suffered in the past, from a coronary heart disease.
- You are suffering, or have suffered in the past, from heart function disturbances or if you recently had a heart attack.
- You have a low heart rate at rest and/or if you know you may develop reduced blood salt levels, as a result of prolonged diarrhea or vomiting or as a result of use of diuretics.
- You are suffering, or have suffered in the past, from symptoms which may indicate heart rate disturbances, such as: rapid or irregular heart rate, fainting, collapse or dizziness when getting up from a sitting or lying position.
- If you have, or had in the past, eye problems, such as certain types of glaucoma (increased intraocular pressure).

#### Warning

Some of the patients that suffer from manic depression may enter into a manic phase, characterized by rapidly changing, unusual ideas, unexplained happiness, and excessive physical activity. If you experience these symptoms, refer to a doctor. Symptoms such as restlessness or difficulty sitting or standing still may also occur in the first few weeks of treatment. If they occur, report to the doctor immediately. Medicines like **Esto** (so called SSRI/SNRI) may cause symptoms of sexual dysfunction (see section 4). In some cases, these symptoms have continued even after stopping treatment.

#### Panic disorders

When treating panic disorders, 2-4 weeks usually pass before any improvement is felt. At the beginning of treatment, some patients may feel increased anxiety, which will disappear during the first and second week of treatment. Therefore, in case of panic disorders, it is recommended to start with a low dosage. It is very important to strictly follow the doctor's instructions and not to stop treatment or change the dosage without consulting the doctor.

#### Suicidal thoughts and worsening of depression or of anxiety disorder

Suicidal thoughts or thoughts of self-injury are common in psychiatric disorders, especially in patients suffering from depression and/or anxiety disorder. These thoughts may

increase at the beginning of treatment with antidepressants, since the effect of these medicines takes time, usually two weeks, but sometimes longer. The chance of occurrence of such thoughts is higher if:

- you have had suicidal thoughts or thoughts of self-injury in the past.
- you are a young adult. Data from clinical trials show that there is an increased risk of suicidal behavior among adults below 25 years of age in a psychiatric state who were treated with antidepressants.

If you have suicidal thoughts or thoughts of self-injury at any point, **refer to your doctor or proceed to a hospital immediately.**

**It is recommended that you tell a relative or close friend that you are suffering from depression or anxiety disorder and to ask them to read this leaflet.** You can ask them to tell you if they think your depression or anxiety disorder has worsened, or if they are concerned about a change that has occurred in your behavior.

#### Children and adolescents

This medicine is usually not intended for use in children and adolescents under the age of 18. In patients under the age of 18 who have taken medicines from this group, there is an increased risk of side effects such as suicide attempts, suicidal thoughts and hostility (particularly aggressiveness, rebellious behavior and anger). Despite this, your doctor can prescribe this medicine for patients under the age of 18 if he/she thinks that this is for their benefit. If the doctor prescribed the medicine for a patient under the age of 18 and you are interested in discussing it – refer to the doctor again. Inform your doctor if some of the listed side effects occurred or worsened in patients under 18 years of age. In addition, the long-term effects of **Esto** on growth, maturation and cognitive-behavioral development have not yet been tested in this age group.

#### Drug Interactions

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

It is especially important to tell the doctor or pharmacist if you are taking:

- Nonselective monoamine oxidase inhibitors (MAOIs) (such as: phenelzine, iproniazid, isocarboxazid, nialamide, tranylcypromine). If you took one of these medicines, wait 14 days before starting treatment with **Esto**, wait 7 days before starting treatment with these medicines.
- Selective, reversible monoamine oxidase inhibitors type A (MAOAs), such as moclobemide (to treat depression). **Do not use Esto in combination with these medicines.**
- Irreversible monoamine oxidase inhibitors type B (MAOBs) such as selegiline (to treat Parkinson's disease). **Do not use Esto in combination with these medicines.** They may increase the risk of side effects.

- The antibiotic linezolid. **Do not use Esto with this antibiotic.**

- Lithium (for treatment of manic depression) and tryptophan.
- Imipramine and desipramine (medicines for treatment of depression).
- Sumatriptan and similar medicines (to treat migraine) and also tramadol and similar medicines (opioids, used to relieve severe pain). They may increase the risk of side effects.
- Cimetidine, lansoprazole and omeprazole (to treat gastric ulcer), fluconazole (to treat fungal infections), fluvoxamine (to treat depression) and ticlopidine (to reduce risk of stroke). These medicines may increase the concentration of escitalopram in the blood.

- An herbal medicine *Hypericum perforatum* (St. John's wort) – for treatment of depression.
- Aspirin (acetylsalicylic acid) and non-steroidal anti-inflammatory drugs (medicines to relieve pain or thin the blood, anticoagulants) – may increase the tendency to bleed.
- Warfarin, dipyrindamole, and phenprocoumon (medicines to thin the blood, anticoagulants): at the beginning and end of treatment with **Esto**, the doctor will definitely check the coagulation time of your blood to be sure that the dosage of the blood thinning medicine you are taking is adequate.

- Medicines which may lower the sensitivity threshold to convulsions: mefloquine (to treat malaria), bupropion (for treatment of depression) and tramadol (to treat severe pain).
- Neuroleptic preparations (medicines to treat schizophrenia and psychosis) and antidepressants (from the tricyclic and SSRI groups of antidepressants), due to possible risk of lowering the threshold for convulsions.
- Flecainide, propafenone and metoprolol (to treat heart and vascular diseases), clomipramine and nortriptyline (antidepressants), risperidone, thioridazine and haloperidol (antipsychotics). The **Esto** dosage may have to be adjusted.
- Medicines that lower the potassium levels or magnesium levels in the blood, since these conditions increase the risk for a life-threatening heart rhythm disturbance.

**Do not take Esto concomitantly with medicines for the treatment of a heart rhythm disturbance or medicines that may have an effect on the heart rhythm**, such as medicines for the treatment of type IA and III arrhythmias, anti-psychotics (e.g., phenothiazine derivatives, pimozide, haloperidol), tricyclic antidepressants, certain antimicrobials (e.g., sparfloracin, moxifloxacin, intravenous erythromycin, pentamidine, antimalarials, especially halofantrine), certain antihistamines (to treat allergy, astemizole, hydroxyzine, mizolastine). **If you have further questions on this matter, refer to a doctor.**

- Antidepressants from the SNRI and SSRI groups may cause serotonin syndrome (rare), which includes symptoms such as nervousness, restlessness, confusion, sweating, high fever, increased reflexes, muscle spasms, tremor, increased heart rate (see section 4: "Side effects"). The syndrome may occur at a higher frequency if you are concomitantly taking other medicines that affect the nervous system (see above). Inform the doctor of any additional medicine that you are taking.

#### Use of the medicine and food

The medicine can be taken with or without food.

#### Use of the medicine and alcohol consumption

Like many medicines, it is recommended not to consume alcohol with **Esto**, although no interaction between **Esto** and alcohol is expected.

#### Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding, think you are pregnant or planning to become pregnant, consult the doctor or pharmacist before using this medicine. Do not use **Esto** if you are pregnant or breastfeeding, unless you have consulted your doctor and discussed with him the risk versus benefit of taking this medicine. If you took **Esto** in the last 3 months of pregnancy, the following signs may appear in the baby that is born: breathing difficulties, cyanosis, seizures, change in body temperature, feeding difficulties, vomiting, low blood sugar level, stiff or flaccid muscles, increased reflexes, tremor, jitteriness, irritability, exhaustion, sleepiness, persistent crying, difficulty sleeping. Refer to the doctor immediately if your baby shows these symptoms. Make sure that the midwife and/or doctor knows that you are taking **Esto**. When taking medicines like **Esto** during pregnancy and particularly during the last 3 months of pregnancy, there is an increased risk of occurrence of a severe condition in babies called

persistent pulmonary hypertension of the newborn (PPHN) that causes the baby to breathe more rapidly and to appear cyanotic. These symptoms generally appear during the first 24 hours following birth. If these symptoms appear in your baby, you should immediately refer to the midwife and/or doctor.

If you are taking **Esto** near the end of your pregnancy, you may have an increased risk of heavy vaginal bleeding shortly after birth, especially if you have had bleeding disorders in the past. Your doctor or midwife should be aware that you are taking **Esto** so that they can advise you.

If you used **Esto** during pregnancy, do not stop taking **Esto** abruptly.

Escitalopram may pass into breast milk and therefore, breastfeeding is not recommended when using the medicine. Animal studies have shown that citalopram, a medicine similar to escitalopram, reduces sperm quality. Theoretically, this may affect fertility, but no such effects on human fertility have yet been observed.

#### Driving and using machines

It is recommended not to drive a car, operate dangerous machines or to engage in activities that require alertness, before you know how **Esto** affects you.

#### Important information about some of the ingredients of the medicine

- This medicine contains lactose. If you have been told by the doctor that you have an intolerance to certain sugars, consult with the doctor before taking this medicine.
- This medicine contains sodium. This medicine contains less than 1 mmol sodium (23 mg) per tablet, and is therefore essentially "sodium-free".

#### 3. HOW SHOULD YOU USE THE MEDICINE?

Always use the preparation according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the preparation. The dosage and treatment regimen will be determined by the doctor only. The recommended dosage is usually:

**Adults**  
Depression: The usual recommended dosage is 10 mg once a day (once-daily dosage). Your doctor can increase the dosage to up to 20 mg per day.

**Panic disorder:** The starting dosage is 5 mg per day (once-daily dosage) for the first week, and afterwards, an increase in the dosage to 10 mg per day. Your doctor can increase the dosage to up to 20 mg per day.

**Social anxiety:** The usual recommended dosage is 10 mg per day (once-daily dosage). Your doctor can lower the dosage to 5 mg per day or increase the dosage to up to 20 mg per day, according to your response to treatment with the medicine.

**Anxiety disorder:** The usual recommended dosage is 10 mg once a day (once-daily dosage). Your doctor can increase the dosage to up to 20 mg per day.

**Obsessive-compulsive disorder:** The usual recommended dosage is 10 mg once a day (once-daily dosage). Your doctor can increase the dosage to up to 20 mg per day.

#### Elderly (above the age of 65)

The usual recommended dosage is 5 mg once a day (once-daily dosage). The doctor can increase the dosage to up to 10 mg per day.

#### Children and adolescents

**Esto** is usually not intended for children and adolescents (see section 2: "Before using the medicine").

#### Impaired kidney function

Caution is advised in patients with severely impaired renal function. Take the medicine as prescribed by the doctor.

#### Impaired liver function

These patients should not receive more than 10 mg of the medicine per day. Take the medicine as prescribed by the doctor.

#### Patients known to be poor metabolisers of the enzyme CYP2C19

Patients with this known genotype should not receive more than 10 mg of the medicine per day. Take the medicine as prescribed by the doctor.

#### Do not exceed the recommended dose.

**Instructions for use:** Swallow the medicine with a little water. The medicine can be taken with or without food. If necessary, the tablet can be halved for immediate use. Do not chew the tablet, since it is bitter! There is no information about crushing the tablet.

#### Duration of treatment:

A few weeks may pass until you start feeling better. Continue taking the medicine even if it takes time until your feeling improves. **Do not change the dosage without consulting the doctor.** Complete the treatment regimen recommended by the doctor. Discontinuation of treatment too early may cause the symptoms to recur. It is recommended to adhere to the treatment for at least 6 months after your feeling improves.

- If you accidentally took an overdose or if a child accidentally swallowed the medicine**, immediately refer to a doctor or proceed to a hospital emergency room and bring the package of the medicine with you. Do so even if you do not feel bad. Possible symptoms of overdose are: dizziness, tremor, nervousness, convulsions, coma, nausea, vomiting, changes in heart rate, reduced blood pressure, change in salt/fluid balance in the body.

- If you forget to take this medicine at the required time, do not take a double dose.** If you forgot to take the medicine and you remembered before going to sleep, take the forgotten dose immediately and continue as usual the following day. If you only remembered during the night or the next day, do not take the forgotten dose and continue as usual.

- Adhere to the treatment regimen recommended by the doctor. Use this medicine at set intervals, as determined by the attending doctor. **Even if there is an improvement in your health condition, do not stop treatment with the medicine without consulting the doctor or pharmacist.**

- If you stop taking the medicine: Do not stop taking Esto before being instructed to do so by the doctor.** Upon completion of treatment, it is usually recommended to gradually reduce the dosage of the medicine over a few weeks. Abrupt discontinuation of treatment may lead to symptoms that occur at high frequency after the end of treatment with **Esto**. The risk of occurrence of these symptoms is higher with longer treatment periods or higher dosages of **Esto** or if the dosage was reduced too rapidly. In most patients, these symptoms are mild or resolve on their own within two weeks. However, in some patients, the symptoms may be more severe or may persist for a longer period of time (2-3 months and more). If you experience these symptoms of treatment withdrawal upon discontinuation of **Esto** treatment, consult a doctor. The doctor will probably ask you to resume taking the medicine and to reduce the dosage more slowly.

Symptoms of treatment discontinuation include: dizziness (unsteadiness or loss of balance), pins and needles sensation, sensation of burning and electrical current in the head (less common), sleep disturbances (vivid dreams, nightmares, inability to sleep), feeling anxious, headaches, nausea, sweating (including night sweats), restlessness or nervousness, tremor, confusion or disorientation, feeling emotional or irritable, diarrhea, visual disturbances, palpitations.

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**Do not take medicines in the dark! Check the label and the dose each time you take a medicine. Wear glasses if you need them. If you have further questions regarding use of the medicine, consult the doctor or pharmacist.**

#### 4. SIDE EFFECTS

As with any medicine, use of **Esto** may cause side effects in some users. Do not be alarmed when reading the list of side effects; you may not suffer from any of them. These effects usually pass after a few weeks of treatment. Note that some of the side effects may be symptoms of your ailment and will therefore improve when you start to feel better.

**Refer to a doctor immediately or proceed to a hospital if the following symptoms occur:**

**Uncommon side effects (frequency of up to 1 in 100 patients):**

- Unusual bleeding, including bleeding in the digestive system.

**Rare side effects (frequency of up to 1 in 1,000 patients):**

- Swelling of the skin, tongue, lips, pharynx or face, urticaria, or difficulty breathing or swallowing (symptoms of a severe allergic reaction).
- High fever, nervousness or restlessness, confusion, tremor, strong contracting of muscles, may be symptoms of a rare condition called serotonin syndrome.
- Side effects of unknown frequency (effects whose frequency has not yet been determined):
  - Difficulty passing urine.
  - Seizures (also see "Special warnings regarding use of the medicine" section).
- Yellowing of the skin and whites of the eye, which are symptoms of liver function problems/hepatitis.
- Rapid and irregular heart rate and fainting, may be symptoms of a life-threatening condition called Torsade de Pointes (arrhythmia).
- Thoughts of self-injury or suicidal thoughts (also see "Special warnings regarding use of the medicine" section).
- Sudden swelling of the skin or mucous membranes (angioedema).

#### Additional side effects:

**Very common side effects (frequency of more than 1 in 10 patients):** Nausea, headache.

**Common side effects (frequency of up to 1 in 10 patients):** nasal congestion (sinusitis), decreased or increased appetite, anxiety, restlessness, abnormal dreams, difficulty falling asleep, sleepiness, dizziness, yawning, tremor, prickling sensation of the skin, diarrhea, constipation, vomiting, dry mouth, increased sweating, muscle and joint pain, sexual function disturbances (delayed ejaculation, problem with erection, decreased sexual desire, difficulty achieving orgasm among women), fatigue, fever, weight gain.

**Uncommon side effects (frequency of up to 1 in 100 patients):** rash, itchy skin, teeth grinding, excitement, nervousness, panic attack, confusion, sleep disturbances, taste disturbances, fainting, enlarged pupils, vision disturbances, ringing in the ears (tinnitus), hair loss, heavy bleeding during the menstrual cycle, unusual menstrual cycle, weight loss, rapid heart rate, swelling of the limbs, nosebleed.

**Rare side effects (frequency of up to 1 in 1,000 patients):** aggressiveness, depersonalization, hallucinations, slow heart rate.

**Side effects of unknown frequency (effects whose frequency has not yet been determined):** reduced blood sodium level (symptoms are: unwell feeling and nausea with muscle weakness or confusion), dizziness when getting up from a sitting or lying position due to low blood pressure, abnormal liver function (increased liver enzyme level in the blood), movement disturbances (involuntary muscle movement), painful erection, bleeding (including bleeding of the skin and mucous membranes), abnormal secretion of the ADH hormone, which causes water retention in the body, thinning of the blood as well as to reduced sodium quantities, milk discharge in men and in women who are not breastfeeding, mania, increased risk of fractures has been observed in patients taking medicines of this kind, change in heart rate (called prolongation of the QT interval, which can be seen in ECG tests of the electrical activity of the heart), heavy vaginal bleeding shortly after birth (see more information in "Pregnancy, breastfeeding and fertility" section that appears in section 2 of the leaflet).

In addition, a number of side effects are known to occur when taking medicines that act in a manner similar to escitalopram (the active ingredient in **Esto**), which are: akathisia (motor restlessness), loss of appetite.

**If a side effect worsens or if you suffer from a side effect not mentioned in the leaflet, consult with the doctor.**

#### Report side effects

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" on the Ministry of Health homepage ([www.health.gov.il](http://www.health.gov.il)) that directs you to the online form for reporting side effects, or by entering the link: <https://sideeffects.health.gov.il>

Additionally, you can report to "Unipharm Ltd."

#### 5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine, and any other medicine, must be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor. Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month. Store below 25°C and in a place protected from light.

#### 6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains: Microcrystalline Cellulose; Lactose Anhydrous; Talc; Croscarmellose Sodium; Colloidal Silicon Dioxide; Magnesium Stearate; Opadry Y-1-7000.

**What the medicine looks like and the contents of the package:** **Esto** is packaged in trays (blisters), which are inserted into a carton package. Each package contains 7, 10, 14, 20, 28 or 30 tablets. Not all package sizes may be marketed.

**Esto 10 and Esto 15** are white, round, film-coated, biconvex tablets, with a break line on one side.

**Esto 20** are white, oval, film-coated, biconvex tablets, with a break line on one side.

**License holder and address:** Unipharm Ltd., P.O.B. 21429, Tel Aviv, 6121301.

**Manufacturer and address:** Unipharm Ltd., "Mevo Carmel" Industrial Park.

**Registration number of the medicine in the National Drug Registry of the Ministry of Health:**

**Esto 10:** 141 60 31712 02

**Esto 15:** 148 65 33637 01

**Esto 20:** 141 61 31970 02

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