

Package leaflet: Information for the patient

Loxentia 20 mg hard gastro-resistant capsules

Loxentia 40 mg hard gastro-resistant capsules

duloxetine

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

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

What is in this leaflet

1. What Loxentia is and what it is used for
2. What you need to know before you take Loxentia
3. How to take Loxentia
4. Possible side effects
5. How to store Loxentia
6. Contents of the pack and other information

1. What Loxentia is and what it is used for

Loxentia contains the active substance duloxetine. Loxentia increases the levels of serotonin and noradrenaline in the nervous system.

Loxentia is a medicine to be taken by mouth to treat Stress Urinary Incontinence (SUI) in women.

Stress urinary incontinence is a medical condition in which patients have accidental loss or leakage of urine during physical exertion or activities such as laughing, coughing, sneezing, lifting, or exercise.

Loxentia is believed to work by increasing the strength of the muscle that holds back urine when you laugh, sneeze, or perform physical activities.

The efficacy of Loxentia is reinforced when combined with a training program called Pelvic Floor Muscle Training (PFMT).

2. What you need to know before you take Loxentia

Do not take Loxentia if you

- are allergic to duloxetine or any of the other ingredients of this medicine (listed in section 6).
- have liver disease
- have severe kidney disease
- are taking or have taken within the last 14 days, another medicine known as a monoamine oxidase inhibitor (MAOI) (see "Other medicines and Loxentia")
- are taking fluvoxamine which is usually used to treat depression, ciprofloxacin or enoxacin which are used to treat some infections

Talk to your doctor if you have high blood pressure or heart disease. Your doctor will tell you if you should be taking Loxentia.

Warnings and precautions

The following are reasons why Loxentia may not be suitable for you. Talk to your doctor before you

take Loxentia if you:

- are taking medicines to treat depression, triptans, antipsychotics, buprenorphine. The use of these medicines together with Loxentia can lead to serotonin syndrome, a potentially life-threatening condition (see sections "Other medicines and Loxentia " and "Possible side effects")
- are taking St. John's Wort, a herbal treatment (*Hypericum perforatum*)
- have kidney disease
- have had seizures (fits)
- have had mania
- suffer from bipolar disorder
- have eye problems, such as certain kinds of glaucoma (increased pressure in the eye)
- have a history of bleeding disorders (tendency to develop bruises), especially if you are pregnant (see "Pregnancy and breast-feeding")
- are at risk of low sodium levels (for example if you are taking diuretics, especially if you are elderly)
- are currently being treated with another medicine which may cause liver damage.
- are taking other medicines containing duloxetine (see "Other medicines and Loxentia")

You should also contact your doctor:

If you experience signs and symptoms of restlessness, hallucinations, loss of coordination, fast heart beat, increased body temperature, fast changes in blood pressure, overactive reflexes, diarrhoea, coma, nausea, vomiting, as you might be suffering a serotonin syndrome.

In its most severe form, serotonin syndrome can resemble Neuroleptic Malignant Syndrome (NMS). Signs and symptoms of NMS may include a combination of fever, fast heart beat, sweating, severe muscle stiffness, confusion, increased muscle enzymes (determined by a blood test).

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

Loxentia may cause a sensation of restlessness or an inability to sit or stand still. You should tell your doctor if this happens to you.

Thoughts of suicide and worsening of depression or anxiety disorder

Although Loxentia is not indicated for the treatment of depression, its active ingredient (duloxetine) is used as an antidepressant medicine. 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
- 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 under 18 years of age

Loxentia should not be used for children and adolescents under 18 years. Also, you should know that 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. Also, the long-term safety effects concerning growth, maturation, and cognitive and

behavioural development of duloxetine in this age group have not yet been demonstrated.

Other medicines and Loxentia

Please tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription.

The main ingredient of Loxentia, duloxetine, is used in other medicines for other conditions:

- diabetic neuropathic pain, depression, anxiety and urinary incontinence

Using more than one of these medicines at the same time should be avoided. Check with your doctor if you are already taking other medicines containing duloxetine.

Your doctor should decide whether you can take Loxentia with other medicines. **Do not start or stop taking any medicines, including those bought without a prescription and herbal remedies, before checking with your doctor.**

You should also tell your doctor if you are taking any of the following:

Monoamine oxidase inhibitors (MAOIs): You should not take Loxentia if you are taking or have recently taken (within the last 14 days) an antidepressant medicine called a monoamine oxidase inhibitor (MAOI). Examples of MAOIs include moclobemide (an antidepressant) and linezolid (an antibiotic). Taking a MAOI together with many prescription medicines, including Loxentia, can cause serious or even life-threatening side effects. You must wait at least 14 days after you have stopped taking a MAOI before you can take Loxentia. Also, you need to wait at least 5 days after you stop taking Loxentia before you take a MAOI.

Medicines that cause sleepiness: These include medicines prescribed by your doctor including benzodiazepines, strong painkillers, antipsychotics, phenobarbital and sedative antihistamines.

Medicines that increase the level of serotonin: Triptans, buprenorphine (a medicine to treat pain or opioid dependence), tramadol, tryptophan, SSRIs (such as paroxetine and fluoxetine), SNRIs (such as venlafaxine), tricyclic antidepressants (such as clomipramine, amitriptyline), pethidine, St John's Wort and MAOIs (such as moclobemide and linezolid). These medicines increase the risk of side effects such as Serotonin syndrome (see section "Warnings and precautions"). If you get any unusual symptom taking any of these medicines together with Loxentia, you should see your doctor.

Oral anticoagulants or antiplatelet agents: Medicines which thin the blood or prevent the blood from clotting. These medicines might increase the risk of bleeding.

Loxentia with food, drink and alcohol

Loxentia may be taken with or without food. You should take extra care if you drink alcohol while taking Loxentia.

Pregnancy and breast-feeding

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

- Tell your doctor if you become pregnant, or you are trying to become pregnant, while you are taking Loxentia. You should use Loxentia only after discussing the potential benefits and any potential risks to your unborn child with your doctor.
- Make sure your midwife and/or doctor knows you are on Loxentia. When taken during pregnancy, similar drugs (SSRIs) 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.
- If you take Loxentia near the end of your pregnancy, your baby might have some symptoms when it is born. These usually begin at birth or within a few days of your baby being born.

These symptoms may include floppy muscles, trembling, jitteriness, not feeding properly, trouble with breathing and fits. If your baby has any of these symptoms when it is born, or you are concerned about your baby's health, contact your doctor or midwife who will be able to advise you.

- If you take Loxentia near the end of your pregnancy there is an increased risk of excessive vaginal bleeding shortly after birth, especially if you have a history of bleeding disorders. Your doctor or midwife should be aware that you are taking duloxetine so they can advise you.
- Available data from the use of Loxentia during the first three months of pregnancy do not show an increased risk of overall birth defects in general in the child. If Loxentia is taken during the second half of pregnancy, there may be an increased risk that the infant will be born early (6 additional premature infants for every 100 women who take Loxentia in the second half of pregnancy), mostly between weeks 35 and 36 of pregnancy.
- Tell your doctor if you are breast-feeding. The use of Loxentia while breastfeeding is not recommended. You should ask your doctor or pharmacist for advice.

Driving and using machines

Loxentia may make you feel sleepy or dizzy. Do not drive or use any tools or machines until you know how Loxentia affects you.

Loxentia contains sucrose

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. How to take Loxentia

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

Loxentia is for oral use. You should swallow your capsule whole with a drink of water.

The recommended dose of Loxentia is 40 mg twice a day (in the morning and late afternoon/evening). Your doctor may decide to start your treatment with 20 mg twice a day for two weeks before increasing the dose to 40 mg twice a day.

To help you remember to take Loxentia, you may find it easier to take it at the same time every day.

Do not stop taking Loxentia, or change your dose, without talking to your doctor. Treating your disorder properly is important to help you get better. If it is not treated, your condition may not go away and may become more serious and difficult to treat.

If you take more Loxentia than you should

Call your doctor or pharmacist immediately if you take more than the amount of Loxentia prescribed by your doctor. Symptoms of overdose include sleepiness, coma, serotonin syndrome (a rare reaction which may cause feelings of great happiness, drowsiness, clumsiness, restlessness, feeling of being drunk, fever, sweating or rigid muscles), fits, vomiting and fast heart rate.

If you forget to take Loxentia

If you miss a dose, take it as soon as you remember. However, if it is time for your next dose, skip the missed dose and take only a single dose as usual. Do not take a double dose to make up for a forgotten dose. Do not take more than the daily amount of Loxentia that has been prescribed for you in one day.

If you stop taking Loxentia

DO NOT stop taking your capsules without the advice of your doctor even if you feel better. If your doctor thinks that you no longer need Loxentia he or she will ask you to reduce your dose over 2 weeks.

Some patients, who suddenly stop taking duloxetine after more than 1 week of therapy, have had symptoms such as:

- dizziness, tingling feelings like pins and needles or electric shock-like feelings (particularly in the head), sleep disturbances (vivid dreams, nightmares, inability to sleep), fatigue, sleepiness, feeling restless or agitated, feeling anxious, feeling sick (nausea) or being sick (vomiting), shaking (tremor), headaches, muscle pain, feeling irritable, diarrhoea, excessive sweating or vertigo.

These symptoms are usually not serious and disappear within a few days, but if you have symptoms that are troublesome you should ask your doctor for advice.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. These effects are normally mild to moderate and often disappear after a short time.

Very common side effects (may affect more than 1 in 10 people)

- feeling sick (nausea), dry mouth, constipation
- fatigue

Common side effects (may affect up to 1 in 10 people)

- lack of appetite
- trouble sleeping, feeling agitated, less sex drive, anxiety, difficulty sleeping
- headache, dizziness, feeling sluggish, feeling sleepy, tremor, numbness, including numbness, pricking or tingling of the skin
- blurred eyesight
- feeling of dizziness or "spinning" (vertigo)
- increased blood pressure, flushing
- diarrhoea, stomach pain, being sick (vomiting), heartburn or indigestion
- increased sweating
- weakness, shivering

Uncommon side effects (may affect up to 1 in 100 people)

- throat inflammation that causes a hoarse voice
- allergic reactions
- decreased thyroid gland activity which can cause tiredness or weight gain
- dehydration
- grinding or clenching the teeth, feeling disorientated, lack of motivation, difficulty or failure to experience orgasm, unusual dreams
- feeling nervous, difficulty concentrating, changes in sense of taste, poor sleep quality
- large pupils (the dark centre of the eye), problems with eyesight, eyes feel dry
- tinnitus (hearing sound in the ear when there is no external sound), ear pain
- feeling the heart pumping in the chest, fast and/or irregular heart beat
- fainting
- increased yawning
- vomiting blood, or black tarry stools (faeces), gastroenteritis, inflammation of the mouth, burping, difficulty swallowing, breaking wind, bad breath
- inflammation of the liver that may cause abdominal pain and yellowing of the skin or whites of the eyes

- (itchy) rash, night sweats, hives, cold sweats, increased tendency to bruise
- muscle pain, muscle tightness, muscle spasm, contraction of the jaw muscle
- difficulty to start urinating, painful urination, needing to pass urine during the night, frequent urination, abnormal urine odour
- abnormal vaginal bleeding, menopausal symptoms
- chest pain, feeling cold, thirst, feeling hot
- weight loss, weight gain
- Loxentia may cause effects that you may not be aware of, such as increases in liver enzymes or blood levels of potassium, creatine phosphokinase, sugar, or cholesterol

Rare side effects (may affect up to 1 in 1 000 people)

- serious allergic reaction which causes difficulty in breathing or dizziness with swollen tongue or lips
- low levels of sodium in the blood (mostly in elderly people; the symptoms may include feeling dizzy, weak, confused, sleepy or very tired, or feeling or being sick, more serious symptoms are fainting, fits or falls), syndrome of inappropriate secretion of anti-diuretic hormone (SIADH)
- suicidal behaviour, suicidal thoughts, mania (over activity, racing thoughts and decreased need for sleep), hallucinations, aggression and anger
- "Serotonin syndrome" (a rare reaction which symptoms may include involuntary, rhythmic contractions of muscles, including the muscles that control movement of the eye, agitation, hallucinations, coma, excessive sweating, tremor, exaggeration of reflexes, increased muscle tension, body temperature above 38°C, nausea, vomiting, diarrhoea), fits, sudden involuntary jerks or twitches of the muscles, sensation of restlessness or an inability to sit or stand still, difficulty controlling movement e.g. lack of coordination or involuntary movements of the muscles, restless legs syndrome
- increased pressure in the eye (glaucoma)
- dizziness, light headedness or fainting on standing up, cold fingers and/or toes
- throat tightness, nose bleeds
- coughing, wheezing and shortness of breath which may be accompanied by a high temperature
- passing bright red blood in your stools, inflammation of the large intestine (leading to diarrhoea)
- liver failure, yellowing of the skin or whites of the eyes (jaundice)
- Stevens-Johnson syndrome (serious illness with blistering of the skin, mouth, eyes and genitals), serious allergic reaction which causes swelling of the face or throat (angioedema), sensitivity to sunlight
- muscle twitching
- difficulty or inability to pass urine, needing to pass more urine than normal, having a decreased urine flow
- abnormal periods, including heavy, painful, irregular or prolonged periods, unusually light or missed periods, abnormal production of breast milk
- excessive vaginal bleeding shortly after birth (postpartum haemorrhage)
- falls (mostly in elderly people), abnormal gait

Very rare side effects (may affect up to 1 in 10 000 people)

- inflammation of the blood vessels in the skin (cutaneous vasculitis)

Frequency not known (cannot be estimated from the available data)

- signs and symptoms of a condition called "stress cardiomyopathy" which may include chest pain, shortness of breath, dizziness, fainting, irregular heart beat

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance, Website: www.hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Loxentia

Keep this medicine out of the sight and reach of children.

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

Do not store above 25°C.

Store in the original package in order to protect from moisture.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Loxentia contains

- The active substance is duloxetine. Each hard gastro-resistant capsule contains 20 mg or 40 mg duloxetine (as duloxetine hydrochloride).
- The other ingredients are:
capsule contents: sugar spheres (sucrose, maize starch), hypromellose 6 cP, sucrose, hypromellose phthalate, talc and triethyl citrate
capsule shell: gelatin, titanium dioxide (E171), indigotine (E132), yellow iron oxide (E172) – only in 40 mg capsules, red iron oxide (E172) – only in 40 mg capsules, ink (shellac, black iron oxide (E172))
See section 2 "Loxentia contains sucrose".

What Loxentia looks like and contents of the pack

20 mg hard gastro-resistant capsules: White to almost white pellets in a hard gelatine capsule size 4 (average length: 14.4 mm). The capsule body and cap are light blue. The capsule body is imprinted with 20 in black.

40 mg hard gastro-resistant capsules: White to almost white pellets in a hard gelatine capsule size 2 (average length: 17.9 mm). The capsule body is light orange and the cap light blue. The capsule body is imprinted with 40 in black.

Loxentia is available in packs containing 7, 10, 14, 28, 30, 56, 60, 90 and 100 hard gastro-resistant capsules in blisters.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

KRKA, d.d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia

Manufacturer

KRKA, d.d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia

TAD Pharma GmbH, Heinz-Lohmann-Straße 5, 27472 Cuxhaven, Germany

This medicine is authorised in the Member States of the European Economic Area under the following names:

Slovakia, Finland, Sweden, Denmark, Ireland	Loxentia
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This leaflet was last revised in