Package leaflet: Information for the patient

Duloxetine Krka 30 mg hard gastro-resistant capsules
Duloxetine Krka 60 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 Duloxetine Krka is and what it is used for

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

Duloxetine Krka is used in adults to treat:
- depression
- generalised anxiety disorder (chronic feeling of anxiety or nervousness)
- diabetic neuropathic pain (often described as burning, stabbing, stinging, shooting or aching or like an electric shock. There may be loss of feeling in the affected area, or sensations such as touch, heat, cold or pressure may cause pain).

Duloxetine Krka starts to work in most people with depression or anxiety within two weeks of starting treatment, but it may take 2-4 weeks before you feel better. Tell your doctor if you do not start to feel better after this time. Your doctor may continue to give you Duloxetine Krka when you are feeling better to prevent your depression or anxiety from returning.

In people with diabetic neuropathic pain it can take some weeks before you feel better. Talk to your doctor if you do not feel better after 2 months.

2. What you need to know before you take Duloxetine Krka

Do not take Duloxetine Krka 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 Duloxetine Krka")
- are taking fluvoxamine which is usually used to treat depression, ciprofloxacin or enoxacin which are used to treat some infections
- are taking other medicines containing duloxetine (see "Other medicines and Duloxetine Krka")

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

Warnings and precautions
The following are reasons why Duloxetine Krka may not be suitable for you. Talk to your doctor before you take Duloxetine Krka if you:
- are taking other medicines to treat depression, triptans, antipsychotics, buprenorphine. The use of these medicines together with Duloxetine Krka can lead to serotonin syndrome, a potentially life-threatening condition (see "Other medicines and Duloxetine Krka" 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 Duloxetine Krka")

You should also contact your doctor:

If you experience signs and symptoms of restlessness, hallucinations, loss of coordination, fast heartbeat, 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 heartbeat, sweating, severe muscle stiffness, confusion, increased muscle enzymes (determined by a blood test).

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

Duloxetine Krka 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 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
- 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
Duloxetine Krka should normally 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. Despite this, your doctor may prescribe Duloxetine Krka for patients under 18 because he/she decides that this is in their best interests. If your doctor has prescribed Duloxetine Krka 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 Duloxetine Krka. 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 Duloxetine Krka
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 Duloxetine Krka, 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 Duloxetine Krka 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 Duloxetine Krka if you are taking, or have recently taken (within the last 14 days) another 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 Duloxetine Krka, can cause serious or even life-threatening side effects. You must wait at least 14 days after you have stopped taking an MAOI before you can take Duloxetine Krka. Also, you need to wait at least 5 days after you stop taking Duloxetine Krka before you take a MAOI.

Medicines that cause sleepiness: These include medicines prescribed by your doctor including benzodiazepines, strong painkillers, antipsychotics, phenobarbital and 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 "Warnings and precautions" and "Possible side effects"). If you get any unusual symptom taking any of these medicines together with Duloxetine Krka, 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.

Duloxetine Krka with food, drink and alcohol
Duloxetine Krka may be taken with or without food. Care should be taken if you drink alcohol while you are being treated with Duloxetine Krka.

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 Duloxetine Krka. You should use Duloxetine Krka 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 Duloxetine Krka. 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 Duloxetine Krka 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 Duloxetine Krka 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 Duloxetine Krka during the first three months of pregnancy do not show an increased risk of overall birth defects in general in the child. If Duloxetine Krka 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 Duloxetine Krka 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 Duloxetine Krka while breastfeeding is not recommended. You should ask your doctor or pharmacist for advice.

Driving and using machines
Duloxetine Krka may make you feel sleepy or dizzy. Do not drive or use any tools or machines until you know how Duloxetine Krka affects you.

Duloxetine Krka 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 Duloxetine Krka

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

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

For depression and diabetic neuropathic pain:
The usual dose of Duloxetine Krka is 60 mg once a day, but your doctor will prescribe the dose that is right for you.

For generalised anxiety disorder:
The usual starting dose of Duloxetine Krka is 30 mg once a day after which most patients will receive 60 mg once a day, but your doctor will prescribe the dose that is right for you. The dose may be adjusted up to 120 mg a day based on your response to Duloxetine Krka.

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

Talk with your doctor about how long you should keep taking Duloxetine Krka. Do not stop taking Duloxetine Krka, 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 Duloxetine Krka than you should
Call your doctor or pharmacist immediately if you take more than the amount of Duloxetine Krka 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 Duloxetine Krka
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 Duloxetine Krka that has been prescribed for you in one day.

If you stop taking Duloxetine Krka
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 Duloxetine Krka he or she will ask you to reduce your dose over at least 2 weeks before stopping treatment altogether.

Some patients who stop taking duloxetine suddenly 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 few weeks.

Very common side effects (may affect more than 1 in 10 people)
- headache, feeling sleepy
- feeling sick (nausea), dry mouth

Common side effects (may affect up to 1 in 10 people)
- lack of appetite
- trouble sleeping, feeling agitated, less sex drive, anxiety, difficulty or failure to experience orgasm, unusual dreams
- dizziness, feeling sluggish, tremor, numbness, including numbness, pricking or tingling of the skin
- blurred eyesight
- tinnitus (hearing sound in the ear when there is no external sound)

- feeling the heart pumping in the chest
- increased blood pressure, flushing
- increased yawning
- constipation, diarrhoea, stomach pain, being sick (vomiting), heartburn or indigestion, breaking wind
- increased sweating, (itchy) rash
- muscle pain, muscle spasm
- painful urination, frequent urination
- problems getting an erection, changes in ejaculation
- falls (mostly in elderly people), fatigue
- weight loss

Children and adolescents under 18 years of age with depression treated with this medicine had some weight loss when they first start taking this medicine. Weight increased to match other children and adolescents of their age and sex after 6 months of treatment.

Uncommon side effects (may affect up to 1 in 100 people)
- throat inflammation that causes a hoarse voice
- suicidal thoughts, difficulty sleeping, grinding or clenching the teeth, feeling disorientated, lack of motivation
- sudden involuntary jerks or twitches of the muscles, sensation of restlessness or an inability to sit or stand still, feeling nervous, difficulty concentrating, changes in sense of taste, difficulty controlling movement e.g. lack of coordination or involuntary movements of the muscles, restless legs syndrome, poor sleep quality
- large pupils (the dark centre of the eye), problems with eyesight
- feeling of dizziness or "spinning" (vertigo), ear pain
- fast and/or irregular heart beat
- fainting, dizziness, light headedness or fainting on standing up, cold fingers and/or toes
- throat tightness, nose bleeds
- vomiting blood, or black tarry stools (faeces), gastroenteritis, burping, difficulty swallowing
- inflammation of the liver that may cause abdominal pain and yellowing of the skin or whites of the eyes
- night sweats, hives, cold sweats, sensitivity to sunlight, increased tendency to bruise
- muscle tightness, muscle twitching
- difficulty or inability to pass urine, difficulty to start urinating, needing to pass urine during the night, needing to pass more urine than normal, having a decreased urine flow
- abnormal vaginal bleeding, abnormal periods, including heavy, painful, irregular or prolonged periods, unusually light or missed periods, pain in the testicles or scrotum
- chest pain, feeling cold, thirst, shivering, feeling hot, abnormal gait
- weight gain
- Duloxetine Krka 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, allergic reactions
- decreased thyroid gland activity which can cause tiredness or weight gain
- dehydration, 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, 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
- increased pressure in the eye (glaucoma)
- coughing, wheezing and shortness of breath which may be accompanied by a high temperature
- inflammation of the mouth, passing bright red blood in your stools, bad breath, 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)
- contraction of the jaw muscle
- abnormal urine odour
- menopausal symptoms, abnormal production of breast milk in men or women
- excessive vaginal bleeding shortly after birth (postpartum haemorrhage)

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 heartbeat

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 Duloxetine Krka

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 Duloxetine Krka contains
- The active substance is duloxetine. Each hard gastro-resistant capsule contains 30 mg or 60 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 60 mg capsules, ink (shellac, black iron oxide (E172))
  See section 2 "Duloxetine Krka contains sucrose ".

What Duloxetine Krka looks like and contents of the pack
30 mg hard gastro-resistant capsules: White to almost white pellets in a hard gelatine capsule size 3 (average length: 15.9 mm). The capsule body is white and the cap dark blue. The capsule body is

imprinted with 30 in black.
60 mg hard gastro-resistant capsules: White to almost white pellets in a hard gelatine capsule size 1 (average length: 19.4 mm). The capsule body is yellowish green and the cap dark blue. The capsule body is imprinted with 60 in black.

Duloxetine Krka 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

Manufacturers
KRKA, d.d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia
TAD Pharma GmbH, Heinz-Lohmann-Straße 5, 27472 Cuxhaven, Germania

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

Name of the Member State	**Name of the medicinal product**
Slovakia, Denmark, Austria, Norway, Iceland	Duloxetin Krka
Finland, Sweden, The Netherlands, Ireland, Belgium	Duloxetine Krka

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