PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S5

EXSIRA 50 mg extended-release tablets

EXSIRA 100 mg extended-release tablets

Desvenlafaxine succinate

Sugar free

Read all of this leaflet carefully before you start taking EXSIRA

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- EXSIRA has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

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

1. What EXSIRA is and what it is used for

EXSIRA tablets are indicated for the treatment of major depressive disorder (MDD).

2. What you need to know before you take EXSIRA

Do not take EXSIRA:

- if you are hypersensitive (allergic) to desvenlafaxine succinate or any of the other ingredients of EXSIRA (listed in section 6)
- if you are taking other so-called MAO inhibitors (MAOI), a special group of anti-depressants. If you have been taking an MAOI then you should only start taking EXSIRA when there has been an interval of at least 14 days since you stopped taking the MAOI. If you stop taking EXSIRA you should wait at least 7 days before taking an MAOI. Serious reactions may occur, such as tremor, muscle twitching, sweating, nausea, vomiting, flushing (redness in the face), dizziness, elevated body temperature, seizures and death
- if you are less than 18 years of age
- if you are pregnant or breastfeeding (see Pregnancy and breastfeeding)

Warnings and precautions

Take special care with EXSIRA:

- Especially at the start of treatment and when the dose is altered, the doctor will observe whether there is deterioration in your symptoms.
- It has not been determined whether EXSIRA is safe and effective in children under the age of 18 years. There have been reports of hostile behaviour, suicidal tendencies and self-harm when medicines from the same group of medicines to which EXSIRA also belongs are used in children under 18 years of age.
- Mania has been reported in patients using EXSIRA. Therefore, EXSIRA should be used with caution, especially if you have a history or family history of mania.
- Serotonin syndrome, which is a potentially life-threatening medicine reaction that causes the body to have too much serotonin (a chemical produced by nerve cells) may occur. Symptoms may include agitation, hallucinations, coma, fast heartbeat, rapid changes in blood pressure, increased body temperature, overactive reflexes, loss of coordination, nausea, vomiting, diarrhoea. Serotonin syndrome most often occurs when two medicines that affect the body's level of serotonin are taken together at the same time. The medicines cause too much serotonin to be released or to remain in the brain area. Examples of medicines that cause this reaction when used together with EXSIRA are: triptans (migraine medicines) and antidepressant medicines such as selective serotonin reuptake inhibitors (SSRIs), selective serotonin/ norepinephrine reuptake inhibitors (SSNRIs) and monoamine oxidase inhibitors

(MAOIs). Tell your doctor if you think you are using any of these medicines.

- Mydriasis (dilation of pupils) can occur when using EXSIRA. Therefore, patients with high internal pressure in the eyes or those with a high risk of narrow angle glaucoma (damage to the nerve of the eye) should be carefully monitored.

Tell your doctor or health care provider:

- if your blood pressure rises during treatment with EXSIRA, especially if you are taking high doses. It is advisable to check your blood pressure at regular intervals
- if you are elderly and your blood pressure drops on standing up, causing you to feel dizzy or faint
- if you have recently suffered a heart attack or suffer from a heart disease which has not been stabilised. Special care is advised and the necessary dose for you should be especially carefully adjusted
- if high cholesterol levels occur under long-term treatment with EXSIRA. Cholesterol examinations should be taken into consideration
- if you suffer or have previously suffered from seizures (especially epilepsy) because EXSIRA should then only be used with care
- if treatment is stopped suddenly because withdrawal symptoms can occur after treatment with EXSIRA depending on the dose which has been taken and the duration of treatment. It is recommended to end treatment by reducing the dose in steps
- if you know that you suffer from blood clotting disorders because it is possible that there is increased risk of skin or mucous membrane bleeding during treatment with EXSIRA
- if you experience headache, difficulty concentrating, memory changes, confusion, weakness and unsteadiness on your feet because you may have low sodium blood levels (hyponatraemia) and/or the so-called “syndrome of inappropriate ADH secretion” (SIADH) that can occur under treatment with EXSIRA. When hyponatraemia is severe or acute in onset, symptoms of cerebral oedema occur (irritability, confusion, seizures and coma). Usually, patients are affected who have reduced quantities of circulating blood or whose bodies contain too little water, such as elderly patients or patients who are being treated with diuretics. Therefore, special care is advised in dealing with these patients
- if you have lung problems including difficulty breathing, cough or chest discomfort

Greater sensitivity to EXSIRA in older patients cannot be ruled out.

Other medicines and EXSIRA

Always tell your health care provider if you are taking any other medicine. (This includes complementary or traditional medicines.) The use of EXSIRA with these medicines may cause undesirable interactions. Please consult your doctor, pharmacist or other health care provider for advice.

Monoamine oxidase inhibitors (MAOIs)

If EXSIRA and certain other anti-depressants belonging to the group of “MAOI” are taken at the same time or immediately after one another, this can give rise to dangerous interactions which can only be controlled with difficulty. If you have been taking an MAOI, including selegiline (for Parkinson’s disease) and linezolid (an antibiotic with MAOI properties), then you should only start taking EXSIRA when there has been an interval of at least 14 days since you stopped taking the MAOI. If you stop taking EXSIRA you should wait at least 7 days before taking an MAOI. Serious reactions may occur, such as tremor, muscle twitching, sweating, nausea, vomiting, flushing (redness in the face), dizziness, elevated body temperature, seizures and death.

Serotonin syndrome

Using EXSIRA with certain medicines may cause a serious and potentially life-threatening reaction called serotonin syndrome (see also the section called ‘Take special care with EXSIRA’). Symptoms may include agitation, hallucinations, coma, fast heartbeat, rapid changes in blood pressure, increased body temperature, overactive reflexes, loss of coordination, nausea, vomiting, diarrhoea. These medicines include: triptans (migraine medicines); other medicines to treat depression such as selective serotonin reuptake inhibitors (SSRIs), selective serotonin/norepinephrine reuptake inhibitors (SSNRIs), monoamine oxidase inhibitors (MAOIs), lithium, St. John’s Wort, tryptophan supplements; and sibutramine (for weight loss), tramadol (a painkiller), pethidine (also a painkiller), linezolid (an antibiotic).

Care needs to be taken when EXSIRA is also used together with the following:

It is especially important if you are using one of the following:

- Alcohol

- Medicines containing ketoconazole (antifungal medicine)
- Tricyclic antidepressants
- Medicines containing codeine
- Sedatives such as midazolam
- Medicines used for schizophrenia such as aripiprazole
- Medicines used for treating breast cancer such as tamoxifen and endoxifen

False-positive drug tests

Due to the urine tests for drug testing being non-specific, a false-positive result for phencyclidine (PCP) and amphetamines may occur when using EXSIRA.

EXSIRA with food and alcohol

You may take your daily dose of EXSIRA with or without food.

You should avoid drinking alcohol while you are using EXSIRA.

Pregnancy and breastfeeding

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before taking this medicine.

You must not use EXSIRA if you are pregnant or breastfeeding.

It has not been proven that EXSIRA is safe to use during pregnancy. If you are pregnant, or are planning to become pregnant, talk to your doctor before receiving EXSIRA.

If you take EXSIRA near the end of your pregnancy there may be an increased risk of heavy 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 EXSIRA so they can advise you.

EXSIRA passes into breast milk in humans. Ask your doctor for advice before breastfeeding your baby.

Driving and using machines

EXSIRA may lower the ability to react quickly and appropriately enough to unexpected or sudden events. Especially at the start of treatment and also if treatment is ended suddenly, you should allow for limitations in your capacity for judgement and reaction. Do not drive a car or other vehicle, do not operate any dangerous electrical tools or machines until you are sure that EXSIRA does not impair your reaction capacity. Especially bear in mind that alcohol and other sedatives can additionally impair your reaction capacity.

It is not always possible to predict to what extent EXSIRA may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which EXSIRA affects them.

3. How to take EXSIRA

Do not share medicines prescribed for you with any other person.

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

EXSIRA should be taken at approximately the same time each day. Tablets must be swallowed whole with fluid and not divided, crushed, chewed, or dissolved.

The recommended dose for EXSIRA is 50 mg once daily, with or without food. Your doctor may increase the dose slowly at an interval of not less than 7 days, up to a maximum daily dose of 100 mg.

Children

Safety and effectiveness in children under 18 years of age has not been established.

Patients with kidney problems

Care should be taken when treating patients with severe renal impairment and end stage renal disease with EXSIRA. You should inform your doctor if you have or have had renal disease. Depending on the condition

of your kidneys, your doctor may reduce the dose to avoid potential side effects. The reduction in kidney function should also be taken into consideration when you are elderly.

Patients with impaired liver function

No dosage adjustment is necessary for patients with liver impairment.

Your doctor will tell you how long your treatment with EXSIRA will last. If you have the impression that the effect of EXSIRA is too strong or too weak, tell your doctor or pharmacist.

If you take more EXSIRA than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

If you forget to take EXSIRA

If you are concerned that you may have missed a dose, talk to your doctor or health care provider. Do not take a double dose to make up for forgotten individual doses.

If you stop taking EXSIRA

If your doctor decides treatment with EXSIRA should be stopped, it will be done by gradually reducing the dose rather than abruptly stopping treatment so that the occurrence of withdrawal symptoms is minimised.

Switching from other antidepressants

If you are already using an antidepressant medicine prescribed by your doctor, you may experience side effects when discontinuing it in order to switch to EXSIRA. Your doctor may gradually reduce the dose of your current antidepressant medication to help to reduce these side effects.

4. Possible side effects

EXSIRA can have side effects.

Not all side effects reported for EXSIRA are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking EXSIRA, please consult your health care provider for advice.

If any of the following happens, stop taking EXSIRA and tell your doctor immediately or go to the casualty department at your nearest hospital:

- allergic reactions (like swelling of the face, mouth, lips, gums, tongue and neck or having trouble breathing)
- angioedema (swelling of the body usually due to an allergic reaction)
- Stevens-Johnson syndrome (an extremely serious allergic skin reaction)
- syncope (fainting), convulsion, dystonia (sustained muscle contractions cause twisting and repetitive movements or abnormal postures)
- increased and/or irregular heartbeat, increased blood pressure
- hypomania (feeling overexcited, euphoric or overly irritable), hallucinations
- thoughts of harming or killing yourself

These are all very serious side effects. If you have them, you may have had a serious reaction to EXSIRA. You may need urgent medical attention or hospitalisation.

Tell your doctor if you notice any of the following:

Frequent side effects:

- decreased appetite
- insomnia (sleeplessness)
- anxiety
- abnormal dreams
- nervousness
- decreased sex drive
- inability to orgasm
- dizziness

- headache
- sleepiness/sedation
- tremor
- paraesthesia (‘pins and needles’)
- taste loss
- disturbance in attention
- blurred vision
- mydriasis (dilation of pupils)
- tinnitus (ringing or buzzing in ears)
- hot flush
- yawning
- nausea
- dry mouth
- constipation
- diarrhoea
- vomiting
- excessive sweating
- rash
- stiffness of the muscles and bones
- erectile dysfunction or failure
- delayed ejaculation (male)
- fatigue
- chills
- lack of energy
- feeling jittery
- irritability
- weight gain
- weight loss

Less frequent side effects:

- low levels of sodium in the blood
- withdrawal syndrome
- abnormal orgasm
- depersonalisation (feeling disconnected or detached from one's body and thoughts)
- orthostatic hypotension (drop in blood pressure when standing up), especially in the elderly
- cold hands and feet
- epistaxis (nosebleeds)
- alopecia (hair loss)
- photosensitivity (sun allergy)
- difficulty starting or maintaining a urine stream
- proteinuria
- abnormal ejaculation (males)
- abnormal sexual function
- increased cholesterol
- abnormal liver function tests
- increased blood prolactin (prolactin is a hormone released by the pituitary gland that stimulates breast development and milk production)

Frequency not known:

- heavy vaginal bleeding shortly after birth (postpartum haemorrhage), see Pregnancy and breastfeeding section for more information

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor or pharmacist or nurse. You can also report side effects to SAHPRA via the **"6.04 Adverse Drug Reaction Reporting Form"**, found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of EXSIRA.

5. How to store EXSIRA

- Store all medicines out of reach of children.
- Store at or below 25 °C.
- Keep well closed.
- Do not remove blister card from the carton until required for use.
- Protect from light and moisture.
- Do not store in the bathroom.
- Do not use after the expiry stated on the label.
- Return all unused medicine to your pharmacist.
- Do not dispose of unused medicine in drains or sewerage systems e.g. toilets.

6. Contents of the pack and other information

WHAT EXSIRA CONTAINS

Each EXSIRA 50 mg extended-release film-coated tablet contains desvenlafaxine succinate equivalent to 50 mg desvenlafaxine.

Each EXSIRA 100 mg extended-release film-coated tablet contains desvenlafaxine succinate equivalent to 100 mg desvenlafaxine.

Excipients:

Hypromellose, microcrystalline cellulose, talc, magnesium stearate, and a film-coating containing:

EXSIRA 50 mg – Polyvinyl alcohol, part hydrolysed; titanium dioxide; macrogol/PEG 3350; talc; yellow iron oxide; red iron oxide

EXSIRA 100 mg – Polyvinyl alcohol, part hydrolysed; titanium dioxide; macrogol/PEG 3350; talc; red iron oxide; FD&C Yellow #6/Sunset Yellow FCF Aluminium Lake

What EXSIRA looks like and contents of the pack

EXSIRA 50 mg extended-release tablets are light pink, square (pyramid, one sided), film-coated tablets, debossed “W” over “50” on the flat side.

EXSIRA 100 mg extended-release tablets are reddish-orange, square (pyramid, one sided), film-coated tablets, debossed “W” over “100” on the flat side.

EXSIRA is available as follows:

A carton containing one or more clear plastic/aluminium foil blister strips containing 7, 14 or 28 tablets

Holder of Certificate of Registration

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