APPROVED PATIENT INFORMATION LEAFLET:

SCHEDULING STATUS:

S5

CETVIO, 37,5 mg/325 mg, film-coated tablets

Tramadol hydrochloride/paracetamol

Sugar free

Read all of this leaflet carefully before you start taking CETVIO:

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.
- CETVIO 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 CETVIO IS AND WHAT IT IS USED FOR

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE CETVIO

3. HOW TO TAKE CETVIO

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6. CONTENTS OF THE PACK AND OTHER INFORMATION

1. WHAT CETVIO IS AND WHAT IT IS USED FOR:

CETVIO contains tramadol and paracetamol.

Tramadol is a painkiller belonging to the class of the opioids that acts on the central nervous system.

It is used for the management of moderate to moderately severe pain.

Paracetamol, the other active substance, has centrally acting analgesic effects.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE CETVIO:

Do not take CETVIO:

- If you are allergic to tramadol, paracetamol, any of the other ingredients mentioned in **section 6.1**, or other opioids such as codeine.
- If you are suffering from acute alcohol poisoning.
- If you are taking sleeping pills, pain relievers or medicines that affect mood and emotions.
- If you are also taking medicines such as tranylcypromine and moclobemide or have taken them in the last 14 days before treatment with CETVIO which are used to treat depression. These medicines are used to treat depression and belong to a group called monoamine oxidase inhibitors (MAOIs).
- If you have a severe liver disorder.
- CETVIO must not be used for narcotic (an addictive substance) withdrawal treatment.
- You should not take CETVIO if you suffer from severe breathing problems.
- You should not take CETVIO if you are suffering from increased intracranial pressure or central nervous system depression, which are characterised by decreased rate of breathing, decreased heart rate, and loss of consciousness.
- You should not take CETVIO if you have fits that are not controlled.

Warnings and precautions:

Take special care with CETVIO:

- If you take other medicines containing paracetamol or tramadol.
- If you have liver problems or disease as your eyes and skin may turn yellow, which may suggest jaundice.
- If you have kidney problems.
- If you have recently suffered from a head injury, shock or severe headaches associated with vomiting (being sick).
- If you are dependent on any medicine (for example morphine).
- If you are taking flucloxacillin antibiotics, as this may cause a serious blood and fluid abnormality
- If you have epilepsy or have experienced fits or seizures.

- Tramadol exerts its effect by converting (metabolising) into its active component. If you convert (metabolise) tramadol to this active component more rapidly and completely than other patients, you are known as an ultra-rapid metaboliser. This means you are more likely to have serious side effects, such as circulatory depression and breathing difficulties, with slow or shallow breathing. If you experience these types of side effects, stop taking CETVIO and consult with your doctor immediately.
- If you abruptly stop treatment with CETVIO you may suffer from panic attacks, severe anxiety (feeling nervous or worried), hallucinations (hearing or seeing things that are not there), paraesthesia (burning or prickling sensation that is usually felt in the hands, arms, legs, or feet) and tinnitus (ringing or buzzing in the ears). Your doctor will gradually decrease your dose of CETVIO to prevent these side effects from occurring.
- CETVIO contains paracetamol. If you are allergic to paracetamol, you may break out in a severe skin rash after you take CETVIO. You should stop using CETVIO at the first appearance of a skin rash or any other sign of allergy.
- CETVIO should not be taken with alcohol containing beverages.
- While taking CETVIO you may experience low levels of sodium in your blood (hyponatraemia). Symptoms may include nausea and vomiting, headaches, feeling confused, feeling very tired, feeling restless, feeling irritable, muscle weakness, spasms or cramps and seizures. Elderly patients and patients taking other medicines that lower sodium in the blood are most at risk for this side effect. If you experience any of these symptoms while taking CETVIO, consult your doctor immediately.
- If you suffer from sleep-related breathing disorders, take special care when taking CETVIO.
- Talk to your doctor if you develop a craving for CETVIO.

Other medicines and CETVIO:

Always tell your healthcare provider if you are taking any other medicine. (This includes all complementary or traditional medicines).

CETVIO should not be administered with the following:

- A group of antidepressants called monoamine oxidase (MAO) inhibitors (such as moclobemide and tranylcypromine). When taken together with CETVIO it can cause diarrhoea, tachycardia (irregular heartbeat), hyperhidrosis (excessive sweating), trembling, confusional state, even coma.
- Carbamazepine (used to treat seizures). When taken together with CETVIO it can cause reduced efficacy and shorter duration due to decreased concentration of tramadol.
- Buprenorphine, nalbuphine or pentazocine (opioid-type pain relievers). The effects of these medicines may be decreased.

Caution is advised when the following medicines are given with CETVIO:

- Tramadol can induce convulsions and increase the potential for certain antidepressants such as citalopram, escitalopram, paroxetine, duloxetine, venlafaxine and amitriptyline, antipsychotics and seizure threshold- lowering medicinal products (such as bupropion, mirtazapine, tetrahydrocannabinol) to cause convulsions.
- Concomitant therapeutic use of tramadol and citalopram, escitalopram, paroxetine, duloxetine, venlafaxine, amitriptyline, moclobemide, tranylcypromine and mirtazapine may cause serotonin toxicity. Symptoms include involuntary, rhythmic contractions of muscles, including the muscles that control movement of the eye, agitation, excessive sweating, tremor, exaggeration of reflexes, increased muscle tension, body temperature above 38 °C.
- If you are taking other pain relievers such as morphine and codeine (also as cough medicine), baclofen (a muscle relaxant), medicines used to lower blood pressure, or medicines to treat allergies as well as sedative medicines such as benzodiazepines (alprazolam, diazepam, lorazepam) or related medicines with CETVIO as there is an increased risk of drowsiness, difficulties in breathing (respiratory depression), coma which may be life-threatening.
- If you are taking warfarin (for blood thinning). The effectiveness of this medicine may be altered, and bleeding may occur.
- If you are taking digoxin used to treat heart problems.
- If you are taking diflunisal used for pain.

- If you are taking ondansetron used to treat vomiting.
- If you are taking flucloxacillin (antibiotic)

CETVIO with food and drink:

Do not drink alcohol during treatment with CETVIO as the effects of CETVIO and alcohol may intensify each other.

Pregnancy, breastfeeding and fertility:

CETVIO must not be taken during pregnancy.

CETVIO must not be taken during breastfeeding since there is no information available regarding safety during 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 healthcare professional for advice before taking this medicine.

Driving and using machines:

Do not drive while taking this medicine until you know how it affects you.

CETVIO can affect your ability to drive as it may make you sleepy or dizzy.

If you feel drowsy while taking CETVIO, do not drive, use tools or use machinery.

CETVIO contains sodium:

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say it is essentially ‘sodium-free’.

3. HOW TO TAKE CETVIO:

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

Always take CETVIO exactly as your doctor or pharmacist has instructed you. You should check with your doctor or pharmacist if you are unsure. Your doctor will tell you how long your treatment with

CETVIO will last. If you have the impression that the effect of CETVIO is too strong or too weak, talk to your doctor or pharmacist.

- Swallow the tablets whole with sufficient liquid.
- Do not break or chew the tablets.

Adults:

The recommended dosage is 1 or 2 tablets every 4 to 6 hours, unless otherwise prescribed by your doctor. If required, further doses may be taken, as instructed by your doctor.

Do not take more than 8 tablets per day.

If you take more CETVIO than you should:

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

Immediate medical advice should be sought in the event of an overdose even if you feel well, because of the risk of delayed, serious liver damage from too much paracetamol. Your kidneys can also become damaged in the absence of liver damage.

If you forget to take CETVIO:

If you forgot to take a dose, take it as soon as you remember unless it is nearly time for your next dose. Do not take a double dose to make up for forgotten individual doses.

If you stop taking CETVIO:

Withdrawal symptoms may occur if CETVIO is discontinued abruptly. You may experience anxiety, nervous excitement, difficulty sleeping, excessive abnormal movements, tremor and gastrointestinal symptoms.

Other symptoms that have very rarely been seen if tramadol hydrochloride is discontinued abruptly include panic attacks, severe anxiety, hallucinations, tingling or prickling sensation and ringing in the ears.

4. POSSIBLE SIDE EFFECTS:

CETVIO can have side effects.

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

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

- severe skin reactions, rash or itching all over the body
- allergic reactions along with breathing problems or closing of the throat
- increased bleeding time.

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

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

The following side effects occur frequently:

- irregular heartbeat that is much rapid and more pronounced than usual
- elevated liver enzymes, resulting in abdominal pain, dark urine, pale stools, weakness, fatigue.

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

Frequent side effects:

- confusional state, sleep disorders, mood changes (anxiety, nervousness, feeling of high spirits)
- dizziness, excessive sleepiness
- headache, trembling

- nausea, vomiting, constipation, dry mouth, diarrhoea, stomach pain, indigestion, stomach gas

Less frequent side effects:

- depression, seeing, hearing, smelling, tasting or imagining things, nightmares
- involuntary muscular contractions, tingling or prickling sensation, loss of memory
- ringing in the ear
- rapid, strong, or irregular heartbeat, very fast heartbeat, dysrhythmia
- difficulty swallowing, blood in faeces
- chills
- chest pain
- problems with urination
- difficulty breathing
- increase in blood pressure, hot flushes
- low blood sugar
- drug dependence
- mental confusion and emotional disruption
- convulsions, fainting, speech disorders
- slurred speech, stumbling, convulsions, syncope, speech disorders
- vision blurred, constriction of the pupil (miosis)
- excessive dilation of the pupils (mydriasis).

In addition, the following side effects have been reported by people using medicines that contain only tramadol or only paracetamol:

- feeling faint when getting up from a lying or sitting position, slow heart rate, fainting
- changes in appetite
- muscle weakness, slower or weaker breathing
- mood changes, changes in activity, changes in perception
- worsening of existing asthma

- inflammation of the pancreas, causing severe abdominal pain.

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, 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 CETVIO.

5. HOW TO STORE CETVIO:

Store all medicine out of reach of children.

Store at or below 25 °C.

Store tablets in the original package until required for use to protect from light.

Keep the container tightly closed in order to protect from moisture.

Do not use the tablets after the expiry date shown on the container.

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 CETVIO contains:

The active ingredients are tramadol hydrochloride and paracetamol.

The other ingredients are:

Tablet core: hydroxypropyl cellulose, macrogol poly (vinyl alcohol) grafted copolymer, magnesium stearate, microcrystalline cellulose 101 & 102, sodium starch glycolate, Type A, starch, pregelatinized.

Tablet coating: Opadry II Beige 85F97409 consisting of iron oxide yellow, iron oxide red, iron oxide black, macrogol/PEG 3350, polvinyl alcohol – part. hydrolysed, talc and titanium dioxide.

What CETVIO looks like and contents of the pack:

Peach, capsule-shaped, film-coated, tablet, engraved ‘A325’ on one side and ‘T37.5’ on the other side.

CETVIO is packaged as follows:

PVC/Aluminium blister packs:

PVC film clear

Foil aluminium-silver plain

The blister pack is packed into a carton box.

Pack sizes: 30 and 60

Bottles:

White, round HDPE bottles with polypropylene cap LNP HS LP-E/PV

Pack sizes: 60 and 100

Not all pack sizes may be marketed.

Holder of Certificate of Registration:

Teva Pharmaceuticals (Pty) Ltd,

Maxwell Office Park,

Magwa Crescent West,

Waterfall City, Midrand, Gauteng, South Africa

2090

Tel: +27 11 055 0200

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