PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S5

CETROMAL, film-coated tablets

Tramadol hydrochloride, paracetamol

Sugar free.

Read all of this leaflet carefully before you start taking CETROMAL.

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

1. What CETROMAL is and what it is used for

Tramadol and paracetamol are the active substances in CETROMAL. They are painkillers that act on the brain and spinal cord to control pain. CETROMAL is used for the management of moderate to moderately severe pain in adults.

2. What you need to know before you take CETROMAL

Do not take CETROMAL

- If you are hypersensitive (allergic) to tramadol, paracetamol, other opioids such as codeine, or any of the other ingredients of CETROMAL (listed in section 6).
- If you have drunk enough alcohol to make you feel woozy or drunk.
- If you have taken more than the prescribed dose of your sleeping tablets, other painkillers or psychotropic medicines (medicines that affect your mood and emotions), which can slow down your breathing and reactions.
- If you have a moderate to severe liver disease.
- If you are taking monoamine oxidase (MAO) inhibitors (medicine used to treat depression) or have taken them in the last 14 days before treatment with CETROMAL (see **Other medicines and CETROMAL**).
- You should not receive CETROMAL for the treatment of withdrawal symptoms caused by narcotics/drugs.
- If you have problems to breathe, if you have a bluish discolouration of your skin (due to decreased oxygen) or have excessive mucus.
- If you have growing pressure inside your skull (headache, blurred vision, weakness) or central nervous system depression due to a head injury, a disorder that affect blood supply to your brain.
- If you suffer from epilepsy (fits) or seizures of any cause.
- If you or your child is younger than 12 years of age.
- If you or your child is younger than 18 years of age and you or your child have had an operation to remove your tonsils or adenoids.

Warnings and precautions

Take special care with CETROMAL:

- If you are taking medicines which may cause seizures/fits such as neuroleptics/antipsychotics (used to treat depression or a psychotic disorder). The risk of having a seizure/fit may increase

if you use CETROMAL at the same time (see **Other medicines and CETROMAL**).

- If you develop any skin adverse reaction, such as toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS), acute generalised exanthematous pustulosis (AGEP), drug rash with eosinophilia and systemic symptoms (DRESS), or drug-induced hypersensitivity syndrome (DIHS) and fixed drug eruptions (FDE), treatment with CETROMAL must immediately be discontinued. These reactions can be life-threatening and are characterised by redness, inflamed or swollen skin, blisters, hives, itching and sometimes peeling or pain. Should you experience any of these symptoms, contact your health care provider immediately.
- If you are taking sedating medicines, also known as central nervous system (CNS) depressants, such as benzodiazepines (used to treat anxiety, panic attacks and insomnia or trouble sleeping) (see **Other medicines and CETROMAL**).
- If you have any biliary tract disorder (disorder involving your gallbladder and/or liver with symptoms such as abdominal pain, yellowing of your skin and eyes, nausea, vomiting and fatigue).
- If you are not as awake/alert, or able to understand or react as you normally would, and the cause is uncertain.
- If you are in a state of shock (cold sweat may be a sign).
- If you have any thoughts of harming or killing yourself.
- If you have any liver or kidney problems.
- If you have been using CETROMAL for a long time and have increased pain, contact your doctor.
- If you suffer from a lung disease.
- If you suffer from emotional disturbance or depression.
- Do not take more than your recommended dose.
- Do not take CETROMAL with any other medicines that contain tramadol or paracetamol.

Sleep-related breathing disorders

CETROMAL contains the active substance, tramadol, that belongs to the group of opioids. Opioids

can cause sleep-related breathing disorders, for example central sleep apnoea (shallow/pause in breathing during sleep) and sleep-related hypoxaemia (low levels of oxygen in the blood). The symptoms can include breathing pauses during sleep, night awakening due to shortness of breath, difficulties to maintain sleep or excessive drowsiness during the day. If you or another person observes these symptoms, contact your doctor. The risk of experiencing central sleep apnoea is dependent on the dose of opioids. Your doctor may consider decreasing your dosage if you experience central sleep apnoea.

Serotonin syndrome

You may experience serotonin syndrome (a serious condition where your body has too much of a chemical called serotonin) after taking CETROMAL in combination with certain antidepressants or CETROMAL alone. Consult your doctor immediately if you have any of the symptoms related to this condition (see section **4. Possible side effects**).

Dependence/addiction and tolerance

CETROMAL may lead to dependence/addiction, especially with long-term use. If you have a history of addiction, especially to medicines of the same class as tramadol (opioids) such as codeine, additional support and monitoring may be necessary.

If you find that treatment with CETROMAL is less effective after long-term use, it could be a sign that you have developed tolerance. If this happens, speak to your doctor about your treatment.

Withdrawal symptoms

You may experience withdrawal symptoms if treatment with CETROMAL is suddenly stopped. Withdrawal symptoms can include agitation, anxiety, difficulty sleeping, restlessness, tremor (uncontrolled shaking) and gastrointestinal (stomach) symptoms.

Your doctor will discuss with you how to gradually reduce your dose of CETROMAL before

stopping.

History of mental health disorders

CETROMAL should be used with particular care if you or any member in your family had mental health problems in the past, characterised by a persistently low or depressed mood (major depression), feeling of fear or worry (anxiety), or the misuse of alcohol and drugs. There is an increased risk of addiction if you or your family have a history of substance abuse or mental health problems.

CETROMAL metabolism

Tramadol, as in CETROMAL, is metabolised in your liver by an enzyme. Some people have a variation of this enzyme, and this can affect people in different ways. In some people, they may not get enough pain relief but other people, known as ultra-rapid metabolisers, are more likely to get serious side effects (such as breathing difficulties, with slow or shallow breathing, confusion, sleepiness, feeling or being sick, constipation and lack of appetite). If you experience any of these side effects, stop taking CETROMAL and consult your doctor immediately.

Low cortisol levels

Discuss it with your doctor if you experience any of the following symptoms while taking CETROMAL: Extreme fatigue, decreased appetite, weight loss, severe stomach pain, feeling or being sick or low blood pressure. This may indicate that you have adrenal insufficiency (a disorder in which your adrenal glands don’t produce enough hormones, mainly cortisol). If you have these symptoms, your doctor will decide if you need to take a hormone supplement.

Low sodium levels

You may experience low levels of sodium in your blood (hyponatraemia) while taking CETROMAL. Symptoms of low blood sodium 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 may lower sodium in the blood are most at risk. If you get any of these symptoms while taking CETROMAL, consult your doctor immediately.

Minor pain

You should not take CETROMAL for minor pain that may be adequately treated with other painkillers.

Children and adolescents

- CETROMAL should not be given to children below 12 years of age.
- CETROMAL should not be given for pain to children below 18 years of age with airflow blockage during sleep (obstructive sleep apnoea) after an operation to remove their tonsils or adenoids.
- CETROMAL is not recommended for use in children with breathing problems, including neuromuscular disorders (conditions that impair the functioning of the muscles, either directly or indirectly, through the nervous system), severe heart or lung conditions, lung infections, several serious injuries or major surgery.

Other medicines and CETROMAL

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

Tell your doctor or pharmacist if you are currently taking:

- Monoamine oxidase inhibitors (used to treat depression) or have taken them in the last 14 days before treatment with CETROMAL (see **Do not take CETROMAL**).
- Sedatives or tranquillisers, also known as central nervous system (CNS) depressants, such as barbiturates and benzodiazepines (used to treat anxiety, panic attacks, insomnia or trouble sleeping).
- Serotonergic medicines (medicines that may increase serotonin levels in your body) such as

selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs) and tricyclic antidepressants (used to treat depression).

- Lithium (used to stabilise your mood).
- Medicines which may cause seizures/fits such as certain antidepressants or antipsychotics (used to treat depression or a psychotic disorder). The risk of having a seizure/fit may increase if you use CETROMAL at the same time (see **Warnings and precautions**).
- Anticoagulants such as warfarin (used to thin your blood). Regular evaluation of your prothrombin time/INR should be performed if you are taking warfarin with CETROMAL.
- Medicines which may reduce certain enzymes known as CYP2D6 and CYP3A4 in your body, such as amitriptyline, fluoxetine and paroxetine (used to treat depression), quinidine (used to stabilise your heart rhythm), ketoconazole (used to treat a fungal infection) and erythromycin (used to treat a bacterial infection).
- Medicines which may increase the CYP3A4 enzyme in your body, such as rifampicin (used to prevent and treat tuberculosis) and phenytoin (used to treat and prevent seizures/fits).
- Carbamazepine (used to treat seizures/fits).
- Ondansetron (used to prevent nausea and vomiting).
- Cimetidine (used to treat stomach ulcers or heartburn).
- Diflunisal (used to relieve mild to moderate pain from various conditions. It also reduces pain, swelling, and joint stiffness caused by arthritis).
- Metoclopramide (used to treat nausea and vomiting).
- Colestyramine (used to lower high cholesterol levels in the blood).

CETROMAL with alcohol

Do not drink alcohol during treatment with CETROMAL as it may have additive sedative effects.

Pregnancy, breastfeeding and fertility

Safe use in pregnancy and breastfeeding has not been established.

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 CETROMAL.

Do not take CETROMAL if you are pregnant or breastfeeding your baby.

Driving and using machines

CETROMAL may cause drowsiness and dizziness and affect your ability to drive a vehicle or use machinery. This is particularly in conjunction with other medicines that may affect your mental state, behaviour or mood, including alcohol.

It is not always possible to predict to what extent CETROMAL may interfere with your daily activities. Do not engage in the above activities until you are aware of the measure to which CETROMAL affects you.

3. How to take CETROMAL

Do not share medicines prescribed for you with any other person.
Always take CETROMAL exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

For use in adults and children over the age of 16 years.

DO NOT TAKE MORE THAN THE RECOMMENDED DOSE.

Tablets are to be taken whole, not broken or chewed, with a sufficient quantity of liquid, with or without meals.

Unless otherwise prescribed by your doctor, the usual dose is:

Adults and children over 16 years:

For the management of pain, the recommended dose is 1 or 2 tablets every 4 to 6 hours as needed for pain relief, up to a maximum of 8 tablets per day.

The lowest pain-relieving dose should be taken for the shortest period of time.

If you have any liver or kidney problems or are over 65 years of age, your doctor may adjust your dosage.

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

If you take more CETROMAL than you should

Possible signs and symptoms of overdosage may include narrowing of the pupil of your eye, nausea (feeling sick), vomiting (being sick), fast heartbeat, loss of sufficient blood flow to maintain consciousness due to sudden dysfunction of the heart, heart stops beating, unconsciousness, coma, convulsions (fits), breathing difficulty (slow and ineffective breathing) and stopped breathing, stomach pain, irritation and discomfort in the stomach and gut, unusually pale skin, weight loss and abnormal heavy sweating.

Cases of abnormal electrical conduction in the heart (QT prolongation) as well as serotonin syndrome have also been reported (see section **4. Possible side effects**).

Even if you feel well after having taken more CETROMAL than you should have, you should still seek medical assistance as there is a risk of delayed, serious liver damage.

Immediate treatment is essential. 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 CETROMAL

Do not take a double dose to make up for forgotten individual doses. If you have missed your dose by only a few hours, take the missed dose as soon as you remember. If it is almost time for your next dose, skip the missed dose and take your CETROMAL tablets at the next regularly scheduled time.

If you stop taking CETROMAL

Treatment with CETROMAL should not be stopped abruptly, as you may experience withdrawal symptoms. If you no longer require treatment or wish to stop treatment due to adverse effects, please tell your doctor. Your doctor will gradually reduce your dose of CETROMAL before you finally stop taking CETROMAL.

If you suddenly stop taking CETROMAL, you may experience withdrawal symptoms such as agitation, anxiety, hallucinations, tingling or prickling (“pins-and-needles”) sensation, ringing in your ears, restlessness, difficulty sleeping (insomnia), uncontrolled shaking (tremors), increased heart/breathing rate, nausea, vomiting, diarrhoea and stomach cramps.

If you experience any of these symptoms, or any other side effects while stopping treatment with CETROMAL, please contact your doctor.

4. Possible side effects

CETROMAL can have side effects.

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

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

- Swelling of your hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing, wheezing.
- A rash or itching.
- Fainting.

These are all very serious side effects. If you have them, you may have had a serious reaction to CETROMAL. 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:

- Serotonin syndrome (agitation, hallucinations, fever, increased heart rate, increased blood pressure, involuntary muscle twitching, muscular rigidity, lack of coordination and/or gastrointestinal symptoms, such as nausea, vomiting and diarrhoea).
- Convulsions/fits.
- Changes in the way your heart beats, such as pounding of your heart, beating faster or slower than normal, irregular heartbeat, skipping a beat, chest pain, lack of blood flow through your body (due to cardiac or circulatory collapse) or to your heart muscle.
- Passing less urine than is normal for you or with difficulty/pain, difficulty in emptying your bladder completely (urinary retention), excess protein in your urine (frequent urination, foamy/bubbly urine), kidney damage (swelling of your hands, feet and face, nausea, weakness), ureteral or biliary spasms (burning or cramping pain in your stomach).
- Slow/ineffective breathing, shortness of breath, excess fluid in your lungs (difficulty breathing, cough), worsening of asthma.
- Yellowing of your skin and eyes, dark urine, fever and tiredness, which may be symptoms of liver problems such as increased liver enzymes.
- Skin reactions such as toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS), acute generalised exanthematous pustulosis (AGEP), drug rash with eosinophilia and systemic symptoms (DRESS) or drug-induced hypersensitivity syndrome (DIHS) and fixed drug eruptions (FDE). These reactions can be life-threatening and are characterised by

redness, inflamed or swollen skin, blisters, hives, itching and sometimes peeling or pain (see **Take special care with CETROMAL**).

- Medicine abuse/dependence, withdrawal reactions (see **If you stop taking CETROMAL**).
- Low blood levels of sodium (tiredness, confusion, muscle twitching, nausea, headache) and/or syndrome of inappropriate antidiuretic hormone secretion (cramping, nausea, vomiting, and in severe cases seizures and coma).
- Stomach pain including inflammation of your pancreas (pain of the upper stomach area that radiates to your back, tenderness, nausea, vomiting, fever).
- Dark black, tarry stool with or without visible blood (may be associated with bleeding in your digestive tract).
- A unique allergic skin reaction that often occurs in the same location after re-exposure to a medicine (known as fixed drug eruption).
- Thoughts of harming or killing yourself.
- Growing pressure inside your skull (headache, blurred vision, weakness).
- Anaemia (a condition in which your body does not have enough healthy red blood cells, with symptoms such as extreme tiredness, pale skin, shortness of breath, dizziness).

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:

- Drowsiness, dizziness, headache, uncontrolled shaking (tremors).
- Nausea (feeling sick), vomiting (begin sick), dry mouth, heartburn, constipation, diarrhoea, stomach pain, excess gas (flatulence).
- Increased sweating.
- Skin itching/rash.
- Fatigue (extreme tiredness / lack of energy), physical weakness.
- Changes in your mood (mostly feeling happy, occasionally irritated/unhappy).
- Feeling confused, sleep disorders (difficulty falling/staying asleep), feeling anxious, nervousness.

- Anorexia (severe weight loss).

Less frequent side effects:

- Difficulty swallowing, swelling of your tongue.
- Changes in your appetite.
- Decline in mental ability (memory/thinking), difficulty concentrating.
- Hallucinations (seeing or hearing things that are not real), nightmares, abnormal thinking.
- Feeling depressed.
- Feeling disconnected or detached from your body and thoughts.
- Erectile dysfunction (impotence).
- Impaired balance or coordination, increased muscle tone making it hard to flex and move around normally, involuntary muscle contractions, speech disorders.
- Migraines (headache of varying intensity, often accompanied by nausea and sensitivity to light and sound).
- Memory loss.
- Tingling or prickling (“pins-and-needles”) sensation.
- Decreased responsiveness.
- Narrowing or excessive widening of your pupils, blurred vision.
- Spinning sensation, ringing in your ears.
- Increased blood pressure (dizziness, headache).
- Postural hypotension (a form of low blood pressure that happens when standing up from sitting or lying down, which may cause dizziness or light-headedness).
- Hot flushes.
- Raised, itchy rash (urticaria).
- Muscle weakness.
- Cold chills (shivering or shaking), low body temperature.
- Increased creatinine and prothrombin levels in the blood when tests are done.
- Changes in your white/red blood cells or platelet count when tests are done.

- Low level of prothrombin in your blood, causing an increased risk of bleeding.

Frequency unknown side effects:

- Low blood sugar levels (light-headedness, tiredness, weakness).
- Restlessness, decreased/increased activity, changes in mental and sensory perception (errors in judgement, changes in senses and recognition), reduced awareness of surroundings.
- Feeling uneasy, unhappy or unwell.
- Widening of your blood vessels, leading to increased blood flow with flushing or warmth.
- Itchy skin rash caused by contact with CETROMAL.
- Muscle stiffness, movement disorders.
- Decreased interest in sexual activity.
- Hiccups.
- Changes in the effects of blood thinners (such as warfarin) including an increase in prothrombin time, causing an increased risk of bleeding.

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 doctor or pharmacist. You can also report side effects to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website. By reporting side effects, you can help provide more information on the safety of CETROMAL.

5. How to store CETROMAL

- Store all medicines out of reach of children.
- Store at or below 25 °C.
- Store in a dry place.
- Keep the blister strips in the outer carton until required for use.

- 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 CETROMAL contains

- The active substances are tramadol hydrochloride and paracetamol.

  Each film-coated tablet contains 37,5 mg tramadol (as tramadol hydrochloride) and 325 mg paracetamol.
- The other ingredients are magnesium stearate, maize starch, microcrystalline cellulose, pregelatinised starch, sodium starch glycolate and Opadry White 03F58991 (containing hypromellose, macrogol, talc and titanium dioxide).

What CETROMAL looks like and contents of the pack

White coloured, capsule shaped, bevel edged, biconvex film-coated tablets debossed with “334” on one side and plain on the other side.

White opaque PVDC/PVC/silver aluminium blister strips, containing 10 tablets each. Each outer carton contains 3 or 6 blister strips.

Pack sizes: 30 or 60 tablets.

Not all pack sizes may be marketed.

Holder of Certificate of Registration

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