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PARTRACET P1530354

PARTRACET P1530354

Professional Information for Medicines for Human Use

SCHEDULING STATUS

S5

1. NAME OF THE MEDICINE
PARTRACET (film-coated tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
PARTRACET:

Each film-coated tablet contains 37,5 mg tramadol hydrochloride and 325 mg paracetamol.
Sugar free.

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM
PARTRACET:

Light yellow, oblong shaped, biconvex film-coated tablets debossed with 'I 03' on one side and plain on the other side.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications
PARTRACET is indicated for the management of moderate to moderately severe pain in adults.
PARTRACET is not recommended for minor pain that may be treated adequately through lesser means.

4.2. Posology and method of administration
Posology

To be used in adults and children over 16 years of age.
DO NOT EXCEED THE RECOMMENDED DOSE.

Adults:

For the management of pain, the recommended dose of **PARTRACET** is 1 or 2 tablets every 4 to 6 hours as needed for pain relief up to a maximum of 8 tablets per day.
As with all analgesic medicines, a titration period of several days with gradual dose increases at the initiation of **PARTRACET** therapy may be beneficial for some patients.
Clinical studies with tramadol in patients with moderate to moderately severe chronic pain indicated that the tolerability of tramadol can be improved by starting at a lower dose with gradual upward titration to reach doses that provide sufficient pain relief.

Special populations
Renal impairment:

For patients with creatinine clearance < 30 mL/min, the dosing interval of **PARTRACET** should be increased not to exceed 2 tablets every 12 hours.

Method of administration

For oral use.
Tablets must be swallowed whole, with a sufficient quantity of liquid. They must not be broken or chewed.

4.3. Contraindications

- **PARTRACET** is contraindicated in patients with a known hypersensitivity to tramadol, paracetamol, or any of the other ingredients mentioned in section 6.1 or other opioids such as codeine.
- **PARTRACET** is also contraindicated in cases of severe liver function impairment and in acute intoxication with alcohol, hypnotics, centrally acting analgesics, opioids or psychotropic medicines.
- **PARTRACET** should not be administered to patients who are receiving Monoamine Oxidase (MAO)-inibitors or within two weeks of their withdrawal.
- **PARTRACET** must not be used for narcotic withdrawal treatment.
- **PARTRACET** should not be given to patients with respiratory depression especially in the presence of cyanosis and excessive bronchial secretions.
- **PARTRACET** should not be given to patients with increased intracranial pressure or central nervous system depression due to head injury or cerebral disease.
- **PARTRACET** is contraindicated in epilepsy not controlled by treatment.

4.4. Special warnings and precautions for use
The maximum dose of 8 tablets of PARTRACET should not be exceeded. In order to avoid inadvertent overdose, patients should be advised not to exceed the recommended dose and not to use any other paracetamol (including over the counter) or tramadol hydrochloride containing products concurrently without the advice of a medical practitioner. (see section 4.9).

In the event of overdosage or suspected overdose and notwithstanding the fact that the person may be asymptomatic, the nearest doctor, hospital or Poison Centre must be contacted immediately.

Dosages in excess of those recommended may cause severe liver damage. Patients suffering from liver or kidney disease should take paracetamol containing products under medical supervision.

Tramadol may only be taken with special care in opioid dependence, reduced level of consciousness of uncertain origin, disorders of the respiratory function and increased intracranial pressure.

Seizures:

Seizures have been reported in patients receiving tramadol at dosages within the recommended dosage range. The risk of seizures is enhanced in patients exceeding the recommended dose, or in patients taking tricyclic anti-depressants or other tricyclic compounds e.g. promethazine, selective serotonin re-uptake inhibitors, MAO-inhibitors and neuroleptics. The risk of seizures may also be increased in patients with epilepsy, with a history of seizures or in patients with a recognised risk for seizures e.g. drug and alcohol withdrawal, intracranial infections, head trauma, metabolic disorders and naloxone administration with tramadol overdose. Patients known to suffer from cerebral convulsions should be carefully monitored during treatment with tramadol.

CYP2D6 ultra-rapid metabolism of tramadol:

Patients who are CYP2D6 ultra-rapid metabolisers may convert tramadol to its active metabolite (M1) more rapidly and completely than other patients. This rapid conversion may lead to higher than expected serum M1 levels which could lead to an increased risk of respiratory depression. Alternative medicine, dose reduction and/or increased monitoring for signs of tramadol overdose, such as respiratory depression is recommended in patients known to be CYP2D6 ultra-rapid metabolisers.

Drug Abuse and Dependence:

Tramadol has a dependence potential and tolerance, psychic and physical dependence of the morphine-type(μ opioid) may develop with long-term use. The medicine has been associated with craving, drug-seeking behaviour and tolerance development. Cases of abuse and dependence on tramadol have been reported. Tramadol should not be used in opioid-dependent patients. Tramadol can reinstate physical dependence in patients that have been previously dependent or chronically using other opioids. In patients with a tendency to drug abuse, a history of drug dependence or who are chronically using opioids, treatment with tramadol is not recommended.

Withdrawal:

Withdrawal symptoms may occur if **PARTRACET** is discontinued abruptly. Panic attacks, severe anxiety, hallucinations, paraesthesia, tinnitus, and unusual CNS symptoms have also been reported with abrupt discontinuation of tramadol hydrochloride. Clinical experience suggests that withdrawal symptoms may be relieved by tapering the medicine.

Serious skin reactions:

Serious skin reactions such as acute generalised exanthematous pustulosis (AGEP), Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN), have been reported in patients receiving paracetamol. Patients should be informed about the signs of serious skin reactions, and use of **PARTRACET** should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.

Precautions – general:

Do not co-administer **PARTRACET** with other tramadol or paracetamol containing products.

Use with alcohol:
PARTRACET should not be taken with alcohol containing beverages.

Use with CNS depressants:

The administration of **PARTRACET** concurrently with central nervous system (CNS) depressants such as alcohol, opioids, anaesthetic medicines, phenothiazines, tranquilisers or sedative hypnotics is likely to intensify and prolong CNS effects.

Use in renal disease:
PARTRACET should be used with caution in patients with impaired renal function and in patients prone to convulsive disorders or in shock.

Hyponatraemia:

Hyponatraemia has been reported with the use of **PARTRACET** usually in patients with predisposing risk factors, such as elderly patients and/or patients using concomitant medicines that may cause hyponatraemia. This hyponatraemia appeared to be the result of the syndrome of inappropriate antidiuretic hormone secretion (SIADH) and resolved with discontinuation of **PARTRACET** and appropriate treatment (e.g. fluid restriction). During **PARTRACET** treatment, monitoring for signs and symptoms of hyponatraemia is recommended for patients with predisposing risk factors.

Sleep-related breathing disorders

Opioids can cause sleep-related breathing disorders including central sleep apnoea (CSA) and sleep-related hypoxemia. Opioid use increases the risk of CSA in a dose-dependent fashion. In patients who present with CSA, consider decreasing the total opioid dosage.

4.5 Interaction with other medicines and other forms of interaction
Concomitant use is contraindicated with:

MAO-inhibitors

- Risk of serotonergic syndrome: diarrhoea, tachycardia, hyperhidrosis, trembling, confusional state, even coma.

In case of recent treatment with MAO-inhibitors, a delay of two weeks should occur before treatment with tramadol.

Concomitant use is not recommended with:

Alcohol

- Alcohol increases the sedative effect of opioid analgesics. The effect on alertness can make driving of vehicles and the use of machines dangerous. Avoid intake of alcoholic drinks and of medicinal products containing alcohol.

Carbamazepine and other enzyme inducers

- Risk of reduced efficacy and shorter duration due to decreased plasma concentrations of tramadol.

Opioid agonists-antagonists (buprenorphine, nalbuphine, pentazocine)

- Decrease of the analgesic effect by competitive blocking effect at the receptors, with the risk of occurrence of withdrawal syndrome.

Concomitant use which needs to be taken into consideration:

- Tramadol can induce convulsions and increase the potential for selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants, antipsychotics and seizure threshold-lowering medicinal products (such as bupropion, mirtazapine, tetrahydrocannabinol) to cause convulsions.
- Concomitant therapeutic use of tramadol and serotonergic medicines such as SSRIs, SNRIs , MAO-inhibitors (see section 4.2), tricyclic antidepressants and mirtazapine may cause serotonin toxicity.
- Serotonin Syndrome is likely when one of the following is observed:
  - Spontaneous clonus
  - Inducible or ocular clonus with agitation or diaphoresis
  - Tremor and hyperreflexia
  - Hypertonia and body temperature > 38 °C and inducible or ocular clonus.

Withdrawal of the serotonergic medicines usually brings about a rapid improvement. Treatment depends on the type and severity of the symptoms.

- Other opioid derivatives (including antitussive medicines and substitutive treatments).

Increased risk of respiratory depression which can be fatal in cases of overdose.

- Other central nervous system depressants, such as other opioid derivatives (including antitussive medicines and substitutive treatments), other anxiolytics, hypnotics, sedative antidepressants, sedative antihistamines, neuroleptics, centrally-acting antihypertensive medicines, thalidomide and baclofen.

These medicines can cause increased central depression. The effect on alertness can make driving of vehicles and the use of machines dangerous.

- Sedating medicinal products such as benzodiazepines or related substances:
  - The concomitant use of opioids with sedative medicines such as benzodiazepines or related medicines increases the risk of sedation, respiratory depression, coma and death because of additive CNS depressant effects. The dose and duration of the concomitant use should be limited (see section 4.4).
- As medically appropriate, periodic evaluation of prothrombin time should be performed when tramadol hydrochloride/paracetamol and warfarin like compounds are administered concurrently due to reports of increased INR.

Post- marketing surveillance of tramadol has revealed rare reports of digoxin toxicity.

Concomitant administration of diflunisal and paracetamol produces a 50 % increase in paracetamol plasma levels in normal volunteers. **PARTRACET** should be used cautiously and patients should be monitored carefully.

Concomitant administration with inhibitors of CYP2D6 such as fluoxetine, paroxetine, quinidine and amitriptyline may inhibit the metabolism of **PARTRACET**.
Ondansetron increased the requirement of tramadol in patients with postoperative pain.

4.6 Fertility, pregnancy and lactation

Safe use in pregnancy and lactation has not been established. **PARTRACET** is not recommended for pregnant mothers because tramadol has been shown to cross the placenta.

Fertility

Post marketing surveillance does not suggest an effect of tramadol on fertility.

4.7 Effects on ability to drive and use machines

Tramadol may cause drowsiness or dizziness, which may be enhanced by alcohol or other CNS depressants. If affected, the patient should not drive or operate machinery.

PARTRACET can impair cognitive function and can affect a patient's ability to drive safely. When prescribing this medicine, patients should be told that **PARTRACET** is likely to affect your ability to drive. Patients should be told to not drive until they know how **PARTRACET** affects them.

4.8 Undesirable effects

Tabulated list of adverse reactions

System Organ Class	Adverse reaction	Frequency
Metabolism and nutrition disorders	hypoglycaemia	Frequency unknown
Psychiatric disorders	confusional state, mood altered, anxiety, nervousness, euphoric mood, sleep disorders, anorexia	Frequent
	depression, hallucinations, depersonalisation, nightmares, delirium, drug dependence, drug abuse, impotence	Less frequent
Nervous system disorders	dizziness, somnolence, headache, trembling	Frequent
	involuntary muscular, contractions, paraesthesia, amnesia ataxia, convulsions, syncope, speech disorders	Less frequent
Eye disorders	vision blurred, miosis, mydriasis	Less frequent
Ear and labyrinth disorders	tinnitus	Less frequent
Blood disorders	anaemia	Less frequent
Cardiac disorders	palpitations, tachycardia, dysrythmia	Less frequent
Gastro-intestinal disorders	nausea, vomiting, constipation, dry mouth, diarrhoea, abdominal pain, dyspepsia, flatulence	Frequent
	dysphagia, meleana	Less frequent
General disorders and administration site conditions	chills, chest pain, asthenia, fatigue, decreased weight	Less frequent
Investigations	transaminases increased	Less frequent
Renal and urinary disorders	albuminuria, micturition disorders (dysuria and urinary retention), oliguria	Less frequent
Respiratory, thoracic and mediastinal disorders	dyspnoea	Less frequent
Skin and subcutaneous tissue disorders	hyperhidrosis, pruritus	Frequent
	dermal reactions(e.g. rash, urticaria)	Less frequent
Vascular disorders	hypertension, aggravated hypertension, hot flush, hypotension	Less frequent

Although not observed during clinical trials, the occurrence of the following undesirable effects known to be related to the administration of tramadol or paracetamol cannot be excluded:
Tramadol

- Postural hypotension, bradycardia, collapse (tramadol).
- Post-marketing surveillance of tramadol has revealed rare alterations of warfarin effect, including elevation of prothrombin times.
- Cases of less frequent: allergic reactions with respiratory symptoms (e.g. dyspnoea, bronchospasm, wheezing, angioedema) and analphylaxis.
- Less frequent: Changes in appetite, motor weakness, and respiratory depression.
- Psychic side-effects may occur following administration of tramadol which vary individually in intensity and nature (depending on personality and duration of medication). These include changes in mood, (usually euphoric mood occasionally dysphoria), changes in activity (usually suppression occasionally increase) and changes in cognitive and sensorial capacity (e.g. decision behaviour perception disorders).
- Worsening of asthma has been reported though a causal relationship has not been established.
- Symptoms of drug withdrawal syndrome, similar to those occurring during opiate withdrawal may occur as follows:
  agitation, anxiety, nervousness, insomnia, hyperkinesia, tremor and gastrointestinal symptoms. Other symptoms that have been seen if tramadol hydrochloride is discontinued abruptly include: panic attacks, severe anxiety, hallucinations, paraesthesia, tinnitus and unusual CNS symptoms.

Paracetamol

- Hypersensitivity including skin rash may occur. There have been reports of blood dyscrasias including thrombocytopenia and agranulocytosis.
- There have been several reports that suggest that paracetamol may produce hypoprothrombinemia when administered with warfarin-like compounds. In other studies, prothrombin time did not change.
- Cases of serious skin reactions have been reported.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the **"6.04 Adverse Medicine Reactions Reporting Form",** found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

The clinical presentation of overdosage may include the signs and symptoms of tramadol toxicity, paracetamol toxicity or both.

DETACH BEFORE DISPENSING

SCHEDULING STATUS: S5

PATIENT INFORMATION LEAFLET
PARTRACET (film-coated tablets)
tramadol hydrochloride 37.5 mg and paracetamol 325 mg.
Sugar free.

Read all this leaflet carefully before you start taking PARTRACET.

- Keep this leaflet. You may need to read it again.
- **PARTRACET** 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
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.

What is in this leaflet:

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

1. What PARTRACET is and what it is used for

PARTRACET 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 PARTRACET

Do not take PARTRACET:

- 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 also taking sleeping pills, pain relievers or other 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 **PARTRACET** 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.
- **PARTRACET** must not be used for narcotic (an addictive substance) withdrawal treatment.
- You should not take **PARTRACET** if you suffer from severe breathing problems.
- You should not take **PARTRACET** if you are suffering from increased intracranial pressure or central nervous system depression (a condition characterised by decreased rate of breathing, decreased heart rate, and loss of consciousness.
- You should not take **PARTRACET** if you have fits that are not controlled.

Warnings and precautions

Take special care with PARTRACET:

- 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 are dependent on any other medicines (for example morphine).
- If you have recently suffered from a head injury, shock or severe headaches associated with vomiting (being sick).
- If you have epilepsy or have experienced fits or seizures.
- If you are dependent on medicines that contain its active component. If you convert (metabolise) Tramadol to the active component more rapidly and in higher than usual amounts, you may experience serious, life-threatening or fatal side effects. This is more likely if you are also taking other painkillers and you are an ultra-rapid metaboliser. This means you are more likely to get these side effects even at usual doses or if you have breathing difficulties, such as breathing difficulties, with slow or shallow breathing. If you experience these types of side effects, stop taking **PARTRACET** and contact your doctor immediately.
- If you abruptly stop treatment with **PARTRACET** 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 **PARTRACET** to prevent these side effects from occurring.
- **PARTRACET** contains paracetamol. If you are allergic to paracetamol, you may break out in a severe skin rash after you take **PARTRACET**. You should stop using **PARTRACET** at the first appearance of a skin rash or any other sign of allergy.
- **PARTRACET** should not be taken with alcohol containing beverages.
- While taking **PARTRACET** 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 **PARTRACET**, consult your doctor immediately.
- If you suffer from sleep-related breathing disorders, take special care when taking **PARTRACET**.
- If to your doctor if you develop a craving for **PARTRACET**.

Other medicines and PARTRACET:

Always tell your healthcare professional if you are taking any other medicine. (This includes all complementary or traditional medicines).
PARTRACET should not be administered with the following:

- A group of antidepressants called Monoamine Oxidase Monoamine Oxidase (MAO)-inhibitors (such as moclobemide and tranylcypromine). When taken together with **PARTRACET** it can cause diarrhoea, tachycardia (irregular heartbeat), hyperhidrosis (excessive sweating). trembling, confusional state, even coma.
- Carbamazepine (used to treat seizures). When taken together with **PARTRACET** 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 **PARTRACET**:

- Tramadol can induce convulsions and increase the potential for certain antidepressants such as citalopram, escitalopram, 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 and amitriptyline, moclobemide and 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 drugs with **PARTRACET** 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 useful to treat vomiting.

PARTRACET with food and drink

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

Pregnancy, breastfeeding and fertility

PARTRACET must not be taken during pregnancy.
PARTRACET 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 **PARTRACET.**

Driving and using machines

Do not drive while taking this medicine until you know how it affects you.
PARTRACET can affect your ability to drive as it may make you sleepy or dizzy.
If you feel drowsy while taking **PARTRACET**, do not drive, use tools or use machinery.

3. How to take PARTRACET

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

Always take **PARTRACET** exactly as your doctor 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 **PARTRACET** will last. If you have the impression that the effect of **PARTRACET** 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 to start with 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 PARTRACET than you should

In the event of over dosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison center.

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 PARTRACET

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 PARTRACET

Withdrawal symptoms may occur if **PARTRACET** 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

PARTRACET can have side effects.

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

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

- 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 **PARTRACET**. 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), anorexia (eating disorder)
- dizziness, excessive sleepiness
- headache, trembling
- nausea, vomiting, constipation, dry mouth, diarrhoea, stomach pain, indigestion, stomach gas, excessive sweating, itching, rash

Less frequent side effects:

- depression, seeing, hearing, smelling, tasting or imagining things, a state in which one's thoughts and feelings seem unreal or not to belong to oneself, nightmares
- involuntary muscular contractions, tingling or prickling sensation, loss of memory
- ringing in the ear

A/s: 420 x 600 mm ■ Black

AUROBINDO Packaging Development		Product Name	Component	Item Code	Date & Time
		PARTRACET	Leaflet	P1530354	16.03.2022 & 04.00 pm
		Country	Version No.	Reason Of Issue	Reviewed / Approved by
		South Africa-APL	04	Commercial	
Team Leader	Pratap Sahu	Dimensions (mm)	Colours: 01		
Initiator	Bhogi	420 x 600 mm	30354		
Artist	Sree Designers	Pharma Code: 30354			
Additional Information:					

Tramadol

The initial symptoms of tramadol overdosage may include respiratory depression and/or seizures.

Primary attention should be given to maintaining adequate ventilation along with general supportive treatment. While naloxone will reverse some, but not all symptoms caused by overdosage, the risk of seizures is also increased with naloxone administration. Treatment of restlessness and/or convulsions is symptomatic and supportive(benzodiazepines/barbiturates).
Tramadol is minimally eliminated from the serum by haemodialysis or haemofiltration. Treatment of acute intoxication with **PARTRACET** with haemodialysis or haemofiltration alone is therefore not suitable for detoxification.

Paracetamol

Prompt treatment is essential. In the event of an overdosage, consult a medical practitioner immediately, or take the person to a hospital directly. A delay in starting treatment may mean that antidote is given too late to be effective. Evidence of liver damage is often delayed until after the time for effective treatment has lapsed. Susceptibility to paracetamol toxicity is increased in patients who have taken repeated high doses (greater than 5 - 10 g/day) of paracetamol for several days, in chronic alcoholism, chronic liver disease, AIDS, malnutrition, and with the use of drugs that induce liver microsomal oxidation such as barbiturates, isoniazid, rifampicin, phenytoin and carbamazepine.

Symptoms of paracetamol overdosage in the first 24 hours include pallor, nausea, vomiting, anorexia and possibly abdominal pain. Mild symptoms during the first two days of acute poisoning do not reflect the potential seriousness of the overdosage.

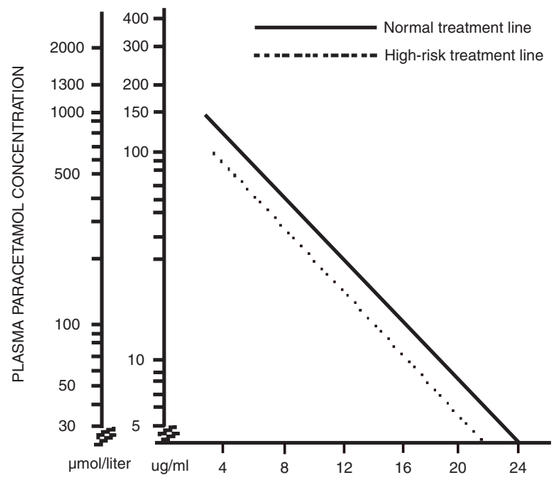
Liver damage may become apparent 12 to 48 hours or later after ingestion, initially by elevation of the serum transaminase and lactic dehydrogenase activity, increased serum bilirubin concentration and prolongation of the prothrombin time. Liver damage may lead to encephalopathy, coma and death.
Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage.

Abnormalities of glucose metabolism and metabolic acidosis may occur. Cardiac dysrhythmias have been reported.

Treatment for paracetamol overdosage:

N-acetylcysteine should be administered to all cases of suspected overdose as soon as possible preferably within eight hours of overdosage, although treatment up to 36 hours after ingestion may still be of benefit, especially if more than 150 mg/kg of paracetamol was taken. An initial dose of 150 mg/kg N–acetylcysteine in 200 mL dextrose injection given intravenously over 15 minutes, followed by an infusion of 50 mg/kg in 500 mL dextrose injection over the next four hours, and then 100 mg/kg in 1000 mL dextrose injection over the next sixteen hours. The volume of intravenous fluid should be modified for children.
Although the oral formulation is not the treatment of choice, 140 mg/kg dissolved in water may be administered initially, followed by 70 mg/kg every four hours for seventeen doses.

A plasma paracetamol level should be determined four hours after ingestion in all cases of suspected overdosage. Levels done before four hours, unless high may be misleading. Patients at risk of liver damage, and hence requiring continued treatment with N-acetylcysteine, can be identified according to their plasma paracetamol level, via the paracetamol overdose nomogram.



Those whose plasma paracetamol levels are above the "normal treatment line", should continue N-acetylcysteine treatment with 100 mg/kg IV over sixteen hours repeatedly until recovery. Patients with increased susceptibility to liver damage as identified above, should continue treatment if concentrations are above the "high risk treatment line". Prothrombin index correlates best with survival.

Monitor all patients with significant ingestions for at least ninety six hours.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A.2.9. Other analgesics, Opioids in combination with non-opioid analgesics, tramadol and paracetamol.
ATC code: N02AJ13

Tramadol is a centrally acting synthetic analgesic compound whose analgesic profile can be attributed to the binding of parent and O-demethylated (M1) metabolite to µ-opioid receptors as well as the weak inhibition of neuronal re-uptake of noradrenaline and serotonin. Paracetamol also has centrally acting analgesic effects.

5.2 Pharmacokinetic properties

Absorption

Tramadol is well absorbed after oral administration, reaching peak activity in 2 to 3 hours. The mean absolute bioavailability of a single 100 mg oral dose is approximately 75 %, increasing to approximately 90 % with multiple dosing. Oral absorption of paracetamol following administration of **PARTRACET** gives a peak plasma concentration of paracetamol within one hour and is not affected by co-administration with tramadol.

Distribution

Tramadol has a high tissue affinity (V_d=203 ± 40 L). It has a plasma protein binding of about 20 %.
Paracetamol appears to be widely distributed throughout most body tissues except fat. Its apparent volume of distribution is about 0.9 L/kg. A relatively small portion (~ 20 %) of paracetamol is bound to plasma proteins.

Metabolism

Tramadol and paracetamol are both extensively metabolised in the liver.

Elimination

Approximately 30 % of tramadol is excreted unchanged in the urine. Tramadol and its metabolites are eliminated primarily by the kidneys. The plasma elimination half-lives of tramadol and its M1 metabolite are approximately 6 and 7 hours respectively.Paracetamol is eliminated from the body primarily by formation of glucuronide and sulfate conjugates in a dose-dependent manner. The half-life of paracetamol is about 2 - 3 hours in adults. Less than 9 % of paracetamol is excreted unchanged in the urine.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

The other ingredients of **PARTRACET** are:
magnesium stearate, maize starch, powdered cellulose, pregelatinized starch, sodium starch glycolate and Opadry light yellow.
Opadry light yellow contains hypromellose, iron oxide yellow (C.I. No: 77492), macrogol, polysorbate 80 and titanium dioxide (C.I. No: 77891).

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store at or below 25 °C.
Keep the blisters in the carton until required for use.
Keep HDPE containers tightly closed.
KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container

PARTRACET

1. Blister pack:
Tablets are packed in white opaque 250 microns PVC coated with 90 g/m^2 PVdC film as the forming material and 20 µ aluminium foil with 7 g/m^2 heat seal lacquer as the lidding material.

Pack size: 60's - Each carton contains 6 blisters of 10 tablets each.

2. HDPE Container Pack:
Tablets are packed in white opaque round 40 mL HDPE container with 33 mm neck finish closed with 33 mm white opaque polypropylene continuous thread closure with wad having induction sealing liner.

Pack size: 60's - One HDPE container contains 60 tablets.

6.6 Special precautions for disposal of a used medicine or waste materials derived from such medicine and other handling of the product

No special requirements for the disposal and handling of **PARTRACET.**

7 NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

AUROGEN SOUTH AFRICA(PTY) LTD
Woodhill Office Park, Building 1, First Floor
53 Phillip Engelbrecht Avenue
Meyersdal, Ext. 12, 1448
Johannesburg
South Africa

8 REGISTRATION NUMBER

47/2.9/1323

9 DATE OF FIRST AUTHORISATION

18 January 2022

P1530354

DETACH BEFORE DISPENSING

SKEDULERINGSTATUS S5

PASIËNTINLIGTINGSPAMFLET

PARTRACET (filmbedekte tablette)

tramadolhidrochloried 37,5 mg en parasetamol 325 mg
Suikervry.

Lees hierdie hele pamflet sorgvuldig deur voordat u PARTRACET begin neem

- Hou hierdie pamflet. U moet dit dalk weer lees.
- **PARTRACET** is vir u persoonlik voorgeskryf en u moet nie u medisyne met ander mense deel nie. Dit kan skadelik vir hulle wees, selfs al het hulle dieselfde simptome as u.
- Indien u enige verdere vrae het, vra asseblief u dokter, apteker, verpleegster of ander gesondheidsorgverskaffer

Wat is in hierdie pamflet

1. Wat **PARTRACET** is en waarvoor dit gebruik word
2. Wat u moet weet voordat u **PARTRACET** gebruik
3. Hoe om **PARTRACET** te gebruik
4. Moontlike newe-effekte
5. Hoe om **PARTRACET** te berg
6. Inhoud van die verpakking en ander inligting

1. Wat PARTRACET is en waarvoor dit gebruik word

PARTRACET bevat tramadol en parasetamol.

Tramadol is 'n pynstiller wat aan die klas van die opioïede behoort wat op die sentrale senuweestelsel inwerk. Dit word gebruik vir matige tot matig ernstige pyn.

Parasetamol, die ander bestanddeel, het santraalwerkende analgetiese effekte.

2. Wat u moet weet voordat u PARTRACET neem

Moenie PARTRACET neem nie:

- Indien u allergies is vir tramadol, parasetamol of vir enige van die ander bestanddele wat in afdeling 6.1 genoem word, of ander opioïede soos kodeïen.
- Indien u ly aan alkoholvergiftiging.
- Indien u slaappille, pynstillers of medisyne gebruik wat gemoed en emosies beïnvloed.
- Indien u ook medisyne soos traniesipromien en moklobemied neem of dit in die laaste 14 dae voor behandeling met **PARTRACET** geneem het wat gebruik word om depressie te behandel. Hierdie medisyne word gebruik om depressie te behandel en behoort aan 'n groep wat monoamienoksidase-inhibeerders (MAOI's) genoem word.
- Indien u 'n ernstige lewerafwyking het.
- Indien u 'n ernstige nierprobleem het ('n verskwende stof) ontrekkingsbehandeling gebruik word nie.
- U moet nie **PARTRACET** neem indien u lyk aan 'n ernstige asemhalingsprobleem, 'n lae asemhalingstempo of verlaagde asemhaling, verlaagde hartklop, en verlies van bewussyn.
- U moet nie **PARTRACET** neem indien u aanvalle het wat onbeheerbaar is nie.

Waarskuwings en voorsorgmaatreëls

Neem spesiale sorg met PARTRACET:

- indien u ander medisyne gebruik wat parasetamol of tramadol bevat
- indien u lewerprobleme of -siekte het. aangesien u oë en vel geel kan word, vat geelsug kan voorstel
- indien u nierprobleme het
- indien u onlangs aan 'n kopbesering, skok of erge hoofpyne gely het, vat met braking geassosieer word (om siek te wees)
- indien u epilepsie het of aanvalle of stuipe ervaar het
- Tramadol oefen sy effek uit deur omskakeling (metabolisering) in sy aktiewe komponent. Indien u Tramadol vinniger of stadiger as normaal metaboliseer, kan u 'n verskeidenheid van effekte ervaar, wat wissel van 'n gebrek aan komponent omskakel (metaboliseer) as ander pasiënte, staan u bekend as 'n ultra-vinnige metaboliseerder. Dit beteken dat u meer geneig is om ernstige newe-effekte te ly, soos asemhalingsprobleme, met stadige of vlak asemhaling. Indien u hierdie tipe newe-effekte ervaar, hou op om **PARTRACET** te neem en raadpleeg onmiddellik u dokter.
- Indien u behandeling met **PARTRACET** skielik staak, kan u aan paniekaanvalle ly, erge angs (voel senuweeagtig of bekommerd), hallusinasies (hoor, voel, baie moeg voel, spierswakheid, spasmas of krampe en aanvalle insluit. Bejaarde pasiënte en pasiënte wat ander medisyne gebruik wat natrium in die bloed verlaag, loop die grootste risiko vir hierdie newe-effek. Indien u enige van hierdie simptome ervaar terwyl u **PARTRACET** neem, raadpleeg u dokter onmiddellik.
- Indien u aan slaapvervaante asemhalingsversteurings ly, wees veral versigtig wanneer u **PARTRACET** neem.
- Praat met u dokter indien u 'n drang vir **PARTRACET** ontwikkel.

Ander medisyne met PARTRACET:

Vertel altyd u gesondheidsorgkundige as u enige ander medisyne neem (dit sluit alle komplementêre of tradisionele medisyne in). Dit is veral belangrik as u enige van die volgende voorgeskryf het:
PARTRACET moet nie saam met die volgende toegedien word nie:

- 'n Groep antidepressante, genaamd monoamieoksidase (MAO)-inhibeerders (soos moklobemied en traniesipromien) of binne twee weke na die laaste dosis **PARTRACET** geneem word, kan dit diarree, tagikardie (onreëlmatige hartklop), hiperhidrose (oormatige sweet), bewing, verwarringstoestand, selfs koma veroorsaak.
- Karbamasepien (gebruik om aanvalle te behandel). Wanneer dit saam met **PARTRACET** geneem word, kan dit verminderde effektiwiteit en korter duur veroorsaak as gevolg van verminderde konsentrasie van tramadol.
- Buprenorfien, nalbufien en pentasosien (opioïed-tipe pynstillers). Die gevolge van hierdie medisyne kan verminder word.

Omsigtigheid word aangeraai wanneer die volgende medisyne saam met **PARTRACET** gegee word:

- **PARTRACET** kalmoniwises veroorsaak en die potensiaal verhoog vir sekere medisyne soos slaappram, esitalopram, duloksetien, venlavaksien en amitriptilien, antipsigotika en medisyne wat aanvaldrempel verlaag (soos bupropion, mirtasapien, tetrahidrokannabinol) om konvulsies te veroorsaak.
- Gelyktydige terapeutiese gebruik van tramadol en slaappram, esitalopram, paroksetien, duloksetien, en amitriptilien, moklobemied en traniesipromien en binnekant twee weke na behandeling met moklobemied kan ernstige newe-effekte veroorsaak. Simptome sluit in onwillekeurige, ritmiese sametrekkings van spiere, insluitend spiere wat die beweging van die arm en been beheer, rossilitend spiere wat die onreëlmatige beweging van die oë beheer, 'n verhoogde liggaamstemperatuur (hipertermie) en 'n verhoogde bloeddruk (hipertensie), bakdoten ('n spierverslapper), medisyne wat gebruik word om bloeddruk te verlaag of medisyne om allergieë te behandel, sowel as kalmeermiddels soos bensodiasepiene (alprasolam, diasepam, lorasepam), is daar 'n verhoogde risiko van lomerigheid, moeilike asemhaling (respiratoriese depressie), koma wat lei tot die dood, en bloeding kan voorkom.
- Indien u warfarien gebruik (vir bloedverdunning). Die effektiwiteit van hierdie medisyne kan verander word, en bloeding kan voorkom.
- Indien u digoksien gebruik, word gebruik om hartprobleme te behandel.
- Indien u diflunisal gebruik vir pyn.
- Indien u ondansetron gebruik, word gebruik om braking te behandel.

PARTRACET met voedsel en drank

Moenie alkohol drink tydens die behandeling met **PARTRACET** nie, aangesien die effekte **PARTRACET** en alkohol mekaar kan versterk.

Swangerskap, borsvoeding en fertiliteit

PARTRACET moet nie tydens swangerskap geneem word nie.
PARTRACET moet nie tydens borsvoeding geneem word nie, aangesien daar geen inligting oor veiligheid tydens borsvoeding beskikbaar is nie.

Indien u swanger is of borsvoed, dink u is dalk swanger of beplan om 'n baba te hê, raadpleeg asseblief u dokter, apteker of ander gesondheidsorgkundige vir advies voordat u **PARTRACET** gebruik.

Bestuur en gebruik van masjinerie

Moenie bestuur tenwyl u hierdie medisyne gebruik totdat u weet hoe dit u beïnvloed nie.
PARTRACET kan u vermoë om te bestuur beïnvloed, aangesien dit u slapheid of duiseligheid kan maak.

Indien u komerig voel terwyl u **PARTRACET** gebruik, moenie bestuur, gereedskap gebruik of masjinerie gebruik nie.

3. Hoe om PARTRACET te neem

Moenie medisyne wat vir u voorgeskryf is met enige ander persoon deel nie.

Neem altyd **PARTRACET** presies soos u dokter u aanbeveel het. Raadpleeg u dokter of apteker indien u onseker is. U dokter sal u vertel hoe lank u behandeling met **PARTRACET** sal duur. Indien u die indruk het dat die effek van **PARTRACET** te sterk of te swak is, praat met u dokter of apteker.

- Sluk die tablette heel met voldoende vloeistof.
- Moenie die tablette breek of kou nie.

Volwassenes:
Die aanbevole dosis is om te begin met 1 of 2 tablette elke 4 tot 6 uur, tensy u dokter dit anders voorgeskryf het. Indien nodig, kan verdere dosisse geneem word, sodat deur u dokter voorgeskryf.
Moenie meer as 8 tablette per dag neem nie.

Indien u meer PARTRACET neem as wat u moet

In die geval van oordosering, raadpleeg u dokter of apteker. Indien geeneen beskikbaar is nie, kontak die naaste hospitaal of giftebeheersentrum.

Onmiddellike mediese advies moet verkry word in die geval van 'n oordosis selfs al voel u goed, weens die risiko van vertraagde, ernstige leverskade as gevolg van te veel parasetamol. U niere kan ook beskadig word in die afwesigheid van leverskade.

Indien u vergeet om PARTRACET te neem

Indien u vergeet het om 'n dosis te neem, neem dit so gou as wat u onthou, tensy dit amper tyd is vir u volgende dosis. Moenie 'n dubbeldosis neem om op te maak vir vergete individuele dosisse nie.

Indien u ophou om PARTRACET te neem

Ontrekkingssimptome kan voorkom indien **PARTRACET** skielik gestaak word. U kan angs, senuweeagtige opwinding, moeilike slaap, oormatige abnormale bewegings, bewing, gastrointestinale simptome ervaar.
Ander simptome, wat baie selde gesien word wanneer tramadolhidrochloried skielik gestaak word, sluit in: paniekaanvalle, erge angs, hallusinasies, tintelende of prikkelende sensasies en gelui in die ore.

4. Moontlike newe-effekte

PARTRACET kan newe-effekte hê.
Nie alle newe-effekte wat vir **PARTRACET** aangemeld is, is in hierdie pamflet ingesluit nie. Indien u algemene gesondheid gaan na die ongewenste effekte ervaar terwyl u **PARTRACET** neem, raadpleeg asseblief u gesondheidsorgverskaffer vir advies.

Indien enige van die volgende gebeur, hou op om **PARTRACET** te neem en vertel u dokter onmiddellik of gaan na die ongevalle-afdeling by u naaste hospitaal:

- Uitslag of jeuk oor die hele liggaam
- Allergiese reaksies saam met asemhalingsprobleme of toetrek van die keel
- Verhoogde bloedingstyd

Dit is almal baie ernstige newe-effekte. Indien u dit ervaar, het u moontlik 'n ernstige reaksie vir **PARTRACET** gehad. U benodig moontlik dringende mediese behandeling of hospitalisasie.

Vertel u dokter onmiddellik of gaan na die ongevalle-afdeling by u naaste hospitaal, indien u enige van die volgende opmerk:

- Ontreëlmatige hartklop wat baie vinnig en meer duidelik is as gewoonlik
- Verhoogde leverensieme, wat lei to abdominale pyn, donker urine, bleek stoelgang, swakheid, moegheid

Dit is almal ernstige newe-effekte. U benodig moontlike dringende mediese behandeling.

Vertel u dokter indien u enige van die volgende opmerk:

Gereelde newe-effekte:

- verwarde toestand, slaapversteurings, gemoedsveranderinge (angs, senuweeagtigheid, gevoel van hoë gemoed), anoreksie (eetversteuring)
- duiseligheid, oormatige slaperigheid
- hoofpyn, bewing
- naarheid, braking, hardlywigheid, droë mond, diarree, maagpyn. slegte spysvertering, maaggas. oormatige sweet, jeuk

Minder gereelde neve-effekte:

- depressie, stem, hoor, ruik, proe of verbeel dinge, 'n toestand waarin 'n mens se gedagtes en gevoelens onwerklik lyk of nie aan jouself behoort nie.
- onwillekeurige spiersametrekkings, tintelende of prikkelende sensasie, geheueverlies
- gelui in die ore
- anemie ['n afname in die rooibloedselle (RBC's) of minder as die normale hoeveelheid hemoglobien in die bloed]