Front Side

400 mm

435 mm

SCHEDULING STATUS: S5

1. NAME OF THE MEDICINE

DOLTREX CO 37.5/325 film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

DOLTREX CO 37.5/325:
Each film-coated tablet contains 37,5 mg tramadol hydrochloride and 325,0 mg paracetamol.
Sugar free
This medicine contains less than 1 mmol sodium (23 mg) per dosage unit, that is to say essentially 'sodium-free'.
For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film –coated tablets
Light yellow coloured, capsule shaped, biconvex, bevelled edge, film-coated tablets debossed with 'L21' on one side and plain on other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications
DOLTREX CO 37.5/325 is indicated for the management of moderate to moderately severe pain in adults.
DOLTREX CO 37.5/325 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 DOLTREX CO 37.5/325 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 minimum period of several days with gradual dose increases at the initiation of DOLTREX CO 37.5/325 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 DOLTREX CO 37.5/325 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
- DOLTREX CO 37.5/325 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.
- DOLTREX CO 37.5/325 is also contraindicated in cases of severe liver function impairment and in acute intoxication with alcohol, hypnotics, centrally acting analgesics, opioids or psychotropic medicines.
- DOLTREX CO 37.5/325 should not be administered to patients who are receiving monoamine oxidase inhibitors or within two weeks of their withdrawal.
- DOLTREX CO 37.5/325 must not be used for narcotic withdrawal treatment.
- DOLTREX CO 37.5/325 should not be given to patients with respiratory depression especially in the presence of cyanosis and excessive bronchial secretions.
- DOLTREX CO 37.5/325 should not be given to patients with increased intracranial pressure or central nervous system depression due to head injury or cerebral disease.

DOLTREX CO 37.5/325 is contraindicated in epilepsy not controlled by treatment.

4.4 Special warnings and precautions for use
The maximum dose of 8 tablets of Tramadol hydrochloride/Paracetamol 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 convulsive 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 (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 reanalize 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 DOLTREX CO 37.5/325 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 generalized 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 DOLTREX CO 37.5/325 should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.

Precautions –general:
Do not co-administer DOLTREX CO 37.5/325 with other tramadol or paracetamol containing products.
Use with alcohol:
DOLTREX CO 37.5/325 should not be taken with alcohol containing beverages.
Use with CNS depressants:
The administration of DOLTREX CO 37.5/325 concurrently with central nervous system (CNS) depressants such as alcohol, opioids, anaesthetic medicines, phenothiazines, tranquillizers or sedative hypnotics is likely to intensify and prolong CNS effects.
Use in renal disease:
DOLTREX CO 37.5/325 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 DOLTREX CO 37.5/325 usually in patients with predisposing risk factors, such as elderly persons and/or patients using concomitant medicines that may cause hyponatraemia. This hyponatraemia appears to be the result of the syndrome of inappropriate antidiuretic hormone secretion (SIADH) and resolves with discontinuation of DOLTREX CO 37.5/325 and appropriate treatment (e.g. fluid restriction). During DOLTREX CO 37.5/325 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:
Monoamine oxidase (MAO) inhibitors
- Risk of serotonergic syndrome, diarrhoea, tachycardia, hyperhidrosis, trembling, confusional state, anorexia.

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 selective serotonin re-uptake inhibitors (SSRIs) serotonin-norepinephrine reuptake inhibitors (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 benzodiazepine 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. DOLTREX CO 37.5/325 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 DOLTREX CO 37.5/325.
Ondansetron increased the requirement of tramadol in patients with post-operative pain.

4.6 Fertility, pregnancy and lactation
Safe use in pregnancy and lactation has not been established. DOLTREX CO 37.5/325 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.
DOLTREX CO 37.5/325 can impair cognitive function and can affect a patient's ability to drive safely. When prescribing this medicine, patients should be told that DOLTREX CO 37.5/325 is likely to affect your ability to drive. Patients should be told to not drive until they know how DOLTREX CO 37.5/325 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, dysrhythmia	Less frequent
Gastro-intestinal disorders:	nausea, vomiting, constipation, dry mouth, diarrhoea, abdominal pain, dyspepsia, flatulence	Frequent
	dysphagia , melaena	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 anaphylaxis.
- 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, hyperkinesias, 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.

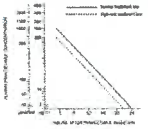
Paracetamol
- Hypersensitivity including skin rash may occur. There have been reports of blood dyscrasias including thrombocytopenia and agranulocytosis.
- There have been several reports that suggest that paracetamol may produce hypoprothrombinaemia when administered with warfarin-like compounds. In other studies, prothrombin time did not change.
- Cases of nausea/ 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 'Med 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.
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 nonrespiratory 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 DOLTREX CO 37.5/325 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. Main 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 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:
Although evidence is limited it is recommended that any adult person who has ingested 5 – 10 g or more of paracetamol (or child who has had more than 140 mg/kg) within the preceding 4 hours should have the stomach emptied by gastric lavage (emesis may be adequate for children) and a single dose of 50 g activated charcoal given via the lavage tube. Ingestion of amounts of paracetamol smaller than this require treatment in patients susceptible to paracetamol poisoning. In patients who are stuporose or comatose endotracheal tubing should precede gastric lavage in order to avoid aspiration.
N-acetylcysteine should be administered to all cases of suspected overdoses 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 15 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 orally, 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 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
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 DOLTREX CO 37.5/325 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 relative 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 sulphate conjugates in a dose-dependent manner. The half-life of paracetamol is about 2 - 3 hours in adults. Less than 5 % of paracetamol is excreted unchanged in the urine.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients
The core tablet contains colloidal silicon dioxide, magnesium stearate, microcrystalline cellulose, povidone, pregelatinized starch, sodium starch glycolate (Type A). The tablets are coated with coating mask up of iron oxide yellow (C.I. No.77492), hypromellose, polyethylene glycol 400, polysorbate 80 and titanium dioxide (C.I. No.77891).
6.2. Incompatibilities
Not applicable.
6.3. Shelf life
24 months from manufacturing date.
6.4. Special precautions for storage
Store at or below 25 °C.
Protect from light and moisture.
Keep the HDPE containers closed.
Keep the blister in the carton until required for use.
KEEP OUT OF REACH OF CHILDREN.
6.5. Nature and contents of container
HDPE container pack (150's):
Tablets are packed in 75 ml round, white, HDPE container, 38-400 mm neck which are closed with 38 mm child resistant closure with pulp and heat seal liner.
Blister pack (10's, 30's and 60's):
Tablets are packed in clear, PVC 250 µm as the forming material and plain 25 um aluminium foil 6 – 8 gsm / m2 , packed in a pre-printed outer carton.
Not all packs and pack sizes are necessarily marketed.
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.
Any unused product or waste material should be disposed of in accordance with local requirements.

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

MacGeods Pharmaceuticals SA (Pty) Ltd
Office block 1, Bassonia Estate Office Park (East),
1 Cussonia Drive, Bassonia Rock, Ext. 12,
Alberton, South Africa.

8. REGISTRATION NUMBER

DOLTREX CO 37.5/325 : 49/2.9/1066

9. DATE OF FIRST AUTHORISATION

15 March 2022

10. DATE OF REVISION OF TEXT

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PATIENT INFORMATION LEAFLET

SCHEDULING STATUS S5

DOLTREX CO 37.5/325
Tramadol hydrochloride 37,5 mg and paracetamol 325 mg.
Sugar free

This medicine contains less than 1 mmol sodium (23 mg) per dosage unit, that is to say essentially 'sodium-free'.

Read all this leaflet carefully before you start taking DOLTREX CO 37.5/325.
- 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.
- DOLTREX CO 37.5/325 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 DOLTREX CO 37.5/325 is and what it is used for
2. What you need to know before you use DOLTREX CO 37.5/325
3. How to use DOLTREX CO 37.5/325
4. Possible side effects
5. How to store DOLTREX CO 37.5/325
6. Contents of the pack and other information

1. What DOLTREX CO 37.5/325 is and what it is used for

DOLTREX CO 37.5/325 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 DOLTREX CO 37.5/325

Do not take DOLTREX CO 37.5/325:
- 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 DOLTREX CO 37.5/325 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 disease.
- DOLTREX CO 37.5/325 must not be used for narcotic (an addictive substance) withdrawal treatment.
- You should not take DOLTREX CO 37.5/325 if you suffer from severe breathing problems.
- You should not take DOLTREX CO 37.5/325 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 DOLTREX CO 37.5/325 if you have fits that are not controlled

Warnings and precautions
Take special care with DOLTREX CO 37.5/325:
- 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 other medicines (for example morphine).
- 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

DOLTREX CO 37.5/325
(film-coated tablet)
PM03603301

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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 breathing difficulties, with slow or shallow breathing. If you experience these types of side effects, stop taking DOLTREX CO 37,5/325 and consult with your doctor immediately.

- If you abruptly stop treatment with DOLTREX CO 37,5/325 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 DOLTREX CO 37,5/325 to prevent these side effects from occurring.
- DOLTREX CO 37,5/325 contains paracetamol. If you are allergic to paracetamol, you may break out in a severe skin rash after you take DOLTREX CO 37,5/325. You should stop using DOLTREX CO 37,5/325 at the first appearance of a skin rash or any other sign of allergy.
- DOLTREX CO 37,5/325 should not be taken with alcohol-containing beverages.
- While taking DOLTREX CO 37,5/325 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 DOLTREX CO 37,5/325, consult your doctor immediately.
- If you suffer from sleep-related breathing disorders, take special care when taking DOLTREX CO 37,5/325.

Talk to your doctor if you develop a craving for DOLTREX CO 37,5/325.

Other medicines and DOLTREX CO 37,5/325:
Always tell your healthcare professional if you are taking any other medicine. (This includes all complementary or traditional medicines).
DOLTREX CO 37,5/325 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 DOLTREX CO 37,5/325 it can cause diarrhoea, tachycardia (irregular heartbeat), hypertensive (excessive sweating), trembling, confusion, stroke, even coma.
- Carbamazepine (used to treat seizures). When taken together with DOLTREX CO 37,5/325 it can cause reduced efficacy and shorter duration due to decreased concentration of tramadol.
- bupropione, nelfinavir and pentazocine (opioid-type pain relievers). The effects of these medicines may be decreased.

Caution is advised when the following medicines are given with DOLTREX CO 37,5/325:

- 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 and amitriptyline, moclobemide and tranylcypromine and mirtazapine may cause serotonin toxicity. Symptoms include convulsions, 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 (diazepam, diazepam, lorazepam) or related medicines with DOLTREX CO 37,5/325 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 diuretics used for pain
- If you are taking ondansetron used to treat vomiting

DOLTREX CO 37,5/325 with food and drink
Do not drink alcohol during treatment with DOLTREX CO 37,5/325 as the effects of DOLTREX CO 37,5/325 and alcohol may intensify each other.

Pregnancy, breastfeeding and fertility
DOLTREX CO 37,5/325 must not be taken during pregnancy.
DOLTREX CO 37,5/325 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.
DOLTREX CO 37,5/325 can affect your ability to drive as it may make you sleepy or dizzy. If you feel drowsy while taking DOLTREX CO 37,5/325, do not drive, use tools or use machinery.

3. How to take DOLTREX CO 37,5/325

Do not share medicines prescribed for you with any other person.
Always take DOLTREX CO 37,5/325 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 DOLTREX CO 37,5/325 will last. If you have the impression that the effect of DOLTREX CO 37,5/325 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 DOLTREX CO 37,5/325 than you should
In the event of over dosage, 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 DOLTREX CO 37,5/325
If you forget 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 DOLTREX CO 37,5/325
Withdrawal symptoms may occur if DOLTREX CO 37,5/325 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

DOLTREX CO 37,5/325 can have side effects.
Not all side effects reported for DOLTREX CO 37,5/325 are included in this leaflet. Should your general health worsen or if you experience any unusual effects while taking DOLTREX CO 37,5/325, please consult your healthcare provider for advice.
If any of the following happens, stop taking DOLTREX CO 37,5/325 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 DOLTREX CO 37,5/325. 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 more 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, sneeze, 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, dysrhythmias
- difficulty swallowing, blood in faeces
- chills
- chest pain
- problems with urination
- difficulty breathing
- increase in blood pressure, hot flashes
- low blood sugar
- drug dependence
- mental confusion and emotional disruption
- convulsions, barking, 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

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

Reporting of side effects
If you get side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects via https://www.mpa.co.za/Publications_Biannual. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store DOLTREX CO 37,5/325

Store at or below 25 °C (room temperature).
Protect from light and moisture.
Keep the HDPE container closed.
Keep the blister in the carton until required for use.
Store all medicines out of reach of children.
Do not store in a bathroom.
Do not use after the expiry date stated on the label / carton / bottle.
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 DOLTREX CO 37,5/325 contains
Each film-coated tablet contains 37,5 mg tramadol hydrochloride and 325,0 mg paracetamol.
Sugar free.
The other ingredients are: Sodium starch glycolate (Type A), pregelatinized starch, colloidal silicon dioxide, povidone, microcrystalline cellulose, magnesium stearate, hypromellose, titanium dioxide (C.I. No.77891), polyethylene glycol 400, iron oxide yellow (C.I.No.77492), polysorbate 80.

What DOLTREX CO 37,5/325 looks like and contents of the pack
Light yellow coloured, capsule shaped, biconvex, bevelled edge, film-coated tablets debossed with "L21" on one side and plain on other side.
Contents of the pack:
HDPE container pack (100's):
Tablets are packed in 75 ml round, white, HDPE container, 38-400 mm neck which are closed with 38 mm child resistant closure with pulp and heat sealliner.

Blister pack (10's, 30's and 60's):
Tablets are packed in clear, PVC 250 µm as the forming material and plain 25 µm aluminium foil 6 - 8 gsm HSL, packed in a one-printed outer carton.
Not all packs and pack sizes are necessarily marketed.

7. NAME, BUSINESS ADDRESS AND TELEPHONE NUMBER OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

MACLEODS PHARMACEUTICALS SA (PTY) LTD,
Office block 1, Bassonia Estate Office Park (East),
1 Cotsend Drive, Bassonia Rock, Ext. 12,
Alberton, South Africa.

8. This leaflet was last revised in

15 March 2022

9. Registration number

DOLTREX CO 37,5/325 : 49/2.9/1066

Access to this corresponding Professional Information
The corresponding professional information can be accessed at https://www.macleodspharma.com or email [redacted] or contact 011 682 1169.

PASIENTINLIGTINGSTUK

SKEDULERINGSTATUS: S5

DOLTREX CO 37,5/325 mg filmbedekte tablette
37,5 mg Tramadolhidrochloried en 325 mg paracetamol
Suikervry

Hierdie medisyne bevat minder as 1 mmol natrium (23 mg) per dosis eenheid, dit wil sê essensieel "natriumvry".

Lees hierdie inligtingstuk sorgvuldig deur voordat jy DOLTREX CO 37,5/325 begin gebruik
- Hou hierdie inligtingstuk. Dit mag nodig wees dat jy dit weer moet lees.
- Vra asseblief jou dokter, apteker, verpleegkundige of ander gesondheidsorgverskaffer, indien jy verdere vrae het.
- DOLTREX CO 37,5/325 is vir jou persoonlik voorgeskryf, so jy moet nie jou medisyne met ander persone deel nie. Dit mag skadelik vir hulle wees, selfs al is het tekenbare dieselfde as joune.

Wat in hierdie inligtingstuk is
1. Wat DOLTREX CO 37,5/325 is en waarvoor dit gebruik word
2. Voordat jy DOLTREX CO 37,5/325 gebruik
3. Hoe om DOLTREX CO 37,5/325 te gebruik
4. Moontlike newe-effekte
5. Hoe om DOLTREX CO 37,5/325 te bewaar
6. Inhoud van die pak en ander inligting

1. Wat DOLTREX CO 37,5/325 is en waarvoor dit gebruik word

DOLTREX CO 37,5/325 bevat tramadol en paracetamol.
Tramadol is 'n pynstiller wat een die opioïedklas behoort wat op die sentrale senuwestelsel inwerk. Dit word gebruik vir die behandeling van matige tot ernstige pyn.
Paracetamol, die ander aktiewe bestanddeel, het sentraalwerkende analgetiese effekte.

2. Wat jy behoort te weet voordat jy DOLTREX CO 37,5/325 gebruik

Moet nie DOLTREX CO 37,5/325 neem

- indien jy allergies is vir tramadol, paracetamol, enige van die ander bestanddele soos genoem in afdeling 6.1, of ander opioïede soos kodeïen.
- indien jy ly aan ernstige alkoholvergiftiging.
- indien jy slaappille, pynstillers of medisyne wat jou sou kon emosies beïnvloed gebruik.
- indien jy ook medisyne wat gebruik word om depressie te behandel, soos monoksidase-inhibeerders en moklobemied neem, of dit in die afgelope 14 dae voor behandeling met DOLTREX CO 37,5/325 geneem het. Hierdie medisyne word gebruik om depressie te behandel en behoort aan 'n groep meestal monoamien oksidase inhibeerders (MAOI's).
- indien jy 'n ernstige lewersiekte het.
- DOLTREX CO 37,5/325 moet nie gebruik word vir die behandeling van ontrekking van narkotiese (verslawende stof) middels nie.
- Jy moet nie DOLTREX CO 37,5/325 neem indien jy aan ernstige asemhalingsprobleme ly nie.
- Jy moet nie DOLTREX CO 37,5/325 neem indien jy aan vernougde intestinale druk of sentrale senuweestelsel onderdrukking, wat gekenmerkteer word deur verlangde asemhalingstempo, verlangde hartklopte, en bewussynsverdowing nie.
- Jy moet nie DOLTREX CO 37,5/325 neem indien jy swanger is nie.

Waarskuwings en voorsorgmaatreëls
Neem spesiale sorg met DOLTREX CO 37,5/325
- Indien jy ander paracetamol- of tramadolbevattende medisyne neem.
- Indien jy lewerprobleme of -siekte het, aangesien jou dosisinterval dan verdoer, wat goedkeuring kan voorsien.
- Indien jy nierprobleme het.
- Indien jy allergies aan 'n hoofbesering, skok of enige hoofpyne gely het wat gepaard gegaan het met bedaling (flauwtes).
- Indien jy uitmaaksiek is van ander medisyne (tyrosienhoudende morfiën).
- Indien jy epileptiese aanvalle of diepliggende epilepsie ervaar het.
- Tramadol reëlen sy effek uit deur omskakeling (metabolisering) na sy aktiewe komponent. Wanneer jy Tramadol vinniger en meer volledig as ander pasiënte na hierdie aktiewe komponent omskakel (metaboliseer), staan jy bekend as 'n ultra-vinnige metaboliseerder. Dit beteken dat jy meer geneig is om ernstige newe-effekte soos probleme met asemhaling, met sluiging of vlak asemhaling te hê. Indien jy hierdie tipe newe-effekte ervaar, staak dan gebruik van DOLTREX CO 37,5/325 en raadpleeg onmiddellik jou dokter.
- Indien jy die behandeling met DOLTREX CO 37,5/325 skielik staak, kan jy aan paniekaanvalle, erge angsgevoel (veel senuweeagtig of bekommerd), hallusinasies (hoor of sien dinge wat nie daar is nie), parestesie (branderige of prikkelende sensasie wat gewoonlik gevoel word in die hande, arms, bene of voete) en tinnitus (gelui of suising in die ore) ly. Jou dokter sal geleidelik jou dosis van DOLTREX CO 37,5/325 verminder om te verhoed dat hierdie newe-effekte voorkom.
- DOLTREX CO 37,5/325 bevat paracetamol. Indien jy allergies is vir paracetamol, kan jy 'n ernstige veluitslag uitbreek nadat jy DOLTREX CO 37,5/325 geneem het. Jy moet die gebruik van DOLTREX CO 37,5/325 staak by die eerste verskyning van 'n velluitslag of enige ander teken van allergie.
- DOLTREX CO 37,5/325 moet nie saam met alkoholbevattende dranksis geneem word nie.
- Jy kan lae natriumvlakte in jou bloed waarneem (hiponatremie) terwyl jy DOLTREX CO 37,5/325 neem. Simptome kan nausheid en braking, hoofpyne, verwardheid, erge moegheid, naarheidsheid, prikkelrigheid, spierswakheid, krampe of krampe en aanvalle insluit. Bejaarde pasiënte en pasiënte wat ander medisyne neem wat natrium in die bloed verlaag, loop die grootste risiko vir hierdie newe-effek. Indien jy enige van hierdie simptome ervaar terwyl jy DOLTREX CO 37,5/325 gebruik, raadpleeg onmiddellik jou dokter.
- Indien jy aan slaapverwante asemhalingsversteurings ly, moet spesiale sorg geneem word wanneer jy DOLTREX CO 37,5/325 neem.

Praat met jou dokter as jy 'n drang vir DOLTREX CO 37,5/325 ontwikkel.

Ander medisyne en DOLTREX CO 37,5/325
Vertel altyd vir jou professionele gesondheidsorgverskaffer indien jy enige ander medisyne neem. (Dit sluit alle komplementêre of tradisionele medisyne in.)
DOLTREX CO 37,5/325 moet nie saam met die volgende toegedien word nie:

- 'n Groep van antidepressante noemlik Monoamien oksidase (MAO) inhibeerders (soos moklobemied en tranielsipromien). Wanneer dit saam met DOLTREX CO 37,5/325 geneem word, kan dit diarree, taglikardie (onreëlmatige hartslag), hipertensie (oormatige sweet), bewing, verwarringsberaand, selfs koma veroorsaak.
- Wanneer karbamasepien (wat gebruik word om aanvalle te behandel) saam met DOLTREX CO 37,5/325 geneem word, kan dit lae doeltreffendheid en verkorte duur veroorsaak as gevolg van die konsentrasie van tramadol wat verlaag word.
- Bupropion, nalfinien of pentazosien (opioied-tipe pynverligters). Die effekte van hierdie middels kan verminder word.

Versigtigheid word aangeraai wanneer die volgende medisyne saam met DOLTREX CO 37,5/325 gegee word:

- Tramadol kan stuiptrekkings indoseer en die potensieel verhoog om konvulsies te veroorsaak vir sekere antidepressante soos sitalopram, essitalopram, paroksetien, duloksetien, venlafaksien en amitriptilien, antipsigotiese middels en medisinale produkte wat die drempel vir aanvalle verlaag (soos bupropion, mirtasapien, tetrahidrokannabinol).
- Gelyktydige terapeutiese gebruik van tramadol en sitalopram, essitalopram, paroksetien, duloksetien, venlafaksien en amitriptilien, moklobemied en tranielsipromien en mirtasapien kan serotoniensiekwaistel veroorsaak. Simptome sluit stuiptrekkings, ritmiese sametrekkings van spiere, insluitend die spiere wat beweging van die oog beheer, rastelosheid, oormatige sweet, bewing, verdrywing van reflekse, verhoogde spierspanning, liggaamstemperatuur bo 38 °C in.
- Indien jy ander pynverligters, soos morfien en kodeïen (ook as hoesmediçyne), baklofen ('n spierverslapper), medisyne wat gebruik word om bloeddruk te verlaag, of medisyne om allergieë te behandel sowel as kalmeermiddels soos bensodiasepyne (diepersitam, diasepam, lorrasipam) of verwante medisyne terselfdertyd as DOLTREX CO 37,5/325 neem, aangesien daar 'n verhoogde risiko is vir lomerigheid, probleme met asemhaling (respiratoriese onderdrukking), koma wat lewensgevaarlik kan wees.
- Indien jy warfarien neem (vir bloedverdunning). Die doeltreffendheid van hierdie medisyne kan beïnvloed word, en bloeding kan voorkom.
- Indien jy digoksien neem wat gebruik word om hartprobleme te behandel.
- Indien jy diuretiese gebruik vir pyn.
- Indien jy ondansetron gebruik wat geneem word om braking te behandel.

DOLTREX CO 37,5/325 met voedsel en drank:
Moet nie alkohol drink tydens behandeling met DOLTREX CO 37,5/325 nie, aangesien die effekte van DOLTREX CO 37,5/325 en alkoholmekaar kan verstaik.

Swangerskap, bevrugting en fertiliteit
DOLTREX CO 37,5/325 moet nie tydens swangerskap gebruik word nie.
DOLTREX CO 37,5/325 moet nie tydens borsvoeding gebruik word nie aangesien daar geen inligting beskikbaar is rakende veiligheid tydens borsvoeding nie.

Indien jy swanger is of borsvoed, vermoed dat jy moontlik swanger kan wees of beplan om 'n baba te hê, raadpleeg asseblief jou dokter, apteker of ander professionele gesondheidsorgwerker vir advies voordat jy hierdie medisyne neem.

Bestuur en gebruik van meslene
Moet nie bestuur terwyl jy hierdie medisyne gebruik nie, totdat jy weet hoe dit jou affekteer.
DOLTREX CO 37,5/325 kan jou vermoë om te bestuur bevoeglikheid aangesien dit jou slaperig of duiselig kan maak.
Indien jy lomerig voel terwyl jy DOLTREX CO 37,5/325 gebruik, moet dan nie bestuur, gereedskap gebruik of meslene hanteer nie.

3. Hoe om DOLTREX CO 37,5/325 te gebruik

Moet nie medisyne wat vir jou voorgeskryf is met enige ander persoon deel nie
Neem altyd DOLTREX CO 37,5/325 presies soos jou dokter dit vir jou voorgeskryf het. Vra vir jou dokter of apteker indien jy onseker is. Jou dokter sal vir jou sê presies hoe lank jou behandeling met DOLTREX CO 37,5/325 sal duur. Indien jy onder die indruk is dat die effek van DOLTREX CO 37,5/325 te sterk of te swak is, praat met jou dokter of apteker.

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

Volwassenes:
Die aanbevole dosis is 1 of 2 tablette elke 4 tot 6 uur, tensy andersis deur jou dokter voorgeskryf. Indien nodig, kan verdere dosisse geneem word, soos deur jou dokter voorgeskryf.
Moet nie meer as 8 tablette per dag neem nie.

Indien jy meer DOLTREX CO 37,5/325 neem as wat jy behoort te neem
In die geval van oordosering, raadpleeg jou dokter of apteker. Indien nie een beskikbaar is nie, kontak die naaste hospitaal of giftebesorgsentrum.

Mediese advies moet onmiddellik ingewin word in die geval van 'n oordosering, selfs al voel jy goed, weens die risiko van vertraagde, ernstige leverskade as gevolg van te veel paracetamol. Jou niere kan ook beskadig word in die afwesigheid van leverskade.

Indien jy vergeet om DOLTREX CO 37,5/325 te neem
Indien jy vergeet om 'n dosis te neem, neem die dosis sy onthou, tensy dit feitlik reg is vir jou volgende dosis. Moet nie 'n dubbele dosis neem om vergete individuele dosisse op te maak nie.
Indien jy ophou om DOLTREX CO 37,5/325 te gebruik
Onttrekkingsimptome kan voorkom as DOLTREX CO 37,5/325 skielik gestaak word. Jy kan angs, senuweeagtige opgewondenheid, probleme om te slaap, oormatige abnormale bewegings, bewing en gastrointestinale simptome ervaar.

Ander simptome wat baie selde gesien is indien tramadolhidrochloried skielik gestaak word, sluit in: paniekaanvalle, erge angs, hallusinasies, tintelende of prikkelende sensasie en gesuis in die ore.

4. Moontlike newe-effekte

DOLTREX CO 37,5/325 kan newe-effekte hê.
Nie al die newe-effekte wat vir DOLTREX CO 37,5/325 gerapporteer is, is in hierdie inligtingstuk ingesluit nie. Sou jou algemene gesondheid versleg of indien jy enige ongewoonste effekte ondervind terwyl jy DOLTREX CO 37,5/325 gebruik, kontak asseblief jou gesondheidsorgverskaffer vir advies.
Indien enige van die volgende gebeur, staak die gebruik van DOLTREX CO 37,5/325 en vertel onmiddellik jou dokter of gaan na die ongevalle afdeling van jou naaste hospitaal:

- Uitslag of jeuk oor die hele liggaam
- Allergiese reaksie saam met asemhalings probleme of bietnis van die keel.
- Verlengde bloedingstyd.

Al hierdie newe-effekte is baie ernstig. Indien jy dit ervaar, het jy moontlik 'n ernstige reaksie op DOLTREX CO 37,5/325 gehad. Jy mag dringende mediese aandag of hospitalisasie benodig.

Sê onmiddellik vir jou dokter of gaan na die ongevalle afdeling van jou naaste hospitaal indien jy enige van die volgende opmerk: Die volgende newe-effekte kom gereeld voor:

- Onreëlmatige hartslag, wat vinniger en meer opvallend is as gewoonlik.
- Verhoogde leverensieme, wat lei tot abdominale pyn, donker urine, bleek stoelgang, swakheid, moegheid.

Al hierdie newe-effekte is ernstig. Jy mag dringende mediese aandag benodig.

Vertel vir jou dokter indien jy enige van die volgende opmerk:
Gereelde newe-effekte:

- verwarringstoestand, slaapversteurings, gemoedsveranderinge (angs, senuweeagtigheid, voel baie gelukkig en opgewonde)
- duiseligheid, oormatige slaaperigheid
- hoofpyn, bewing
- naarheid, braking, hardlywigheid, droë mond, diarree, maagpyn, slegte spysvertering, misagtes

Minder gereelde newe-effekte:

- depressie, sien, hoor, reik, proe of verbeel dinge, nagmerries
- onwillekeurige spiersametrekkings, tintelende of prikkelende sensasie, geheueverlies
- gesuis in die oor
- vinnige, sterk of onreëlmatige hartslag, baie vinnige hartslag, disrimieë
- sluk moeilik, bloed in stoelgang
- koue rillings
- borspyn
- probleme met urinering
- moeilike asemhaling
- koorsame en bloedrush, warm gevoel
- lae bloedsuiker
- dwelmafhanklikheid
- geestelike verwarring en emosionele onderbreking
- stuipreklings, floutes, spraak versteurings
- slaapspraak, stukkelig, tonvalsies, floute, spraak versteurings.
- dowwe visie, vernouing van die pupille (miose)
- oormatige vergroting van die pupille (mariase)

Daarbenewens is die volgende newe-effekte aangemeld deur mense wat medisyne gebruik wat slegs tramadol of slegs paracetamol bevat:

- veel duiseligheid wanneer uit 'n liggings of sittende posisie opstaan, stadige hartslamp, floutes
- veranderinge in eetlus
- spiersmagheid, stadiger of swakker asemhaling
- gemoedsveranderinge, veranderinge in aktiwiteit, veranderinge in persepsie
- verergering van bestaande asma

Jy moet asseblief jou dokter of apteker in indien jy enige newe-effekte opmerk wat nie in hierdie inligtingstuk genoem word nie.

Aanmelding van newe-effekte
Indien jy newe-effekte kry praat met jou dokter, apteker of verpleegkundige. Dit sluit enige moontlike newe-effekte in wat nie in hierdie inligtingstuk gelys is nie. Jy kan ook newe-effekte via https://www.sahpra.org.za/Publications/Index/8 rapporteer.
Deur newe-effekte aan te meld kan jy help om meer inligting beskikbaar te stel aangaande die veiligheid van hierdie medisyne.

5. Hoe om DOLTREX CO 37,5/325 te bewaar

Bewaar by of benede 25 °C (kamertemperatuur).
Beskerm teen lig en vog.
Hou die HDPE houer dig toe.
Hou die sluisstrook in die buitenste karton totdat dit benodig word vir gebruik.
Bewaar alle medisyne buite bereik van kinders.
Moet nie in 'n badkamer bêre nie.
Moet nie na die vervaldatum wat aangebring is op die etiket/karton/bottel gebruik nie.
Neem alle ongebruikte medisyne terug na jou apteker.
Moet nie ongebruikte medisyne in afvoere of rioolstelsels (bv. toilette) gooi nie.

6. Inhoud van die pak en ander inligting

Wat DOLTREX CO 37,5/325 bevat
Elke filmbedekte tablet bevat 37,5 mg tramadolhidrochloried en 325,0 mg paracetamol.
Suikervry.
Die ander bestanddele is: Natriumstysselglikolaat (Tipe A), voorgelatiniseerde stysel, kolloïdale silikondioksied povidon, mikrokristallyne sellulose, magnesiumsteraat, hipromellose, titaandioksied (C.I. nr. 77891), poliëtileenglikol 400, geel ysteroksied (C.I. nr. 77492), polisorbaat 80.

Hoe DOLTREX CO 37,5/325 lyk en inhoud van die pak
Liggeel kleurige, kapsulevormige, bikonvekse, skuins gerande, filmbedekte tablette gedruk met "L21" aan die een kant en glad aan die ander kant.
Inhoud van die pak:
HDPE houer verpakking (100's):
Tablette word in 75 ml ronde, wit, HDPE houer verpak, met 38-400 mm nek wat toegemaak is met 'n 38 mm kinderbestande sluiting met pulp en hittesel toevoering.

Stulpverpakkings (10's, 30's en 60's):
Tablette word verpak in helder PVC 250 µm as die vormgemateriaal en gewone 25 µm aluminiumfoelie 6 - 8 gsm HSL, verpak in 'n voorafgedrukte buitenste karton.
Nie alle verpakkings en verpakkingsgroottes word noodwendig bemark nie.

7. Naam, besigheidsadres en telefoonnommer van die Houer van die Registrasiesertifikaat

MACLEODS PHARMACEUTICALS SA (Edms) Bpk
Kantoorblok 1, Bassonia Estate Kantoorpark (Oos),
Cassonia Weg 1, Bassonia Rock, Ulitte. 12,
Alberton, Suid Afrika

8. Hierdie inligtingstuk was hersien in

15 Maart 2022

9. Registrasienommer

DOLTREX CO 37,5/325 : 49/2.9/1066

Toegang tot die ooreenstemmende Professionele inligting
Die ooreenstemmende professionele inligting kan verkry word by https://www.macleodspharma.com of e-pos macleodsrsa@rmdeodspharma.com of kontak 011 682 11 69.

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MACLEODS

Restricted Circulation

PACKAGING RESEARCH & DEVELOPMENT

(Front Page)

ARTWORK / PRINTPROOF APPROVAL FORM

1. Product: DOLTREX CO 37.5/325 (Tramadol Hydrochloride and Paracetamol Tablets 37,5 mg / 325 mg)	
2. Country: South Africa (Private Market)	3. Packaging component: Package Insert & Patient Information Leaflet
4. No. of Colours: 1 Colour	5. Pantone Shade No.: Black
6. Specification: 40 gsm bible paper	
7. Machine Layout No.: NA	8. Dimensions: 435 (L) x 400(W) mm
9. Design / Style: Booklet	10. Item code No.: PM03932301
11. Artwork has been made: Actual Size	12. Pharma code No.: 31830 mini
13. Barcode/NDC no: NA	14. Supersedes Item code No: NA
15. Revision no: 00	16. AW File name: T:\Tramadol HCL and Acetaminophen Tablets\SA Private Market\Tramadol HCL and Acetaminophen PI & PIL- PM03932301.cdr
Approved By:	17. Location: Baddi

PRD	M.A. HOLDER	MEDICAL/RAD	QC	PRODN	QA
23/09/22	Vanita Rajool	23/09/22	30/09/22	6/10/22	03/12/22

Note: 1. To follow overleaf checklist for approval of Artwork / Print proof.

Instructions to Vendor :

1. Before processing, please ensure First pull out / Commercial supply should match with approved Artwork with respect to Design, Size, Fonts & Text.
2. Print proof to represent full printing area with Station Numbers.

FRM/CQA/021/04-02

Reason for revision :	Item code	Artwork Release Date	Artwork Implementation Date
1) New Artwork for South Africa Private Market	PM03932301		

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