SUMMARY OF PRODUCT CHARACTERISTICS

Tramadol Hydrochloride

(PAM TRAMADOL CAPSULES)

1 NAME OF THE MEDICINAL PRODUCT

PAM TRAMADOL CAPSULES

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each effervescent tablet contains:

Tramadol Hydrochloride BP….50 mg

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Capsule.

Green and white capsules.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

PAM TRAMADOL CAPSULES is indicated for the symptomatic treatment of moderate to severe pain.

The use of PAM TRAMADOL CAPSULES should be restricted to patients whose moderate to severe pain is considered to require a combination of tramadol hydrochloride (see also section 5.1).

4.2 Posology and method of administration

Adults and adolescents over 12 years:

The recommended starting dose, unless otherwise prescribed by your doctor is 2 capsules for adults and adolescents over 12 years.

If required, further doses may be taken, as instructed by your doctor.

The shortest time between doses must be at least 6 hours.

Do not take more than 8 tablets per day.

Children under 12 years of age:

Not recommended Older people:

In elderly patients (above 75 years) the excretion of tramadol may be delayed. If this applies to you, your doctor may recommend prolonging the dosage interval.

If required, further doses may be taken, as instructed by your doctor.

The shortest time between doses must be at least 6 hours.
Do not take more than 8 capsules per day.

Method of administration
Oral use
Capsules should be taken in a glass of drinking water.

4.3 Contraindications

- Hypersensitivity to the active substances, or to any of the excipients listed in section 6.1
- acute intoxication with alcohol, hypnotic medicinal products, centrally-acting analgesics opioids or psychotropic medicinal products,
- PAM TRAMADOL CAPSULES should not be administered to patients who are receiving monoamine oxidase inhibitors or within two weeks of their withdrawal (see section 4.5)
- severe hepatic impairment,
- epilepsy not controlled by treatment (see section 4.4).

4.4 Special warnings and precautions for use *Warnings:*

- In adults and adolescents 12 years and older. The maximum dose of 8 capsules of PAM TRAMADOL CAPSULES 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 tramadol hydrochloride containing products concurrently without the advice of a physician.
- In severe renal insufficiency (creatinine clearance <10 ml/mm), PAM TRAMADOL CAPSULES is not recommended.
- In patients with severe hepatic impairment PAM TRAMADOL CAPSULES should not be used (see section 4.3). In moderate cases prolongation of dosage interval should be carefully considered.
- In severe respiratory insufficiency, PAM TRAMADOL CAPSULES is not recommended.
- Tramadol hydrochloride is not suitable as a substitute in opioid-dependent patients. Although it is an opioid agonist, tramadol hydrochloride cannot suppress morphine withdrawal symptoms.
- Convulsions have been reported in tramadol hydrochloride-treated patients susceptible to seizures or taking other medications that lower the seizure threshold, especially selective serotonin re-uptake inhibitors, tricyclic antidepressants, antipsychotics, centrally acting analgesics or local anaesthesia. Epileptic patients controlled by a treatment or patients susceptible to seizures should be treated with PAM TRAMADOL CAPSULES only if there are compelling circumstances. Convulsions have been reported in patients receiving tramadol

hydrochloride at the recommended dose levels. The risk may be increased when doses of tramadol hydrochloride exceed the recommended upper dose limit.

- Concomitant use of opioid agonists-antagonists (nalbuphine, buprenorphine, pentazocine) is not recommended (see section 4.5).

Precautions for use

Risk from concomitant use of sedative medicines such as benzodiazepines or related drugs

Concomitant use of PAM TRAMADOL CAPSULES and sedative medicines such as benzodiazepines or related drugs may result in sedation, respiratory depression, coma and death. Because of these risks, concomitant prescribing with these sedative medicines should be reserved for patients for whom alternative treatment options are not possible. If a decision is made to prescribe PAM TRAMADOL CAPSULES concomitantly with sedative medicines, the lowest effective dose should be used, and the duration of the concomitant treatment should be as short as possible.

Tolerance and physical and/or psychological dependence may develop, even at therapeutic doses. The clinical need for analgesic treatment should be reviewed regularly (see section 4.2). In opioid-dependent patients and patients with a history of drug abuse or dependence, treatment should only be for short period and under medical supervision. PAM TRAMADOL CAPSULES should be used with caution in patients with cranial trauma, in patients prone to convulsive disorder, biliary tract disorders, in a state of shock, in an altered state of consciousness for unknown reasons, with problems affecting the respiratory center or the respiratory function, or with an increased intracranial pressure.

Symptoms of withdrawal reaction, similar to those occurring during opiate withdrawal, may occur even at therapeutic doses and for short term treatment (see section 4.8). Withdrawal symptoms may be avoided by tapering it at the time of discontinuation especially after long treatment periods. Rarely, cases of dependence and abuse have been reported (see section 4.8).

4.5 Interaction with other medicinal products and other forms of interaction *Concomitant use is contraindicated with:*

• Non-selective MAO Inhibitors

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

• Selective-A MAO Inhibitors

Extrapolation from non-selective MAO inhibitors

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

• Selective-B MAO Inhibitors

Central excitation symptoms evocative of a 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 hydrochloride *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 re-uptake inhibitors (SSRIs), serotonin-norepinephrine re-uptake inhibitors (SNRIs), tricyclic antidepressants, antipsychotics and seizure threshold-lowering medicinal products (such as bupropion, mirtazapine, tetrahydrocannabinol) to cause convulsions.
- Concomitant therapeutic use of tramadol hydrochloride and serotonergic drugs such as selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), MAO inhibitors (see section 4.3), 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 drugs usually brings about a rapid improvement. Treatment depends on the type and severity of the symptoms.
- Other opioid derivatives (including antitussive medicinal products and substitutive treatments), benzodiazepines and barbiturates. 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 medicinal products and substitutive treatments), barbiturates, benzodiazepines, other anxiolytics,

hypnotics, sedative antidepressants, sedative antihistamines, neuroleptics, centrallyacting antihypertensive medicinal products, thalidomide and baclofen.

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

- As medically appropriate, periodic evaluation of prothrombin time should be performed when PAM TRAMADOL CAPSULES and warfarin like compounds are administered concurrently due to reports of increased INR.
- In a limited number of studies the pre- or postoperative application of the antiemetic 5-HT3 antagonist ondansetron increased the requirement of tramadol hydrochloride in patients with postoperative pain.

4.6 Fertility, pregnancy and lactation

Pregnancy

Since PAM TRAMADOL CAPSULE contains the active substance tramadol hydrochloride, it should not be used during pregnancy.

Tramadol hydrochloride should not be used during pregnancy as there is inadequate evidence available to assess the safety of tramadol hydrochloride in pregnant women. Tramadol hydrochloride administered before or during birth does not affect uterine contractility. In neonates it may induce changes in the respiratory rate which are usually not clinically relevant. Long-term treatment during pregnancy may lead to withdrawal symptoms in the newborn after birth, as a consequence of habituation.

Breast-feeding:

Data regarding tramadol hydrochloride:

Approximately 0.1% of the maternal dose of tramadol is excreted in breast milk. In the immediate post-partum period, for maternal oral daily dosage up to 400 mg, this corresponds to a mean amount of tramadol ingested by breast-fed infants of 3% of the maternal weight-adjusted dosage. For this reason tramadol should not be used during lactation or alternatively, breastfeeding should be discontinued during treatment with tramadol. Discontinuation of breastfeeding is generally not necessary following a single dose of tramadol.

Fertility

Animal studies did not show an effect of tramadol on fertility. No study on fertility was accomplished with tramadol.

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.

• The medicine is likely to affect your ability to drive

• Do not drive until you know how the medicine affects you

• It is an offence to drive while under the influence of this medicine

• However, you would not be committing an offence (called 'statutory defence') if:

o The medicine has been prescribed to treat a medical or dental problem and o You have taken it according to the instructions given by the prescriber and in the information provided with the medicine and

o It was not affecting your ability to drive safely

4.8 Undesirable effects

The most commonly reported undesirable effects during the clinical trials performed with the paracetamol/tramadol hydrochloride combination were nausea, dizziness and somnolence, observed in more than 10 % of the patients.

The frequencies are defined as follows:

Very common: ≥1/10
Common: ≥1/100 to <1/10
Uncommon: ≥1/1000 to <1/100 Rare: ≥1/10 000 to <1/1000
Very rare: <1/10 000
Unknown: Frequency cannot be estimated from the available data

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Cardiac disorders:

• Uncommon: arrhythmia, tachycardia, palpitations.

Eye disorders:

• Rare: vision blurred, miosis, mydriasis *Ear and labyrinth disorders:*

• Uncommon: tinnitus *Gastrointestinal disorders:*

• Very common: nausea

• Common: vomiting, constipation, dry mouth, diarrhoea, abdominal pain, dyspepsia, flatulence

• Uncommon: dysphagia, melaena.

General disorders and administration site conditions:

• Uncommon: chills, chest pain. *Investigations:*

• Uncommon: transaminases increased. *Metabolism and nutrition disorders:*

• Unknown: hypoglycaemia *Nervous system disorders:*

• Very common: somnolence, dizziness

• Common: headache, trembling

• Uncommon: muscular contractions involuntary, paraesthesia, amnesia

• Rare: convulsions, ataxia, syncope, speech disorders.

Psychiatric disorders:

• Common: confusional state, mood altered, anxiety, nervousness, euphoric mood, sleep disorders

• Uncommon: depression, hallucinations, nightmares

• Rare: delirium, drug dependence

Post marketing surveillance Very rare: abuse.

Renal and urinary disorders:

• Uncommon: albuminuria, micturition disorder (dysuria and urinary retention). *Respiratory, thoracic and mediastinal disorders:*

• Uncommon: dyspnoea

Skin and subcutaneous tissue disorders:

• Common: hyperhidrosis, pruritus

• Uncommon: dermal reactions (e.g.rash, urticaria). *Vascular disorders:*

• Uncommon: hypertension, hot flush

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

• Postural hypotension, bradycardia, collapse.

• Post-marketing surveillance of tramadol hydrochloride has revealed rare alterations of warfarin effect, including elevation of prothrombin times.

• Rare cases (≥ 1/10000 to < 1/1000): allergic reactions with respiratory symptoms (e.g. dyspnoea, bronchospasm, wheezing, angioneurotic oedema) and anaphylaxis

• Rare cases (≥ 1/10000 to < 1/1000): changes in appetite, motor weakness, and respiratory depression

• Psychic side-effects may occur following administration of tramadol hydrochloride 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 very rarely been seen if tramadol hydrochloride is discontinued abruptly include: panic attacks, severe anxiety, hallucinations, paraesthesia, tinnitus and unusual CNS symptoms.

4.9 Overdose

In case of overdose, the symptoms may include the signs and symptoms of toxicity of tramadol hydrochloride.

Symptoms of overdose from tramadol hydrochloride:

In principle, on intoxication with tramadol hydrochloride, symptoms similar to those of other centrally acting analgesics (opioids) are to be expected. These include in particular, miosis, vomiting, cardiovascular collapse, consciousness disorders up to coma, convulsions and respiratory depression up to respiratory arrest.

Emergency treatment:

- Transfer immediately to a specialised unit.
- Maintain respiratory and circulatory functions
- Prior to starting treatment, a blood sample should be taken as soon as possible after overdose in order to measure the plasma concentration of paracetamol and tramadol and in order to perform hepatic tests.
- Perform hepatic tests at the start (of overdose) and repeat every 24 hours. An increase in hepatic enzymes (ASAT, ALAT) is usually observed, which normalizes after one or two weeks. - Empty the stomach by causing the patient to vomit (when the patient is conscious) by irritation or gastric lavage.
- Supportive measures such as maintaining the patency of the airway and maintaining cardiovascular function should be instituted; naloxone should be used to reverse respiratory depression; fits can be controlled with diazepam.
- Tramadol hydrochloride is minimally eliminated from the serum by haemodialysis or haemofiltration. Therefore treatment of acute intoxication with PAM TRAMADOL CAPSULES with haemodialysis or haemofiltration alone is not suitable for detoxification.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Analgesics ATC code: N02AJ13

ANALGESICS

Tramadol is an opioid analgesic that acts on the central nervous system. Tramadol is a pure non selective agonists of the μ, δ, and κ opioid receptors with a higher affinity for the μ receptors. Other mechanisms which contribute to its analgesic effect are inhibition of neuronal reuptake of noradrenaline and enhancement of serotonin release. Tramadol has an antitussive effect. Unlike morphine, a broad range of analgesic doses of tramadol has no respiratory depressant effect. Similarly, the gastro-intestinal motility is not modified. The cardiovascular effects are generally slight. The potency of tramadol is considered to be one-tenth to one-sixth that of morphine.

The precise mechanism of the analgesic properties of paracetamol is unknown and may involve central and peripheral effects.

PAM TRAMADOL CAPSULES is positioned as a step II analgesic in the WHO pain ladder and should be utilised accordingly by the physician.

5.2 Pharmacokinetic properties

Tramadol hydrochloride is administered in racemic form and the [-] and [+] forms of tramadol and its metabolite M1, are detected in the blood. After a single oral administration of a tramadol hydrochloride, mean peak plasma concentration of 94.1 ng/ml for racemic tramadol is reached after 1.1 h. The mean terminal phase half-life are 5.7 h for racemic tramadol.

During pharmacokinetic studies in healthy volunteers after single and repeated oral administration of PAM TRAMADOL CAPSULES, no clinical significant change was observed in the kinetic parameters of the active ingredient.

Absorption:

Racemic tramadol is rapidly and almost completely absorbed after oral administration. The mean absolute bioavailability of a single 100 mg dose is approximately 75%. After repeated administration, the bioavailability is increased and reaches approximately 90%.

The oral administration of PAM TRAMADOL CAPSULES with food has no significant effect on the peak plasma concentration or extent of absorption of either tramadol so that PAM TRAMADOL CAPSULES can be taken independently of meal times.

Distribution:

Tramadol has a high tissue affinity. 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 is extensively metabolized after oral administration. About 30% of the dose is excreted in urine as unchanged drug, whereas 60% of the dose is excreted as metabolites.

Tramadol is metabolised through O-demethylation (catalysed by the enzyme CYP2D6) to the metabolite M1, and through N-demethylation (catalysed by CYP3A) to the metabolite M2. M1 is further metabolised through N-demethylation and by conjugation with glucuronic acid. The plasma elimination half-life of M1 is 7 hours. The metabolite M1 has analgesic properties and is more potent than the parent drug. The plasma concentrations of M1 are several-fold lower than that of tramadol and the contribution to the clinical effect is unlikely to change on multiple dosing.

Elimination:

Tramadol and its metabolites are eliminated mainly by the kidneys.

6. Pharmaceutical particulars

6.1 List of excipients

Microcrystalline cellulose, Sodium starch glycolate, Lactose monohydrate.

6.4 Special precautions for storage

Store below 30°C. Protect form moisture and light. Keep out of reach & sight of children.

6.5 Nature and contents of container

Finished product is packed in Aluminium/PVC foil contain 1 strip of 10 capsules. - Such 2 Strips packed in carton along with pack insert

6.6 Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorisation holder and Manufacturing Site Addresses

Plot No 5, Sector 2, Block A, South Akwapim District

P. O. Box 625, Nsawam, Eastern Region, Ghana

Phone No : +233 245 720301

E. Mail : info@pampharma.com

8. Marketing Authorisation Number.

FDA/SD.215-04614

9. Date Of First Authorisation or Renewal

5/1/2026

10. Date Of Revision of the Text.

11/2025