SUMMARY OF PRODUCT CHARACTERISTICS

1. **Name of the medicinal product**

SUPRIDOL

(Tramadol Injection BP)

Strength

50 mg/ml – 2 ml

2. **Qualitative and quantitative composition**

Sr. No.	Particulars	Grade	Qty./ml	Overages	Function
1.	Tramadol Hydrochloride	BP	50mg	3%	Active

For Full list of Excipients Refer section 6.1

3. **Pharmaceutical form**

A clear colourless solution.

4. **Clinical Particulars**

4.1 Therapeutic indications

Tramadol hydrochloride indicated for the management (treatment and prevention) of moderate to severe pain.

4.2 Posology and method of administration

As with all analgesic drugs, the dose of Tramadol should be adjusted according the severity of the pain and clinical responses of the individual patient.

Adults and children aged 14 years and above

Parenteral Administration :

Tramadol injection may be administered intramuscularly, by slow intravenous injection, or diluted in solution for administration by infusion or patients controlled analgesia.The usual dose is 50 or 100 mg 4-6 hourly by the intravenous or intramuscular route. Dosage should be adjusted according to pain severity and response.Intravenous injection must be given slowly over 2-3 minutes.For postoperative pain administer an initial bolus of 100mg.

During the 90 minutes following the initial bolus, further dose of 50 mg may be given every 30 minutes, up to a total of 250 mg including the initial bolus, Subsequent doses should be 50mg or 100mg 4-6 hourly up to a total daily dose of 600 mg.

Oral Administration:

DOSAGE AND DIRECTIONS FOR USE :

The dosage should be adjusted to the intensity of pain and the individual's response to the analgesic action of Tramadol Hydrochloride Capsules. Supridol Capsules should not be used for the treatment of minor pain.

Adults and children over the age of 14 years :

Oral administration : Initial dose of 50 mg, followed by 100 mg twice daily. The dose may be increased to 150 mg or 200 mg twice daily. A total daily dose of more than 400 mg per day must not be exceeded.

Elderly: The usual doses may be used except in patients 75 years of age and over. A downward adjustment of the dose and/or prolongation of the interval between doses are recommended.

Renal impairment : The elimination of SUPRIDOL CAPSULES may be prolonged. The usual initial dose should be used, but for patients with creatinine clearance <30 ml/min, the dosage interval should be increased to 12 hours.

Hepatic impairment : The elimination of SUPRIDOL CAPSULES may be prolonged. The usual initial dose should be used but in severe hepatic impairment, the dosage interval should be increased to 12 hours. Treatment periods should usually be limited and intermittent. Treatment should be given only where there exists a medical need.

Elderly
The usual dosages may be used although it should be noted that in volunteers aged over 75 years the elimination half – life of tramadol was increased by 17% following oral administration.

Renal Impairment/Dialysis
The elimination of tramadol may be prolonged. The usual initial dosage should be used. For patients with creatinine clearance < 30 ml/min, the dosage interval should be increased to 12 hours. Tramadol is not recommended for patients with severe renal impairment (creatinine clearances < 10 ml/min).
As tramadol is only removed very slowly by haemodialysis or haemofiltration, post-dialysis administration to maintain analgesia is not usually necessary.

Hepatic Impairment
The elimination of tramadol may be prolonged. The usual dosage should be used, but in severe hepatic impairment the dosage interval should be increased to 12 hours.

Children under 14 years: Not recommended.

4.3 Contraindications

Tramadol should not be administered to patients who have previously demonstrated hypersensitivity to it or in cases of acute intoxication with alcohol, hypnotics centrally acting analgesics, opioids or psychotropic drugs. In common with other opioid analgesics it should not be administered to patients who are receiving monoamine oxidase inhibitors or within two weeks of their withdrawal.

4.4 Special warnings and precautions for use

Tramadol has been shown to have a low potential to cause physical dependence, however cases of abuse and dependence have occurred.Tramadol is not suitable as a substitute in opioid-dependent patients. Although it is an opioid agonist, Tramadol cannot suppress morphine withdrawal symptoms. Tramadol may cause drowsiness and this effect may be potentiated by alcohol and other CNS depressants. Ambulant patients should be warned not to drive or operate machinery if affected. Tramadol should be used with caution in patients with head

injury, increased intracranial pressure, severe impairment of hepatic and renal function and in patients prone to convulsive disorders or in shock.
Care should be taken when treating patients with respiratory depression, or if concomitant CNS depressant drugs are being administered, as the possibility of respiratory depression cannot be excluded in these situations. At therapeutic doses respiratory depression has infrequently been reported. In one study use of Tramadol during general anaesthesia with enflurane and nitrous oxide was reported to enchance intraoperative recall. Until further information is available use of Tramadol during planes of general anaesthesia should be avoided.

Pharmaceutical Precautions: Tramadol Injection is physically and chemically compatible for up to 24 hours with the following infusion solutions:
4.2% Sodium Bicarbonate
0.9% Sodium Chloride
0.18% Sodium Chloride and 5% Glucose
Sodium Lactate Compound
5% Glucose, Haemaccel and Ringer's Solution
Precipitation will occur if Tramadol Injection is mixed in the same syringe with injections of Diazepam, Diclofenac sodium, Indomethacin, Midazolam and Piroxicam.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant administration of Tramadol with other centrally acting drugs including alcohol may potentiate CNS depressant effects. Simultaneously administration with cimetidine is associated with clinically insignificant changes in serum concentrations of tramadol. Therefore no alteration of the Tramadol dosage regimen is recommended for patients receiving chronic cimetidine therapy. Simultaneous administration of carbamazepine markedly decreases serum concentration of tramadol to an extent that a decrease in analgesic effectiveness and a shorter duration of action may occur. There is a theoretical possibility that tramadol could interact with lithium and 5HT and noradrenaline potentiating anti-depressants due to their respective mechanisms of action. There have been no reports of this potential interaction.

4.6 Pregnancy and lactation:

Fertility, reproductive performance and development of offspring were unaffected, There is inadequate evidence available on the safety of tramadol in human pregnancy, therefore Tramadol should not be used in pregnant women.

LACTATION
Tramadol and its metabolites are found in small amounts in human breast milk. An infant could ingest about 0.1% of the dose given to the mother. Tramadol should not be administered during breast feeding.

4.7 Effects on ability to drive and operate machines

Even when taken according to instructions, tramadol may cause effects such as somnolence and dizziness and therefore may impair the reactions of drivers and machine operators. This applies particularly in conjunction with other psychotropic substances, particularly alcohol.

4.8 Undesirable effects

Rapid intravenous administration may be associated with a higher incidence of adverse effects and therefore should be avoided.

Gastrointestinal System

Nausea, vomiting and occasionally dry mouth.

Central Nervous System And Psychiatric

Tiredness, fatigue, drowsiness, somnolence, dizziness and infrequently headache or respiratory depression. Epileptiform convulsions, which in most instances followed intravenous use, dependence and dysphoria have been rarely reported.

Other Adverse Events

Diaphoresis have been reported. Skin rashes, tachycardia, orthostatic hypotension, increase in blood pressure, bradycardia, flushing, syncope and anaphylaxis have been rarely reported. Cases of blood dyscrasias have been rarely observed during treatment with tramadol, but causality has not been established.

4.9 Overdosage

Symptoms of overdosage are typical of other opioid analgesics, and include miosis, vomiting, cardiovascular collapse, sedation and coma, seizures and respiratory depression.Supportive measures such as maintaining the potency 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 is minimally eliminated from the serum by haemodialysis or haemofiltraton. Therefore treatment of acute intoxication with Tramadol with haemodialysis or haemofiltration alone is not suitable for detoxification.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Tramadol produces analgesia by interacting with specific receptors in the central nervous system i.e. the spinal cord, thalamus and cerebral cortex, where unlike peripheral acting agents, they act indirectly to suppress the painful experience, alters the appreciation or perception and removes the feeling of impending doom. The onset and duration of analgesic action is comparable to morphine and longer than that of codeine and dextropropoxyphene. Tramadol interacts with the opioid receptors (mu, kappa and delta) where it exhibits only agonistic effects. Tramadol is rapidly and completely metabolised and its main active metabolite, O-demethyl tramadol also has analgesic effect. Unlike opiates, Tramadol Hydrochloride has a remarkably low dependence potential.

5.2 Pharmacokinetic properties

Tramadol hydrochloride is readily absorbed following oral administration. Oral bioavailability is approximately 68% after a single dose and increases to 90% at steady state. Onset of action is dose dependent but generally occurs within one hour of dosing, peaking within 2 to 3 hours. Duration of analgesia is about 6 hours. The rate or extent of absorption is not significantly affected by co-administration with food.The bioavailability of tramadol hydrochloride after intramuscular injection or intravenous administration is the same; the mean peak serum concentration is achieved after 45 minutes. Tramadol hydrochloride is primarily metabolized in the liver (90%) with one of its metabolites, mono-Odesmethyltramadol (M1), being 2 to 4 times as potent as the parent compound. Tramadol hydrochloride has a linear pharmacokinetic profile within the therapeutic dosage range. Tramadol hydrochloride and its metabolites are excreted mainly in the urine. The elimination half-life is 5 to 7 hours, but is prolonged in impaired hepatic and renal function. Tramadol hydrochloride crosses the blood-brain and placental barrier. Small amounts are excreted in breast milk unchanged or as the metabolite M1.

5.3 Pre-clinical Safety Data

On repeated oral parenteral administration of tramadol for 6-26 weeks in rats and dogs and oral administration for 12 months in dogs haematological, clinicochemical and histological investigations showed no evidence of any substance-related changes. Central nervous manifestations only occurred after high doses considerably above the therapeutic range: restlessness, salivation, convulsions, and reduced weight gain. Rats and dogs tolerated oral doses of 20mg/kg and 10mg/kg body weight respectively, and dogs rectal doses of 20mg/kg body weight without any reactions. In rats tramadol dosages from 50 mg/kg/day upwards caused toxic effects in dams and raised neonate mortality. In the offspring retardation occurred in the form of ossification disorders and delayed vaginal and eye opening. Male fertility was not affected. After higher doses (from 50 mg/kg/day upwards) females exhibited a reduced pregnancy rate. In rabbits there were toxic effects in dams from 125 mg/kg upwards and skeletal anomalies in the offspring. In some in vitro test systems there was evidence of mutagenic effects. In vivo studies showed no such effects. According to knowledge gained so far, tramadol can be classified as non-mutagenic.Studies on the tumourigenic potential of tramadol hydrochloride have been carried out in rats and mice. The study in rats showed no evidence of any substance-related increase in the incidence of tumours. In the study in mice there was an increased incidence of liver cell adenomas in male animals (a dose-dependent, non-significant increase from 15 mg/kg upwards) and an increase in pulmonary tumours in females of all dosage groups (significant, but not dose-dependent).

6. Pharmaceutical particulars

6.1 List of excipients

Sodium Acetate BP
Water for Injections BP (Bulk)

6.2 Incompatibilities

Precipitation will occur if TRADOL injection is mixed in the same syringe with injections of diazepam, non-steroidal anti-inflammatory drugs and anion-forming drugs. This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6

6.3 Shelf life

24 Months

6.4 Special precautions for storage

Store below 25°C, protected from light. Do not freeze..

6.5 Nature and contents of container

Ampoules Flint 2ml Black band snap off. Such 5 ampoules are packed in a blister such 2 blister packed in an inner printed carton along with direction slip.

6.6 Special Precautions for Handling and Disposal

Chemical and physical in-use stability has been demonstrated for 24 hours at 25°C with the following infusion fluids. 0.9% Sodium Chloride. 0.18% Sodium Chloride and 4% Glucose 5% Glucose Haemaccel For single use only. Any unused product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorization holder:

M/s. NEON LABORATORIES LIMITED
140, Damji Shamji Industrial Complex,
28, Mahal Industrial Estate, M. Caves Road,
Andheri (E), Mumbai – 400 093.
INDIA

8. Marketing Authorization Number (s):

08270/08569/REN/2022

9. Date of first authorization/ Renewal of the authorization:

Date of first authorisation: 26-12-2022

10. Date of revision of the text:

July 2023