WARNING: To be sold by retail on the prescription of Medical Specialist for use in Hospital / Institutional setup only.
SCHEDULE H1 PRESCRIPTION DRUG - CAUTION
- It is dangerous to take this preparation except in accordance with the medical advice.
- Not to be sold by retail without the prescription of a Registered Medical Practitioner.

TAPRISE NS

(Tapentadol Hydrochloride Nasal Spray) टेप्राइज़ एनएस

1. Generic Name

Tapentadol Hydrochloride Nasal Spray 225 mg/ml (22.5 mg/spray)

2. Qualitative and quantitative composition

Tapentadol Hydrochloride Nasal Spray 225 mg/ml

Each Spray (0.1 ml) contains:
Tapentadol Hydrochloride I.P. .....22.5 mg
Preservative:
Benzalkonium Chloride Solution (50%) I.P. .....0.02 %w/v
Excipients .....q.s.

3. Dosage form and strength

Dosage Form: Nasal Spray
Strength: 22.5 mg/Spray

4. Clinical particulars

4.1 Therapeutic indication

TAPRISE NS is indicated for treatment of moderated to severe post- operative pain in hospital admitted patients.

4.2 Posology and method of administration

Posology

As with many centrally-acting analgesic medications, the dosing regimen should be individualized according to the severity of pain being treated, the previous experience with similar drugs and the ability to monitor the patient. Use exactly as prescribed by your doctor. Do not use in larger or smaller amounts or for longer than recommended. Follow the directions as suggested by your physician only.

The recommended dose is 45 mg (one spray in each nostril) every 4-6 hr for a period not exceeding 5 days. Additional one dose of TAPRISE NS may be administered after 1 hr of first dose if adequate pain relief is not attained with the first dose. Your doctor may change your dose after your symptoms improve. Daily doses greater than 315 mg on the first day of therapy and 270mg on subsequent days have not been studied.

Instructions for use:

1. Remove the plastic cap (see figure 1).

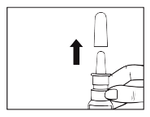


Figure 1

2. Before you use Taprise nasal spray for the first time, prime the pump by pressing downwards 6 times on the shoulders of the white nasal applicator, using your index finger and middle finger, while holding the base of the bottle with your thumb (see figure 2).

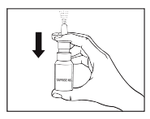


Figure 2

3. Gently blow your nose to clear the nostrils. Insert half of the nasal applicator (about 1 cm) into the nostril tilting it towards outside of your nose, away from the centre (See figure 3) Press down and release the pump once

Figure 3

You may feel slight irritation/burning sensation, which is normal and transient.

Do not breathe deeply after administration.

You may also experience a slightly sweet taste in throat upon dosing.

4.3 Contraindications

TAPRISE NS is contraindicated in:

- patients with hypersensitivity to active substances or to any of the excipients of this product
- situations where active substances with mu-opioid receptor agonist activity are contraindicated, i.e., patients with significant respiratory depression (in unmonitored settings or the absence of resuscitative equipment), and patients with acute or severe bronchial asthma or hypercapnia
- any patient who has or is suspected of having paralytic ileus
- patients who are receiving monoamine oxidase (MAO) inhibitors or who have taken them within the last 14 days due to potential additive effects on norepinephrine levels which may result in adverse cardiovascular events

4.4 Special warnings and precautions for use

Potential for Abuse and Addiction/Dependence Syndrome

TAPRISE NS has a potential for abuse and addiction in a manner similar to other opioid agonists. This should be considered when prescribing or dispensing TAPRISE NS in situations where there is concern about an increased risk of misuse, abuse, addiction, or diversion. Concerns about abuse and addiction should not prevent the proper management of pain. However, all patients treated with mu-opioid agonists require careful monitoring for signs of abuse and addiction.

Generally, tolerance and/or withdrawal are more likely to occur the longer a patient is on continuous opioid therapy. In a safety study where tapentadol HCl was administered up to 90 days, 82.7% of patients who stopped abruptly without initiating alternative therapy and were assessed 2 to 4 days after discontinuation, did not have objective signs of opioid withdrawal. Withdrawal symptoms if any may be reduced by tapering the dose.

Risk from concomitant use of sedating medicinal products such as benzodiazepines or related substances

Concomitant use of TAPRISE NS and sedating medicinal products such as benzodiazepines or related substances may result in sedation, respiratory depression, coma and death. Because of these risks, concomitant prescribing with these sedating medicinal products should be reserved for patients for whom alternative treatment options are not possible. If a decision is made to prescribe TAPRISE NS concomitantly with sedating medicinal products, the reduction of dose of one or both agents should be considered and the duration of the concomitant treatment should be as short as possible. The patients should be followed closely for signs and symptoms of respiratory depression and sedation. In this respect, it is strongly recommended to inform patients and their caregivers to be aware of these symptoms (see section Drugs interactions).

Respiratory Depression

At high doses or in mu-opioid receptor agonist sensitive patients, TAPRISE NS may produce dose-related respiratory depression. Therefore, TAPRISE NS should be administered with caution to patients with impaired respiratory functions. Alternative non-mu-opioid receptor agonist analgesics should be considered and TAPRISE NS should be employed only under careful medical supervision at the lowest effective dose in such patients. If respiratory depression occurs, it should be treated as any mu-opioid receptor agonist-induced respiratory depression (see section Overdose).

Head Injury and Increased Intracranial Pressure

TAPRISE NS should not be used in patients who may be particularly susceptible to the intracranial effects of carbon dioxide retention such as those with evidence of increased intracranial pressure, impaired consciousness, or coma. Analgesics with mu-opioid receptor agonist activity may obscure the clinical course of patients with head injury. TAPRISE NS should be used with caution in patients with head injury and intracranial lesions.

Seizures

Tapentadol HCl has not been systematically evaluated in patients with a seizure disorder, and such patients were excluded from clinical studies. TAPRISE NS should be prescribed with care in patients with a history of a seizure disorder or any condition that would put the patient at risk of seizures.

Renal Impairment

TAPRISE NS has not been studied in controlled efficacy trials in patients with severe renal impairment, therefore the use in this population is not recommended.

Hepatic Impairment

Subjects with hepatic impairment show higher serum concentrations than in those with normal hepatic function hence TAPRISE NS should be used with caution in patients with moderate hepatic impairment, especially upon initiation of treatment.

TAPRISE NS has not been studied in patients with severe hepatic impairment and therefore, use in this population is not recommended.

Use in Pancreatic/Biliary Tract Disease

No difference in the risk of pancreatitis complications or clinically serious adverse events between opioids and other analgesia options have been reported in independent small studies. Mu-opioid receptor agonist activity may cause spasm of the sphincter of Oddi. However mu opioid agonists like tapentadol HCl have been used patients with biliary tract disease, including acute pancreatitis with individual dose titration.

Mixed opioid agonists/antagonists

Care should be taken when combining TAPRISE NS with mixed mu-opioid agonist/antagonists (like pentazocine, nalbuphine) or partial mu-opioid agonists (like buprenorphine). In patients maintained on buprenorphine for the treatment of opioid dependence, alternative treatment options (like e.g. temporary buprenorphine discontinuation) should be considered, if administration of full mu-agonists (like tapentadol HCl) becomes necessary in acute pain situations. On combined use with buprenorphine, higher dose requirements for full mu-receptor agonists have been reported and close monitoring of adverse events such as respiratory depression is required in such circumstances.

4.5 Drugs interactions

Sedative medicines such as benzodiazepines or related drugs

Depression Patients receiving other mu-opioid agonist analgesics, general anesthetics, phenothiazines, other tranquilizers, sedatives, hypnotics, or other CNS depressants (including alcohol) concomitantly with TAPRISE NS may exhibit additive CNS depression. When such combined therapy is contemplated, a dose reduction of one or both agents should be considered (see section Special warnings and precautions for use).

Mixed opioid agonists/antagonists

Care should be taken when combining TAPRISE NS with mixed mu-opioid agonist/antagonists (like pentazocine, nalbuphine) or partial mu-opioid agonists (like buprenorphine) (see also section Special warnings and precautions for use).

Serotonin Syndrome Risk

The development of a potentially life-threatening serotonin syndrome may occur, particularly with concomitant use of serotonergic drugs such as Selective Serotonin Reuptake Inhibitors (SSRIs), SNRIs, tricyclic antidepressants (TCAs), MAOIs and triptans, and with drugs that impair metabolism of serotonin (including MAOIs). This may occur within the recommended dose. Serotonin syndrome may include mental-status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular aberrations (e.g., hyperreflexia, incoordination) and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea). Withdrawal of the serotoninergic medicinal products usually brings about a rapid improvement. Treatment depends on the nature and severity of the symptoms.

The major elimination pathway for tapentadol HCl is conjugation with glucuronic acid mediated via uridine diphosphate transferase (UGT) mainly UGT1A6, UGT1A9 and UGT2B7 isoforms. Thus, concomitant administration with strong inhibitors of these isoenzymes may lead to increased systemic exposure of tapentadol HCl.

For patients on tapentadol HCl treatment, caution should be exercised if concomitant drug administration of strong enzyme inducing drugs (e.g. rifampicin, phenobarbital, St John's Wort (hypericum perforatum)) starts or stops, since this may lead to decreased efficacy or risk for adverse effects, respectively

4.6 Use in special populations

Pregnancy

There is very limited amount of data from the use in pregnant women.

Reported studies in animals have not shown teratogenic effects. However, delayed development and embryotoxicity were observed at doses resulting in exaggerated pharmacology (mu-opioid-related CNS effects related to dosing above the therapeutic range).

TAPRISE NS should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

Labour and Delivery

The effect of tapentadol HCl on labour and delivery in humans is unknown. TAPRISE NS is not recommended for use in women during and immediately before labour and delivery. Due to the mu-opioid receptor agonist activity of tapentadol HCl, newborn infants whose mothers have been taking tapentadol HCl should be monitored for respiratory depression.

Lactation

There is no information on the excretion of tapentadol HCl in human milk. From a reported study in rat pups suckled by dams dosed with tapentadol HCl it was concluded that tapentadol HCl is excreted in milk. Therefore, a risk to the suckling child cannot be excluded. TAPRISE NS should not be used during breast feeding.

4.7 Effects on ability to drive and use machines

TAPRISE NS may have major influence on the ability to drive and use machines, because it may adversely affect central nervous system functions (see section Undesirable effects). This has to be expected especially at the beginning of treatment, when any change of dosage occur as well as in connection with the use of alcohol or tranquilisers (see section Special warnings and precautions for use). Patients should be cautioned as to whether driving or use of machines is permitted.

4.8 Undesirable effects

Summary of the safety profile

The efficacy and safety of oral tapentadol HCl in the treatment of moderate to severe acute pain has been established in randomized, double-blind, placebo- and active-controlled studies of moderate to severe acute pain from first metatarsal bunionectomy and chronic pain from end-stage degenerative joint disease.

Safety and tolerability of TAPRISE NS over a dose range of 17.5 mg to 45 mg has been established in a single and multiple ascending dose phase 1 study conducted in healthy human subjects. There was no serious AE reported in the study and all the AEs reported were mild to moderate in nature. The most frequently reported AEs were rhinorrhea observed after endoscopic evaluation, heart rate decreased and somnolence. Other AEs reported were isolated instances of burning sensation, nasal discomfort, nasal inflammation, post nasal drip, oropharyngeal pain, nasal crusting, nasal obstruction, sneezing, throat irritation, nasopharyngitis, dizziness, vomiting and pyrexia There were no abnormalities observed in ECG, blood pressure, respiratory rate, SpO2, physical examination parameters and laboratory assessment. Tapentadol HCl NS was found to be safe and well tolerated.

The safety of TAPRISE NS has also been evaluated in a phase 3 clinical study conducted in patients with post-operative moderate to severe pain. No incidences of deaths or SAE were observed with the use of TAPRISE NS and majority of AEs observed were mild in severity and were unlikely to be related to study drug treatment. The number of AEs were comparable between the two treatment groups. Almost all the AEs were reported as recovered except 1 AE of anaemia where outcome was unknown.

The most commonly reported TEAEs with TAPRISE NS included vomiting, nausea, headache, pyrexia, ALT increased, AST increased and GGT increased..

Summary of adverse reactions

Adverse drug reactions (ADRs) based upon pooled data are shown by system organ class and by preferred term are listed below.

Gastrointestinal disorders: Vomiting, Nausea, Constipation, Gastroesophageal reflux disease*
Nervous system disorders: Headache, Somnolence*, Hypoaesthesia*
Vascular disorders: Hypertension*
Psychiatric disorders: Sleep disorder*
Respiratory, thoracic and mediastinal disorders: Nasal discomfort, Nasal crusting, Epistaxis*, Nasal pruritus
Skin and subcutaneous tissue disorders: Pruritus*, Pruritus generalised*
Cardiac disorders: Tachycardia*
Infections and infestations: Postoperative wound infection*
Renal and urinary disorders: Dysuria*
General disorders and administration site conditions: Pyrexia
Investigations: ALT increased*, AST increased*, GGT increased*, Blood glucose increased*, Glucose urine present*
*Treatment Emergent Adverse Events (TEAEs) observed during study were not necessarily causality related to TAPRISE NS.

Table 1: Adverse drug reactions that were identified from reported clinical trials

Display of adverse events in phase 1 multiple ascending dose clinical trial

		Dose level and treatment N(%)				Total	
System Organ Class	**Preferred Term (MedDRA)**	**22.5 mg /0.1 ml in one nostril**		**22.5 mg /0.1 ml in both nostrils**		**Active N=20**	**Placebo N=04**
		A N=10	**P N=02**	**A N=10**	**P N=02**		
Respiratory, thoracic and mediastinal disorder	Rhinorrhea	6 (60)	-	5 (50)	-	11 (55)	-
	Nasal discomfort	-	-	2 (20)	-	2 (10)	-
	Nasal inflammation	-	-	1 (10)	-	1 (5)	-
Nervous system disorder	dizziness	-	-	1 (10)	-	1 (5)	-
Gastrointestinal system disorder	vomiting	-	-	1 (10)	-	1 (5)	-

Table 2: Summary of TEAEs in ≥2% Patients in phase 3 clinical trial

System Organ Class/ Preferred Term	Tapentadol HCl (N=149)	Tramadol HCl (N=145)	Total (N=294)
Patients with at least 1 TEAE	36 (24.2) [59]	28 (19.3) [46]	64 (21.8) [105]
Gastrointestinal Disorders	11 (7.4) [14]	11 (7.6) [17]	22 (7.5) [31]
Vomiting	7 (4.7) [7]	9 (6.2) [9]	16 (5.4) [16]
Nausea	5 (3.4) [5]	5 (3.4) [5]	10 (3.4) [10]
Investigations	6 (4.0) [15]	2 (1.4) [7]	8 (2.7) [22]
ALT increased	5 (3.4) [5]	2 (1.4) [2]	7 (2.4) [7]
AST increased	4 (2.7) [4]	2 (1.4) [2]	6 (2.0) [6]
GGT increased	4 (2.7) [4]	2 (1.4) [2]	6 (2.0) [6]
General Disorders And Administration Site Conditions	4 (2.7) [4]	8 (5.5) [9]	12 (4.1) [13]
Pyrexia	4 (2.7) [4]	8 (5.5) [9]	12 (4.1) [13]
Nervous System Disorders	9 (6.0) [10]	3 (2.1) [3]	12 (4.1) [13]
Headache	5 (3.4) [5]	2 (1.4) [2]	7 (2.4) [7]

ALT=alanine aminotransferase, AST=aspartate aminotransferase, GGT=gamma-glutamyl aminotransferase, MedDRA=Medical Dictionary for Regulatory Activities, PT=preferred term, SOC=system organ class, TEAE=treatment-emergent adverse event.
Note 1: SOC and PT are coded using the MedDRA Version 22.
Note 2: TEAEs are represented as Patient count (Percentage of patients) [Event Count].

- **Reporting of side effects**
  If you get any 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 directly via any point of contact of Torrent Pharma available at: http://www.torrentpharma.com/Index.php/site/info/adverse_event_reporting.

4.9 Overdose

Symptoms

Human experience with overdose of tapentadol HCl is very limited. Reported preclinical data suggest that symptoms similar to those of other centrally acting analgesics with mu-opioid receptor agonist activity are to be expected upon intoxication with tapentadol HCl. In principle, these symptoms include, referring to the clinical setting, in particular miosis, vomiting, cardiovascular collapse, consciousness disorders up to coma, convulsions and respiratory depression up to respiratory arrest.

Management

Management of overdose should be focused on treating symptoms of mu-opioid agonism. Primary attention should be given to re-establishment of a patent airway and institution of assisted or controlled ventilation when overdose of tapentadol HCl is suspected. Pure opioid receptor antagonist such as naloxone is specific antidote to respiratory depression resulting from opioid overdose. Respiratory depression following an overdose may outlast the duration of action of the opioid receptor antagonist. Administration of an opioid receptor antagonist is not a substitute for continuous monitoring of airway, breathing, and circulation following an opioid overdose. If the response to opioid receptor antagonists is suboptimal or only brief in nature, an additional dose of antagonist (e.g. naloxone) should be administered as directed by the manufacturer of the product.

5. Pharmacological properties

5.1 Mechanism of Action

Tapentadol HCl is a centrally-acting synthetic analgesic. Although its exact mechanism is unknown, analgesic efficacy is thought to be due to mu-opioid agonist activity and the inhibition of norepinephrine reuptake.

5.2 Pharmacodynamic properties

Tapentadol HCl is a centrally-acting synthetic analgesic. It is 18 times less potent than morphine in binding to the human mu-opioid receptor and is 2-3 times less potent in producing analgesia in animal models. Tapentadol HCl has been shown to inhibit norepinephrine reuptake in the brains of rats resulting in increased norepinephrine concentrations. In preclinical models, the analgesic activity due to the mu-opioid receptor agonist activity of tapentadol HCl can be antagonized by selective mu-opioid antagonists (e.g., naloxone), whereas the norepinephrine reuptake inhibition is sensitive to norepinephrine modulators. Tapentadol HCl exerts its analgesic effects without a pharmacologically active metabolite.

Effects on the cardiovascular system: Reportedly, there was no effect of therapeutic and supratherapeutic doses of tapentadol HCl on the QT interval. In a reported randomized, double-blind, placebo- and positive-controlled crossover study, healthy subjects were administered five consecutive doses of Tapentadol HCl 100 mg every 6 hr, Tapentadol HCl 150 mg every 6 hr, placebo and a single oral dose of moxifloxacin. Similarly, Tapentadol HCl had no relevant effect on other ECG parameters (heart rate, PR interval, QRS duration, T-wave or U-wave morphology).

Clinical Studies

The efficacy and safety of TAPRISE NS 22.5 mg and 45 mg in comparison to Tramadol IR capsule and IV injection has been evaluated in 294 patients with post-operative moderate to severe pain in a phase 3 multi-centric, randomized, comparative clinical trial.

TAPRISE NS was found to be non-inferior to Tramadol IV on Pain Intensity Difference (PID) at 60 minutes and Patient Global Assessment (PGA) at 24 hour. The Sum of Pain Intensity Difference (SPID) at 60 minutes, 24 hrs, 26 hrs, 28 hrs, and 120 hrs achieved with TAPRISE NS was comparable to Tramadol oral. The median time to onset of pain relief was not significantly different between TAPRISE NS and Tramadol oral, however a more consistent relief was seen with TAPRISE NS. The proportion of patients who required rescue medication for nausea and vomiting was also similar between the two treatment groups. Overall, TAPRISE NS was found to be non-inferior to Tramadol IV and produced same degree of pain relief as seen with Tramadol IV.

5.3 Pharmacokinetic properties

Pharmacokinetics and dose proportionality of TAPRISE NS over a dose range of 17.5 mg to 45 mg has been evaluated in phase 1 single and multiple ascending dose study in healthy human subjects. The rate and extent of absorption of tapentadol HCl obtained from intra-nasal route showed higher bioavailability and early T_{max} as compared to oral route. $AUC_{(0-6)}$, C_{max} and Cavg of TAPRISE NS 22.5 mg and 45 mg was within the therapeutic range of reported AUC (0-6), C_{max} and C_{avg} of approved strengths of oral Tapentadol HCl 50 mg and 100 mg, respectively.

The range obtained for $AUC_{(0-6h)}$, C_{max} and C_{avg} with TAPRISE NS 22.5 mg at steady state was 104 to 207 hr*ng/mL, 22 to 64 ng/mL and 17 to 35 ng/mL respectively, as compared to 76 to 310 hr*ng/mL, 22 to 78 ng/mL and 13 to 52 ng/mL, respectively obtained with oral Tapentadol HCl 50 mg. The results for AUC(0-6h), C_{max} and Cavg with TAPRISE NS 45 mg at steady state were 247 to 569 hr*ng/mL, 56 to 128 ng/mL and 41 to 95 ng/mL, respectively as compared to oral Tapentadol HCl 100 mg, which ranged from 248 to 740 hr*ng/mL for $AUC_{(0-6h)}$, 52 to 184 ng/mL for C_{max} and 41 to 123 ng/mL for Cavg.

The median T_{max} after nasal administration ranged from 0.12 to 1.01 hr indicating rapid absorption compared to 1.00 to 4.00 hr with oral dose.The mean elimination half-life ranged between 3.66 and 4.39 hr following single and multiple intranasal dose administration, which were well within the range produced with IR Tablet.

Tapentadol HCl is widely distributed throughout the body, the volume of distribution (Vz) for Tapentadol HCl is 540 +/- 98 L. The plasma protein binding is low and amounts to approximately 20%.

In humans, the metabolism of Tapentadol HCl is extensive. About 97% of the parent compound is metabolized. Tapentadol HCl is mainly metabolized via Phase II pathways, and only a small amount is metabolized by Phase 1 oxidative pathways. The major pathway of Tapentadol HCl metabolism is conjugation with glucuronic acid to produce glucuronides. Approximately 70% (55% O-glucuronide and 15% sulfate of Tapentadol HCl) of the dose is excreted in urine in the conjugated form. A total of 3% of drug was excreted in urine as unchanged drug. Tapentadol HCl is additionally metabolized to N-desmethyl Tapentadol HCl (13%) by CYP2C9 and CYP2C19 and to hydroxy Tapentadol HCl (2%) by CYP2D6, which are further metabolized by conjugation. Therefore, drug metabolism mediated by cytochrome P450 system is of less importance than Phase II conjugation.

None of the metabolites contributes to the analgesic activity.

Tapentadol HCl and its metabolites are excreted almost exclusively (99%) via the kidneys. The terminal half-life is on average 4 hr after oral administration. The total clearance is 1530 +/- 177 ml/min.

6 Nonclinical properties

6.1 Animal Toxicology or Pharmacology

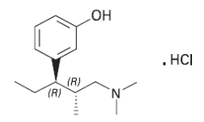
Pre-clinical studies showed that tapentadol HCl is absorbed rapidly (0.13 hr) intra-nasally compared to oral dose (1.63 hr) in NZW rabbits with same plasma exposure. Tapentadol HCl formulation in normal saline instillation was found nonirritant to nasal mucosa after multiple repeated administration. In repeat dose toxicity study in rats, the No Observed Adverse Effect Level (NOAEL) in "2 Week Repeated Multiple Dose Intra-Nasal Toxicity and Toxicokinetics Study of Tapentadol HCl in Wistar rats" is considered to be 32 mg/kg/day (5.4 mg/day) In a four week repeat dose toxicity study in non-rodent species, rabbit, 100.8 mg/day (40 mg/kg/day) dose level of Tapentadol HCl was established as the NOAEL.

7 Description

Tapentadol Hydrochloride is centrally acting analgesic having both mu-opioid receptor agonist and noradrenaline (norepinephrine) reuptake inhibition activity with minimal serotonin reuptake inhibition.

Chemical name: 3-[(1R,2R)-3-(dimethylamino)-1-ethyl-2methylpropyl] phenol monohydrochloride

Structure:



. HCl

a) Empirical Formula: $C_{14}H_{23}NO.HCL$
b) Molecular Weight: 257.80
c) Appearance & Properties: White to off white powder
d) Solubility: Freely Soluble in methanol and water
e) Hygroscopic Properties: Slightly hygroscopic
f) Melting Point, boiling point: Between 198-208°C
g) pKa (acid-base dissociation constant) other characteristic values: 9.34 and 10.45
h) Specific Rotation: Between -24.5° and -28.5°
i) Polymorphic Form (XRPD): Crystalline Form
j) Stability: Tapentadol Hydrochloride is reported to be a stable compound at room temperature.

8 Pharmaceutical particulars

8.1 Incompatibilities

None Stated

8.2 Shelf-life

Do not use later than the date of expiry.

8.3 Packaging information

10ml, HDPE Vial Snap fit with nasal spray pump of 100µl & fitted with actuator and cap

9 Patient Counselling Information

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 9.4.

What is in this leaflet:

9.1 What TAPRISE NS is and what it is used for

The full name of your medicine is 'Tapentadol Hydrochloride Nasal Spray'. It is referred to as 'TAPRISE NS' in the rest of this leaflet.

Tapentadol Hydrochloride - the active substance in TAPRISE NS - is a strong painkiller which belongs to the class of opioids. TAPRISE NS is used for treatment of moderated to severe post- operative pain in hospital admitted patients.

9.2 What you need to know before you use TAPRISE NS

Do not take TAPRISE NS

- if you are allergic to Tapentadol HCl or any of the other ingredients of this medicine
- if you have asthma or if your breathing is dangerously slow or shallow (respiratory depression, hypercapnia)
- if you have no bowel movement as shown by severe constipation and bloating which may be accompanied by pain or discomfort in the lower stomach
- if you are on monoamine oxidase inhibitors (MAOIs – certain medicines for the treatment of depression) or have taken these during the last 14 days.

Warnings and precautions

Talk to your doctor before taking TAPRISE NS if you:

- have slow or shallow breathing
- suffer from increased pressure in the brain or are not fully conscious
- have had a head injury or brain tumors
- suffer from liver or kidney problems
- suffer from a pancreatic disease including inflammation of the pancreas (pancreatitis) or disease of the bile duct (biliary tract disease)
- are taking medicines referred to as mixed opioid agonist/antagonists (e.g., pentazocine, nalbuphine) or partial mu-opioid agonists (e.g. buprenorphine)
- have a tendency towards epilepsy or fits or if you are taking other medicines known to increase the risk of seizures because the risk of a fit may increase.
- have a tendency to abuse medicines or if you are dependent on medicines, as TAPRISE NS may lead to addiction. In this case, you should only take TAPRISE NS for short periods of time and under strict medical supervision.

Other medicines and TAPRISE NS

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Your doctor will tell you which medicines are safe to take with TAPRISE NS.

- The risk of side effects increases if you are taking medicines which may cause convulsions (fits), such as certain antidepressants or antipsychotics. The risk of having a fit may increase if you take TAPRISE NS at the same time. Your doctor will tell you whether TAPRISE NS is suitable for you.
- Concomitant use of TAPRISE NS and sedative medicines such as benzodiazepines or related drugs (certain sleeping pills or tranquillizers (e.g. barbiturates) or pain relievers such as opioids, morphine and codeine (also as cough medicine), antipsychotics, H1-antihistamines, alcohol) increases the risk of drowsiness, difficulties in breathing (respiratory depression), coma and may be life-threatening. Because of this, concomitant use should only be considered when other treatment options are not possible. However if your doctor does prescribe TAPRISE NS together with sedative medicines the dose and duration of concomitant treatment should be limited by your doctor. Please tell your doctor about all sedative medicines you are taking, and follow your doctor's dose recommendation closely. It could be helpful to inform friends or relatives to be aware of the signs and symptoms stated above. Contact your doctor when experiencing such symptoms.
- If you are taking a type of medicine that affects serotonin levels (e.g. certain medicines to treat depression), speak to your doctor before taking TAPRISE NS as there have been cases of "serotonin syndrome". Serotonin syndrome is a rare, but life-threatening condition. The signs include involuntary, rhythmic contractions of muscles, including the muscles that control movement of the eye, agitation, excessive sweating, tremor, exaggeration of reflexes, increased muscle tension and body temperature above 38°C. Your doctor can advise you on this.
- TAPRISE NS may not work as well if taken with opioid like medicines (e.g. those containing pentazocine, nalbuphine or buprenorphine). Tell your doctor if you are currently being treated with one of these medicines.
- Taking TAPRISE NS with products (e.g. rifampicin, phenobarbital or St John's Wort) that affect the enzymes required to remove TAPRISE NS from the body, may affect how well TAPRISE NS works or may cause side effects. The effects may occur especially when the other medication is started or stopped.

Please keep your doctor informed about all medicines you are taking.

Taking TAPRISE NS with food, drink and alcohol

Do not drink alcohol whilst you are on TAPRISE NS, because some side effects such as drowsiness may be increased. You can take TAPRISE NS with or without food.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Do not take TAPRISE NS:

- if you are pregnant, unless your doctor has instructed you to do so
- if you become pregnant during treatment with TAPRISE NS. Check with your doctor.
- during childbirth, as it could lead to dangerously slow or shallow breathing (respiratory depression)
- in the newborn
- if you are breast-feeding, as it may pass into the breast milk.

Driving and using machines

If you feel drowsy, dizzy, have blurred vision or a slow reaction time whilst taking TAPRISE NS, then do not drive, use tools or machinery.

Any such effects are more likely to occur when you start taking TAPRISE NS, when the dose of TAPRISE NS is changed, or when you drink alcohol or take tranquilizers.

Please ask your doctor before driving a car or using machinery.

9.3 How to use TAPRISE NS

Use exactly as prescribed by your doctor. Do not use in larger or smaller amounts or for longer than recommended. Follow the directions as suggested by your physician only.

The recommended dose is 45 mg (one spray in each nostril) every 4-6 hr for a period not exceeding 5 days. Additional one dose of TAPRISE NS may be administered after 1 hr of first dose if adequate pain relief is not attained with the first dose. Your doctor may change your dose after your symptoms improve. Daily doses greater than 315 mg on the first day of therapy and 270mg on subsequent days have not been studied.

Instructions for use:

1. Remove the plastic cap (see figure 1).

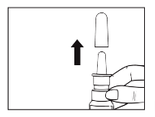


Figure 1

2. Before you use Taprise nasal spray for the first time, prime the pump by pressing downwards 6 times on the shoulders of the white nasal applicator, using your index finger and middle finger, while holding the base of the bottle with your thumb (see figure 2).

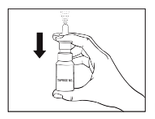


Figure 2

3. Gently blow your nose to clear the nostrils. Insert half of the nasal applicator (about 1 cm) into the nostril tilting it towards outside of your nose, away from the centre (See figure 3) Press down and release the pump once.

Figure 3

You may feel slight irritation/burning sensation, which is normal and transient.

Do not breathe deeply after administration.

You may also experience a slightly sweet taste in throat upon dosing.

You should not take more TAPRISE NS than the recommended dose.
Taking too much TAPRISE NS may be life-threatening.
Immediate medical advice should be sought in the event of an overdose, even if you feel well.

Very high doses of TAPRISE NS may cause the following:

- pin-point pupils in the eyes
- being sick (vomiting)
- drop in blood pressure
- fast heart beat
- altered consciousness, collapse or deep unconsciousness (coma)
- epileptic fits
- dangerously slow or shallow breathing or stopping breathing.

If you forget to take TAPRISE NS

If you forget to take the dose of TAPRISE NS, your pain is likely to return. Do not take a double dose to make up for a forgotten dose; simply continue taking the TAPRISE NS as before.

If you stop taking TAPRISE NS

If you interrupt or stop treatment too soon, your pain is likely to return. If you wish to stop treatment, please tell your doctor first before stopping treatment.

Generally there will be no withdrawal effects when treatment is stopped. However, on uncommon occasions, people who have been taking TAPRISE NS for some time may feel unwell if they suddenly stop taking them.

Symptoms may be:

- feeling restless, irritable, anxious, weak or sick (nausea), loss of appetite, being sick (vomiting),
- diarrhoea
- watery eyes, runny nose, increase in size of the pupils in the eyes (dilated pupils)
- difficulty in sleeping, yawning
- sweating, shivering
- muscle or joint pain, backache, abdominal cramps
- increase in blood pressure, breathing or heart rate.

If you experience any of these complaints after stopping TAPRISE NS, please contact your doctor.

Do not stop taking this medicine unless your doctor tells you to. If your doctor wants you to stop taking TAPRISE NS, he/she will tell you how to do this. This may include a gradual reduction of the dose.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

9.4 Possible Side Effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

- Feeling sick (Nausea)
- Being sick (Vomiting)
- Constipation
- Headache
- Nasal discomfort
- Dryness in nose(Nasal crusting)
- Itching in nose (Nasal pruritus)
- Fever (Pyrexia)
- **Reporting of side effects**

If you get any 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 directly via any point of contact of Torrent Pharma available at: http://www.torrentpharma.com/Index.php/site/info/adverse_event_reporting.

By reporting side effects, you can help provide more information on the safety of this medicine.

9.5 How to store TAPRISE NS

Store below 30°C in upright condition

Do not use TAPRISE NS after the expiry date.

9.6 Contents of the pack and other information

What TAPRISE NS contains:

The active substance is Tapentadol Hydrochloride.

The excipients are Hypromellose (6cps), Poloxamer 188, Neotame, Benzalkonium Chloride, Spearmint supreme (Novamint spearmint flavour).

10 Details of manufacturer

M/s Torrent Pharmaceuticals Limited,
C/o M/s Biodeal Pharmaceuticals Pvt. Ltd.,
Village Sainimajra, Nalagarh-Ropar Road,
Nalagarh, Dist: Solan, HP.

11 Details of permission or licence number with date

L/13/1225/MNB dated 18-08-2025

12 Date of revision

Aug-2025

TORRENT PHARMA

Manufactured by:
TORRENT PHARMACEUTICALS LTD., INDIA.
At: Village: Saini Majra, Nalagarh-Ropar Road,
Nalagarh, Dist.: Solan (HP) 174101., INDIA.

IN/TAPRISE NS 22.5 mg/0.1 ml/Aug-2025/04/PI

European Patent Number: EP2753302B1
Indian Patent Number: IN355890

8105277

PRODUCT NAME :	TAPRISE NS	**COUNTRY :** Domestic LL	**LOCATION :** -	**Supercedes A/W No. :**			
ITEM / PACK :	PIL	**NO. OF COLORS :** 3	**REMARK :**				
DESIGN STYLE :	Front / Back	**PANTONE SHADE NOS.:**	**SUBSTRATE :**				
CODE :	8105277	485 C	**Activities**	**Department**	**Name**	**Signature**	**Date**
DIMENSIONS (MM) :	180 x 440 mm	432 C	Prepared By	**Pkg.Dev**			
ART WORK SIZE :	S/S	Black	Reviewed By	**Pkg.Dev**			
DATE :	04-12-2025		Reviewed By	**CR**			
			Approved By	**Quality**			
			Approved By	**Quality**			

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