TOPSEA PENTAZOCINE INJECTION BP 30MG/ML

1.3.1. SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. Name of the medicinal product:

TOPSEA PENTAZOCINE INJECTION BP 30MG/ML

2 Qualitative and quantitative composition:

Each ml contains:
PentazocineBP
(Prepared as lactate) 30mg
Water for Injection BP Q.S.

3. Pharmaceutical Form

Injection
A clear colourless solution.

4. Clinical particulars

4.1 Therapeutic indications

TOPSEA PENTAZOCINE INJECTION is indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. TOPSEA PENTAZOCINE INJECTION may also be used for preoperative or preanesthetic medication and as a supplement to surgical anesthesia.

Limitations of Use

Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve TOPSEA PENTAZOCINE INJECTION for use in patients for whom alternative treatment options [e.g., non-opioid analgesics or opioid combination products]:

- Have not been tolerated, or are not expected to be tolerated.
- Have not provided adequate analgesia, or are not expected to provide adequate analgesia.

4.2 Posology and method of administration

Adults, Excluding Patients in Labor

The recommended single parenteral dose is 30 mg by intramuscular, subcutaneous, or intravenous route. This may be repeated every 3 to 4 hours. Doses in excess of 30 mg intravenously or 60 mg intramuscularly or subcutaneously are not recommended. Total daily dosage should not exceed 360 mg. Elderly patients may be more sensitive to the analgesic effects of TOPSEA PENTAZOCINE INJECTION than younger patients. Elderly patients generally should be started on low doses of TOPSEA PENTAZOCINE INJECTION and observed closely.

The subcutaneous route of administration should be used only when necessary because of possible severe tissue damage at injection sites). When frequent injections are needed, the drug should be administered intramuscularly. In addition, constant rotation of injection sites (e.g., the upper outer quadrants of the buttocks, mid-lateral aspects of the thighs, and the deltoid areas) is essential.

Patients in Labor

A single, intramuscular 30 mg dose has been most commonly administered. An intravenous 20 mg dose has given adequate pain relief to some patients in labor when contractions become regular, and this dose may be given two or three times at two- to three-hour intervals, as needed.

Pediatric Patients Excluding Patients Less Than One Year Old

The recommended single parenteral dose as premedication for sedation is 0.5 mg/kg by intramuscular route.

CAUTION: TOPSEA PENTAZOCINE INJECTION should not be mixed in the same syringe with soluble barbiturates because precipitation will occur.

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4.3 Contraindications

TOPSEA PENTAZOCINE INJECTION is contraindicated in patients with:

- Significant respiratory depression.
- Acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitativeequipment.
- Known or suspected gastrointestinal obstruction, including paralytic ileus.
- Hypersensitivity to pentazocine.

4.4 Special warnings and precautions for use

Addiction,Abuse, and Misuse

TOPSEA PENTAZOCINE INJECTION exposes patients and other users to the risks of opioid addiction, abuse, and misuse,whichcanleadto overdose and death. Assess each patient's risk prior to prescribing it, and monitor all patients regularly for the development of these behaviours and conditions.

Life-Threatening Respiratory Depression

Serious, life-threatening, or fatal respiratory depression may occur with use of TOPSEA PENTAZOCINE INJECTION. Monitor for respiratory depression, especially during initiation of TOPSEA PENTAZOCINE INJECTION or following a dose increase.

Neonatal OpioidWithdrawal Syndrome

Prolonged use of TOPSEA PENTAZOCINE INJECTION during pregnancycanresultin neonatal opioidwithdrawal syndrome, which may be life-threatening if not recognizedandtreated, andrequiresmanagementaccording to protocols developed by neonatology experts. Ifopioiduseis required for a prolonged period in a pregnant woman, advise the patient of the riskofneonatal opioidwithdrawal syndrome and ensure that appropriate treatment will be available.

Risks from Concomitant Use with Benzodiazepines or Other CNS Depressants

Concomitantuseofopioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may resultinprofoundsedation, respiratory depression, coma, and death.

- Reserve concomitant prescribing of TOPSEA PENTAZOCINE INJECTION Injection and benzodiazepines or other CNS depressants for use in patients for whom alternative treatment options are in adequate.
- Limit dosages and durations to theminimumrequired.
- Follow patients for signs and symptoms of respiratory depression and sedation.

4.5 Interaction with other medicinal products and other forms of interaction

Table 1 Clinically SignificantDrug Interactions

Interactions with PENTAZOCINE LACTATE INJECTION Benzodiazepines and other Central Nervous System(CNS)Depressants	
Clinical Impact:	Dueto additivepharmacologiceffect, the concomitant useofbenzodiazepines orotherCNSdepressants includingalcohol, increases the risk of respiratory depression, profound sedation, coma, and death.
Intervention:	Reserve concomitant prescribingofthesedrugsforusein patients forwhomalternativetreatment options areinadequate.Limit dosages and durations to the minimum required. Follow patients closelyforsigns of respiratorydepression and sedation.
Examples:	Benzodiazepines and othersedatives/hypnotics, anxiolytics, tranquilizers,muscle relaxants, generalanesthetics, antipsychotics, otheropioids, alcohol.
Serotonergic Drugs	
Clinical Impact:	The concomitant useof opioids with otherdrugs that affect theserotonergicneurotransmitter systemhas resulted in serotonin syndrome.
Intervention:	If concomitant useis warranted, carefullyobservethepatient, particularly duringtreatment initiation and dose adjustment. DiscontinuePENTAZOCINE LACTATE INJECTIONifserotonin syndromeis suspected.
Examples:	Selectiveserotonin reuptakeinhibitors (SSRIs), serotonin and norepinephrine reuptakeinhibitors (SNRIs), tricyclic antidepressants (TCAs), triptans, 5-HT3 receptor antagonists, drugs that effect theserotonin neurotransmitter system (e.g., mirtazapine, trazodone, tramadol), monoamineoxidase (MAO)inhibitors (those intended to treat psychiatricdisorders and also others, such as linezolid and intravenous methyleneblue).
Mixed Agonist/Antagonist and Partial Agonist Opioid Analgesics	
Clinical Impact:	May reducethe analgesic effect ofPENTAZOCINE LACTATE INJECTION and/orprecipitatewithdrawalsymptoms.
Intervention:	Avoid concomitantuse.
Examples:	Butorphanol, nalbuphine,pentazocine, buprenorphine.
Muscle Relaxants	
Clinical Impact:	Pentazocinemay enhancetheneuromuscularblocking action ofskeletal muscle relaxants and produce anincreased degreeof respiratorydepression.
Diuretics	
Clinical Impact:	Opioids can reducethe efficacy ofdiuretics byinducingthe releaseof antidiuretichormone.
Intervention:	Monitorpatients forsigns of diminished diuresis and/or effectson bloodpressure andincrease the dosage of the diuretic asneeded.
PENTAZOCINE LACTATE INJECTION is used concomitantlywith anticholinergicdrugs.	

4.6 Fertility, pregnancy and lactation

Pregnancy:

Prolonged use of opioid analgesics during pregnancy may cause neonatal opioid withdrawal syndrome. Availabledatawith PENTAZOCINE LACTATE INJECTION in pregnant womenareinsufficient to informadrug-associated risk for majorbirth defects andmiscarriage.

In animal reproduction studies, pentazocine administered subcutaneously to pregnant hamsters during the early gestational period produced neural tubedefects (i.e., exencephalyandcranioschisis) at 4.4 times the maximum dailydose. Based on animal data, advisepregnant women ofthepotential risk to a fetus. The estimated backgroundrisk ofmajorbirth defects and miscarriage fortheindicated population is unknown. All pregnancies haveabackground risk ofbirth defect, loss, orother adverseoutcomes.

In theU.S. general population, the estimated backgroundrisk ofmajorbirth defectsand miscarriagein clinicallyrecognized pregnancies is 2-4%and 15-20%, respectively.

Lactation:

Thedevelopmentaland health benefits ofbreastfeedingshould beconsidered alongwith themother's clinical need forPENTAZOCINE LACTATE INJECTIONand anypotential adverse effects on thebreastfed infant from PENTAZOCINE LACTATE INJECTIONor from theunderlyingmaternal condition.

Fertility:

Chronic use of opioids may cause reduced fertility in females and males of reproductive potential. It is not known whether these effects on fertility are reversible.

4.7 Effects on ability to drive and use machines

PENTAZOCINE LACTATE INJECTION may impair the mental or physical abilities needed to perform potentially hazardous activities such as driving a car or operating machinery. Warn patients not to drive or operate dangerous machinery unless they are tolerant to the effects of PENTAZOCINE LACTATE INJECTION and know how they will react to the medication.

4.8 Undesirable effects

The most commonly occurring reactions are: nausea, dizziness or lightheadedness, vomiting, euphoria.

Dermatologic Reactions

Soft tissue induration, nodules, and cutaneous depression can occur at injection sites. Ulceration (sloughing) and severe sclerosis of the skin and subcutaneous tissues (and, rarely, underlying muscle) have been reported after multiple doses. Other reported dermatologic reactions include diaphoresis, sting on injection, flushed skin including plethora, dermatitis including pruritus.

Infrequently occurring reactions are—respiratory: respiratory depression, dyspnea, transient apnea in a small number of newborn infants whose mothers received PENTAZOCINE LACTATE INJECTION during labor; cardiovascular: circulatory depression, shock, hypertension; CNS effects: dizziness, lightheadedness, hallucinations, sedation, euphoria, headache, confusion, disorientation; infrequently weakness, disturbed dreams, insomnia, syncope, visual blurring and focusing difficulty, depression; and rarely tremor, irritability, excitement, tinnitus; gastrointestinal: constipation, dry mouth; other: urinary retention, headache, paresthesia, alterations in rate or strength of uterine contractions during labor.

Rarely reported reactions include—neuromuscular and psychiatric: muscle tremor, insomnia, disorientation, hallucinations; gastrointestinal: taste alteration, diarrhea and cramps; ophthalmic: blurred vision, nystagmus, diplopia, miosis; hematologic: depression of white blood cells (especially granulocytes), which is usually reversible, moderate

transient eosinophilia; other: tachycardia, weakness or faintness, chills; allergic reactions including edema of the face, toxic epidermal necrolysis.

4.9 Overdose

Clinical Presentation

Acuteoverdosewith PENTAZOCINE LACTATE INJECTIONcan bemanifested byrespiratorydepression, somnolenceprogressingto stuporor coma, skeletal muscle flaccidity, cold and clammyskin, constricted pupils, and, in some cases, pulmonaryedema, bradycardia, hypotension, partial or complete airwayobstruction, atypical snoring, and death. Marked mydriasis rather than miosis maybeseen with hypoxiain overdosesituations.

Treatment ofOverdose

Incaseofoverdose, priorities arethereestablishment ofapatentand protected airwayand institutionof assisted or controlled ventilation, ifneeded.

Employothersupportivemeasures (includingoxygen and vasopressors)in themanagement of circulatoryshock and pulmonaryedema as indicated. Cardiacarrest or arrhythmias will require advanced life-supporttechniques.

Inan individual physicallydependent on opioids, administration ofthe recommended usual dosageofthe antagonist will precipitate an acutewithdrawal syndrome. Theseverityofthewithdrawal symptoms experienced will dependon thedegreeofphysicaldependence and thedoseofthe antagonist administered.Ifadecision is madeto treat seriousrespiratorydepression inthephysicallydependentpatient, administration ofthe antagonist should bebegunwith care and bytitration with smallerthan usual doses ofthe antagonist.

5. Pharmacological properties

MechanismofAction

Pentazocineis amixed agonist-antagonist at opioid receptors. Pentazocineis partial agonist at themu opioid receptorand an agonist at thekappaopioid receptor.

5.1 Pharmacodynamic properties

Effects on theCentral Nervous System

Pentazocine produces respiratory depression by direct action on brain stem respiratory centers. The respiratorydepression involves a reduction in the responsiveness of the brain stem respiratory centres to both increases in carbondioxidetension and electrical stimulation.

Pentazocine causes miosis, even in total darkness.Pinpoint pupils are assign of opioid overdose but are not pathognomonic(e.g.,pontinelesions ofhemorrhagicorischemicorigins may produce similar findings). Marked mydriasis rather than miosis may be seen due to hypoxiain overdose situations.

Effects on theGastrointestinal Tract and OtherSmooth Muscle

Pentazocine causesa reduction in motility associated with an increase in smooth muscletone in the antrum of the stomach and duodenum. Digestion of food in thesmall intestineis delayed and propulsive contractions aredecreased.

Propulsiveperistalticwaves in the colon aredecreased, whiletonemaybe increased to thepoint ofspasm resultingin constipation. Otheropioid-induced effects mayincludea reduction in biliary and pancreatic secretions, spasm of sphincter of Oddi, and transient elevations in serum amylase.

Effects on theCardiovascularSystem

Pentazocine produces peripheral vasodilation which mayresult in orthostatichypotension orsyncope. Manifestations ofhistamine release and/orperipheral vasodilation mayincludepruritus, flushing,red eyes and sweatingand/ororthostatichypotension.

Effects on theEndocrineSystem

Opioids inhibit thesecretion of adrenocorticotropichormone (ACTH), cortisol, and luteinizinghormone (LH)in humans. Theyalso stimulateprolactin, growth hormone (GH)secretion, and pancreaticsecretion ofinsulin and glucagon.
Chronicuseofopioids mayinfluencethehypothalamic-pituitary-gonadal axis,leadingto androgen deficiencythat maymanifest as low libido, impotence, erectiledysfunction, amenorrhea, orinfertility. The causal roleofopioids in the clinical syndromeofhypogonadism is unknown becausethevarious medical, physical, lifestyle, and psychological stressors that mayinfluencegonadal hormonelevels have not been adequatelycontrolled forin studies conducted to date.
Effects on theImmuneSystem
Opioids havebeen shown to haveavarietyofeffects on components oftheimmunesystem in *in vitro* and animal models. The clinical significanceofthesefindings is unknown. Overall, the effects ofopioids appearto bemodestlyimmunosuppressive.

5.2 Pharmacokinetic properties

Pentazocineis metabolized in the liver and excreted primarily in theurine. Clinical dataindicatethat differences in various pharmacokineticparameters maybeobserved with increasingage.In onestudy, elderlypatients exhibited alongermeanelimination half-life, alowermean total plasma clearance,and alargermeanareaunderthe concentration-time curvethanyoungerpatients.

5.3 Preclinical safety data

The safety of the additive should be considered separately.

6. Pharmaceutical particulars

6.1 List of Excipients:

Refer dossier

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 Months

6.4 Special precautions for storage

Store below 30°C, Protect from light.
Keep all medicines away from children

6.5 Nature and contents of container

10 X 1 ML glass ampoule.

6.6 Special precautions for disposal and other handling

None stated.

Manufactured by:
Alpa Laboratories Ltd.,
33/2 A. B Road, Pigdamber,
India.

7. Marketing authorisation holder

TOPSEA STANDARD PHARMACEUTICAL CO. LTD,
Onitsha, Anambra State, Nigeria.

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