

1.3.1. SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. Name of the medicinal product:

PENTAZOCINE LACTATE 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

PENTAZOCINE LACTATE INJECTION is indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. PENTAZOCINE LACTATE 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 PENTAZOCINE LACTATE 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 PENTAZOCINE LACTATE INJECTION than younger patients. Elderly patients generally should be started on low doses of PENTAZOCINE LACTATE 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: PENTAZOCINE LACTATE INJECTION should not be mixed in the same syringe with soluble barbiturates because precipitation will occur.

4.3 Contraindications

PENTAZOCINE LACTATE INJECTION is contraindicated in patients with:

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

4.4 Special warnings and precautions for use

Addiction, Abuse, and Misuse

PENTAZOCINE LACTATE INJECTION exposes patients and other users to the risks of opioid addiction, abuse, and misuse, which can lead to overdose and death. Assess each patient's risk prior to prescribing PENTAZOCINE LACTATE INJECTION, 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 PENTAZOCINE LACTATE INJECTION. Monitor for respiratory depression, especially during initiation of PENTAZOCINE LACTATE INJECTION or following a dose increase.

Neonatal Opioid Withdrawal Syndrome

Prolonged use of PENTAZOCINE LACTATE INJECTION during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated, and requires management according to protocols developed by neonatology experts. If opioid use is required for a prolonged period in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.

Risks from Concomitant Use with Benzodiazepines or Other CNS Depressants

Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death.

- Reserve concomitant prescribing of PENTAZOCINE LACTATE INJECTION and benzodiazepines or other CNS depressants for use in patients for whom alternative treatment options are inadequate.
- Limit dosages and durations to the minimum required.
- Follow patients for signs and symptoms of respiratory depression and sedation.

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4.5 Interaction with other medicinal products and other forms of interaction

Table 1 Clinically Significant Drug Interactions

Interactions with PENTAZOCINE LACTATE INJECTION Benzodiazepines and other Central Nervous System(CNS)Depressants	
Clinical Impact:	Due to additive pharmacologic effect, the concomitant use of benzodiazepines or other CNS depressants including alcohol, increases the risk of respiratory depression, profound sedation, coma, and death.
Intervention:	Reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate. Limit dosages and durations to the minimum required. Follow patients closely for signs of respiratory depression and sedation.
Examples:	Benzodiazepines and other sedatives/hypnotics, anxiolytics, tranquilizers, muscle relaxants, general anesthetics, antipsychotics, other opioids, alcohol.
Serotonergic Drugs	
Clinical Impact:	The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Intervention:	If concomitant use is warranted, carefully observe the patient, particularly during treatment initiation and dose adjustment. Discontinue PENTAZOCINE LACTATE INJECTION if serotonin syndrome is suspected.
Examples:	Selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), triptans, 5-HT ₃ receptor antagonists, drugs that effect the serotonin neurotransmitter system (e.g., mirtazapine, trazodone, tramadol), monoamine oxidase (MAO) inhibitors (those intended to treat psychiatric disorders and also others, such as linezolid and intravenous methylene blue).
Mixed Agonist/Antagonist and Partial Agonist Opioid Analgesics	
Clinical Impact:	May reduce the analgesic effect of PENTAZOCINE LACTATE INJECTION and/or precipitate withdrawal symptoms.
Intervention:	Avoid concomitant use.
Examples:	Butorphanol, nalbuphine, pentazocine, buprenorphine.
Muscle Relaxants	
Clinical Impact:	Pentazocine may enhance the neuromuscular blocking action of skeletal muscle relaxants and produce an increased degree of respiratory depression.
Diuretics	
Clinical Impact:	Opioids can reduce the efficacy of diuretics by inducing the release of antidiuretic hormone.
Intervention:	Monitor patients for signs of diminished diuresis and/or effects on blood pressure and increase the dosage of the diuretic as needed.
PENTAZOCINE LACTATE INJECTION is used concomitantly with anticholinergic drugs.	

4.6 Fertility, pregnancy and lactation

Pregnancy:

Prolonged use of opioid analgesics during pregnancy may cause neonatal opioid withdrawal syndrome. Available data with PENTAZOCINE LACTATE INJECTION in pregnant women are insufficient to inform drug-associated risk for major birth defects and miscarriage.

In animal reproduction studies, pentazocine administered subcutaneously to pregnant hamsters during the early gestational period produced neural tube defects (i.e., exencephaly and cranioschisis) at 4.4 times the maximum daily dose. Based on animal data, advise pregnant women of the potential risk to a fetus. The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Lactation:

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for PENTAZOCINE LACTATE INJECTION and any potential adverse effects on the breastfed infant from PENTAZOCINE LACTATE INJECTION or from the underlying maternal 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

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

4.9 Overdose

Clinical Presentation

Acute overdose with PENTAZOCINE LACTATE INJECTION can be manifested by respiratory depression, somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, constricted pupils, and, in some cases, pulmonary edema, bradycardia, hypotension, partial or complete airway obstruction, atypical snoring, and death. Marked mydriasis rather than miosis may be seen with hypoxia in overdose situations.

Treatment of Overdose

In case of overdose, priorities are the reestablishment of a patent and protected airway and institution of assisted or controlled ventilation, if needed.

Employ other supportive measures (including oxygen and vasopressors) in the management of circulatory shock and pulmonary edema as indicated. Cardiac arrest or arrhythmias will require advanced life-support techniques.

In an individual physically dependent on opioids, administration of the recommended usual dosage of the antagonist will precipitate an acute withdrawal syndrome.

The severity of the withdrawal symptoms experienced will depend on the degree of physical dependence and the dose of the antagonist administered. If a decision is made to treat serious respiratory depression in the physically dependent patient, administration of the antagonist should be begun with care and by titration with smaller than usual doses of the antagonist.

5. Pharmacological properties

Mechanism of Action

Pentazocine is a mixed agonist-antagonist at opioid receptors. Pentazocine is partial agonist at the μ opioid receptor and an agonist at the κ opioid receptor.

5.1 Pharmacodynamic properties

Effects on the Central Nervous System

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

Pentazocine causes miosis, even in total darkness. Pinpoint pupils are a sign of opioid overdose but are not pathognomonic (e.g., pontine lesions of the hemorrhagic or ischemic origins may produce similar findings). Marked mydriasis rather than miosis may be seen due to hypoxia in overdose situations.

Effects on the Gastrointestinal Tract and Other Smooth Muscle

Pentazocine causes a reduction in motility associated with an increase in smooth muscle tone in the antrum of the stomach and duodenum. Digestion of food in the small intestine is delayed and propulsive contractions are decreased.

Propulsive peristaltic waves in the colon are decreased, while tone may be increased to the point of spasm resulting in constipation. Other opioid-induced effects may include a reduction in biliary and pancreatic secretions, spasm of sphincter of Oddi, and transient elevations in serum amylase.

Effects on the Cardiovascular System

Pentazocine produces peripheral vasodilation which may result in orthostatic hypotension or syncope. Manifestations of histamine release and/or peripheral vasodilation may include pruritus, flushing, red eyes and sweating and/or orthostatic hypotension.

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Opioids inhibit the secretion of adrenocorticotrophic hormone (ACTH), cortisol, and luteinizing hormone (LH) in humans. They also stimulate prolactin, growth hormone (GH) secretion, and pancreatic secretion of insulin and glucagon. Chronic use of opioids may influence the hypothalamic-pituitary-gonadal axis, leading to androgen deficiency that may manifest as low libido, impotence, erectile dysfunction, amenorrhea, or infertility. The causal role of opioids in the clinical syndrome of hypogonadism is unknown because the various medical, physical, lifestyle, and psychological stressors that may influence gonadal hormone levels have not been adequately controlled for in studies conducted to date.

Effects on the Immune System

Opioids have been shown to have a variety of effects on components of the immune system in *in vitro* and animal models. The clinical significance of these findings is unknown. Overall, the effects of opioids appear to be modestly immunosuppressive.

5.2 Pharmacokinetic properties

Pentazocine is metabolized in the liver and excreted primarily in the urine. Clinical data indicate that differences in various pharmacokinetic parameters may be observed with increasing age. In one study, elderly patients exhibited a longer mean elimination half-life, a lower mean total plasma clearance, and a larger mean area under the concentration-time curve than younger patients.

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.

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:

Radiant Parenterals Ltd.

7. Marketing authorisation holder

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