SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

Pentazocine Injection BP 30 mg/ml

1. NAME OF THE DRUG PRODUCT

Pentazocine Injection BP 30 mg/ml

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

- Pentazocine BP 30 mg (as lactate)
- Sodium Chloride BP 2.8 mg
- Water for Injection BP q.s.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

A colourless or almost colourless solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Pentazocine is used to relieve moderate to severe pain. It is in a class of medications known as opiate (narcotic) analgesics, and works by changing the way the brain and nervous system respond to pain. It is also sometimes used to help control pain during labour.

4.2 Posology and method of administration

Route of administration: Pentazocine Injection may be administered subcutaneously, intramuscularly or intravenously.

Adults: The usual starting dose is 30 mg to 60 mg according to severity. The dose should be adjusted according to response and repeated as necessary every three to four hours. A dose should not normally exceed 1 mg/kg body weight subcutaneously or intramuscularly, or 0.5 mg/kg intravenously. The maximum daily dose is 360 mg.

Children: In patients between 1 year and 12 years, the maximum single dose of parenteral pentazocine should be calculated on the basis of 1 mg/kg body weight, intravenously. Pentazocine Injection is not recommended for use in children under one year.

Elderly: Since impaired renal or hepatic function is often associated with ageing, elderly patients may require smaller doses of pentazocine.

4.3 Contraindications

Pentazocine Injection should not be administered to patients with established respiratory depression, especially in the presence of cyanosis and excessive bronchial secretion. It is also contraindicated in acute alcoholism, head injuries, conditions in which intracranial pressure is raised, acute bronchial asthma, heart failure secondary to chronic lung disease, and in patients known to be hypersensitive to pentazocine or any excipient.

4.4 Special warnings and precautions for use

Respiratory depression is a common effect but is subject to a ceiling effect, such that beyond a certain dose the degree of respiratory depression does not increase further with increasing dose.

High doses may cause elevated blood pressure or heart rate. Intravenous administration may increase cardiac workload following myocardial infarction; this route should be avoided where possible in this setting.

4.5 Interaction with other drug products and other forms of interaction

Monoamine oxidase inhibitors may enhance the opioid effects of pentazocine; the two may also interact through their respective effects on catecholamine breakdown and release.

Agents with sedative action, including phenothiazines, tricyclic antidepressants and ethyl alcohol, can enhance the central depressant effects of pentazocine, which are opposed by respiratory stimulants such as doxapram.

Tobacco smoking appears to enhance the metabolic clearance rate of pentazocine, reducing the clinical effectiveness of a standard dose.

Pentazocine can antagonise the effects of stronger opioid agonists such as diamorphine (heroin) and morphine, and is itself antagonised by naloxone.

Because pentazocine has narcotic antagonist activity, it may provoke withdrawal symptoms if given to narcotic addicts, and should be given with caution to patients recently treated with large doses of narcotics.

4.6 Fertility, pregnancy and lactation

There is evidence to indicate that exposure to pentazocine during pregnancy may have a teratogenic effect on the foetus. The likelihood and severity of defects may be affected by the level of exposure and the stage of pregnancy at which exposure occurred. Reported signs include:

- Retarded foetal growth
- Extra digits
- Heart defects

4.7 Effects on ability to drive and use machines

NA.

4.8 Undesirable effects

The following adverse reactions have been reported (consolidated from multiple, overlapping lists in the source document):

- Dizziness, drowsiness, exaggerated sense of well-being
- Lightheadedness or fainting spells
- Nausea, vomiting
- Injection-site reactions (redness, swelling, irritation)
- Severe allergic reactions (rash, hives, difficulty breathing, tightness in the chest, swelling of the mouth, face, lips or tongue)
- Blurred vision or other vision problems
- Confusion, hallucinations, seizures
- Trouble sleeping
- Trouble urinating or decreased urination
- Unusual weakness
- Slow or fast heartbeat
- Nervousness or restlessness
- Constipation, dry mouth
- Headache, itching
- Rare: agranulocytosis, erythema multiforme, toxic epidermal necrolysis

4.9 Overdose

Symptoms and signs of overdose resemble those of morphine and other opioids, and may include somnolence, respiratory depression, hypotension, hypertension, tachycardia, hallucinations or seizures. Circulatory failure and deepening coma may occur in more severe cases, particularly in patients who have also taken other CNS depressants such as alcohol, sedatives/hypnotics or antihistamines.

Management: Adequate measures to maintain ventilation and general circulatory support should be employed. Gastric lavage and gastric aspiration should be considered where appropriate. For respiratory depression due to overdosage or unusual sensitivity to pentazocine, parenteral naloxone is a specific and effective antagonist. Initial doses of 0.4 to 2.0 mg of naloxone are recommended, repeated at 2–3 minute intervals if needed, up to a total of 10 mg. Anticonvulsant therapy may be necessary.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Benzomorphan derivatives.

Mechanism of action: Pentazocine is a mixed agonist-antagonist with low intrinsic activity at receptors of the μ-opioid type (morphine-like) and is also an agonist at κ-opioid receptors. Its interactions with these receptors in the central nervous system apparently mediate most of its pharmacological effects, including analgesia.

Pharmacodynamic effects: In addition to analgesia, CNS effects include depression of spontaneous respiratory activity and cough, stimulation of the emetic centre, miosis and sedation. Effects possibly mediated by non-CNS mechanisms include alteration in cardiovascular resistance and capacitance, bronchomotor tone, gastrointestinal secretory and motor activity, and bladder sphincter activity.

In an animal model, the dose of pentazocine tartrate required to antagonise morphine analgesia by 50% was similar to that for nalorphine, less than that for pentazocine, and more than that for naloxone. The pharmacological activity of pentazocine metabolites has not been studied in humans; in animal studies, pentazocine metabolites have demonstrated some analgesic activity.

In human studies, sedation is commonly noted at doses of 0.5 mg or more. Narcosis is produced by 10–12 mg doses administered over 10–15 minutes intravenously. Pentazocine, like other mixed agonist-antagonists with high affinity for the κ-receptor, may produce unpleasant psychotomimetic effects in some individuals.

Nausea and/or vomiting may be produced by doses of 1 mg or more administered by any route. In studies involving individuals without significant respiratory dysfunction, 2 mg of pentazocine IV and 10 mg of morphine sulfate IV depressed respiration to a comparable degree; at higher doses the magnitude of respiratory depression with pentazocine is not appreciably increased, though its duration is longer. Respiratory depression after pentazocine administration by any route is reversed by naloxone. Pentazocine tartrate demonstrates antitussive effects in animals at doses lower than those required for analgesia. Hemodynamic changes noted during cardiac catheterisation in patients receiving single 0.025 mg/kg intravenous doses have included increases in pulmonary artery pressure, wedge pressure and vascular resistance, and increases in left ventricular end-diastolic pressure and systemic arterial pressure.

5.2 Pharmacokinetic properties

Absorption: Rapidly absorbed after intramuscular injection, with peak plasma levels reached in 20–40 minutes. Following its initial absorption/distribution phase, the single-dose pharmacokinetics of pentazocine by the intravenous, intramuscular and nasal routes of administration are similar.

Distribution: Serum protein binding is independent of concentration over the range achieved in clinical practice (up to 7 ng/mL), with a bound fraction of approximately 80%.

5.3 Preclinical safety data

Not provided.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Sodium chloride
- Lactic acid
- Water for injection

6.2 Incompatibilities

This medicinal product should not be mixed with preparations containing bisulfite, metabisulfite, long-chain or high molecular weight anions, or any solution having an alkaline pH.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store at a temperature not exceeding 30°C. Protect from light.

6.5 Nature and contents of container

10 × 1 mL, USP Type I flint glass ampoules, with a blue dot at the constriction.

6.6 Special precautions for disposal of a used or unused drug product and other handling of the product

No special requirements.

7. APPLICANT / HOLDER OF CERTIFICATE OF PRODUCT REGISTRATION

Alpa Laboratories Limited

33/2 A.B. Road, Pigdamber, Indore (MP), Pin Code – 453446, India

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8. DRUG PRODUCT MANUFACTURER

9. NAFDAC REGISTRATION NUMBER(S)