1.3.1 Summary of product Characteristics (SmPC)

1. Name of the Medicinal Product

Pentazocine Injection BP 30mg/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

Batch size 70 liter

S.NO.	INGREDIENTS	GRADE	TYPE	STANDARD QUANTITY REQUIRED FOR 70.0 LIT.	UNIT QUANTITY
1	Pentazocine (as lactate)	BP	A	2.200 kg	31.4 mg
2	Sodium chloride	BP	E	0.196 kg	2.8 mg
3	Lactic acid	BP	E	87.5 ml	0.00125 ml
4	Water for injection	BP	E	Q.S to make 70 liters	Q.S to make 1 ml

3. Pharmaceutical Form

Liquid Injection

5. Pharmacological Class

Benzomorphan derivatives.

6. Product Description

A colourless or almost colourless solution filled in flint glass sealed ampoule with blue dot at constriction.

7. Clinical Particular

7.1 Therapeutic Indication

Pentazocine is used to relieve moderate to severe pain. Pentazocine is in a class of medications called opiate (narcotic) analgesics. It works by changing the way the brain and nervous system respond to pain.

7.2 Posology and method of administration

Adults

Pentazocine Injections may be administered subcutaneously, intramuscularly or intravenously. The usual starting dose is 30mg to 60mg according to the severity. The dose should be adjusted according to response and repeated as necessary every three to four hours. A dose should not normally exceed 1mg/kg body weight SC or IM, or 0.5mg/kg iv.

The maximum daily dose is 360mg.

Children

In the case of patients between 1 year and 12 years, the maximum single dose of parenteral Pentazocine should be calculated on the basis of 1mg/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.

8. Contraindication

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

9. Special warnings and precautions for use

Dizziness; drowsiness; exaggerated sense of well-being; lightheadedness; nausea; redness, swelling, or irritation at injection site; vomiting. 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; fainting; hallucinations; seizures; trouble sleeping; trouble urinating; unusual weakness;

10. Interaction with other medicinal products and other forms of Interaction.

Monoamine oxidase inhibitors may enhance the opioid effects of pentazocine and the agents may 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 it should be given with caution to patients recently being treated with large doses of narcotics.

11. Teratogenicity

There is evidence to indicate that exposure to Pentazocine during pregnancy may have a teratogenic effect on the fetus. A teratogen is a substance that can cause birth defects. The likelihood and severity of defects may be affected by the level of exposure and the stage of pregnancy that the exposure occurred at.

The list of signs and symptoms mentioned in various sources for Pentazocine - Teratogenic Agent includes the 3 symptoms listed below:

- Retarded fetal growth
- Extra digits
- Heart defects

12. Antidote in the events of Over dosage

The symptoms and clinical signs of pentazocine overdose will resemble those of morphine and other opioids. They may therefore 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 ingested other CNS depressants such as alcohol, sedatives / hypnotics, or antihistamines. 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 over dosage or unusual sensitivity to pentazocine, parenteral naloxone is a specific and effective antagonist. Initial doses of 0.4 to 2.0mg of naloxone are recommended, repeated at 2-3-minute intervals if needed, up to a total of 10mg. Anti-convulsant therapy may be necessary.

13. Undesirable effects

Side Effects

- Slow or fast heartbeat
- Seizures
- Unusual weakness
- Confusion
- Hallucinations (seeing or hearing things that are not really there)
- Lightheadedness or fainting spells
- Nervousness or restlessness
- Constipation
- Decrease or difficulty passing urine
- Dry mouth
- Headache
- Itching

14. Pharmacological Properties

14.1 Pentazocine relieves moderate to severe pain. Pentazocine is sometimes used to help control pain during labor. Pentazocine injection will be given as an injection into a muscle or through your vein by a trained health care provider.

Pentazocine is a mixed agonist-antagonist with low intrinsic activity at receptors of the μ-opioid type (morphine-like). It is also an agonist at k-opioid receptors.

Its interactions with these receptors in the central nervous system apparently mediate most of its pharmacologic effects, including analgesia. In addition to analgesia, CNS effects include depression of spontaneous respiratory activity and cough, stimulation of the emetic center, 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 antagonize 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 of pentazocine, sedation is commonly noted at doses of 0.5 mg or more. Narcosis is produced by 10–12 mg doses of pentazocine administered over 10–15 minutes intravenously. Pentazocine, like other mixed agonist-antagonists with a high affinity for the k- 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 human 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; however, the duration of respiratory depression is longer. Respiratory depression noted after administration of pentazocine to humans by any route is reversed by treatment with naloxone, a specific opioid antagonist. Pentazocine tartrate demonstrates antitussive effects in animals at doses less than those required for analgesia. Hemodynamic changes noted during cardiac catheterization in patients receiving single 0.025 mg/kg intravenous doses of

pentazocine have included increases in pulmonary artery pressure, wedge pressure and vascular resistance, increases in left ventricular end diastolic pressure and in systemic arterial pressure.

14.2 Pharmacokinetic properties

This Injection is rapidly absorbed after IM injection and peak plasma levels are reached in 20–40 minutes. After nasal administration, mean peak blood levels of 0.9–1.04 ng/mL occur at 30–60 minutes after a 1 mg dose. The absolute bioavailability of injection NS is 60–70% and is unchanged in patients with allergic rhinitis. In patients using a nasal vasoconstrictor (oxymetazoline) the fraction of the dose absorbed was unchanged, but the rate of absorption was slowed. The peak plasma concentrations were approximately half those achieved in the absence of the vasoconstrictor. Following its initial absorption/distribution phase, the single dose pharmacokinetics of Pentazocine by the intravenous, intramuscular, and nasal routes of administration are similar.

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%.

15. Toxicology

Side effects are similar to those of morphine, but pentazocine, due to its action at the kappa opioid receptor is more likely to invoke psychotomimetic effects. High dose may cause high blood pressure or high heart rate. It may also increase cardiac work after myocardial infarction when given intravenously and hence this use should be avoided where possible. Respiratory depression is a common side effect, but is subject to a ceiling effect, such that at a certain dose the degree of respiratory depression will no longer increase with dose increases. Likewise rarely it has been associated with agranulocytosis, erythema multiforme and toxic epidermal necrolysis.

16. Pharmaceutical Excipient

16.1. List of excipients

Sodium chloride

Lactic acid

Water for Injection

16.2. Incompatibilities

Pentazocine Injection BP 30mg/ml Should not be mixed with preparations containing bisulfite, metabisulfite, long-chain or high molecular anions or any solution having an alkaline pH.

16.3. Shelf life

36 months

16.4. Special Precautions for Storage

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

16.5. Nature and contents of container.

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

16.6. Special precautions for disposal and other handling

None

17. Marketed By:

M/S. KFC PHARMACEUTICAL LTD.,
NO. 16, KING FAISAL STREET,
ASOKORO, ABUJA, NIGERIA.,

18. Manufactured By:

M/S SAKAR HEALTHCARE PVT. LTD.,

406, SILVER OAKS COMM. COMPLEX, OPP.
ARUN SOCIETY, PALDI,
AHMEDABAD-380007, GUJARAT, INDIA.,

19. Marketing authorization number (s)

To be allocated

20. Date of first authorization / renewal of authorization

To be allocated

21. Date of revision of the text

To be allocated