SAKAR HEALTHCARE LTD

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

PENTAFORT INJECTION

[Pentazocine Lactate BP 30mg/ml]

PRODUCT INFORMATION FOR HEALTH PROFESSIONALS (FOR ALL PRODUCTS SUBJECT TO MEDICAL PRESCRIPTION)

Enclosed herewith:

1. Name of the medicinal product:

1.1 Name of the medicinal product :
Pentafort Injection
(Pentazocine BP 30mg)

1.2 Strength :
Pentazocine Lactate BP
eq. to Pentazocine ..... 30 mg/ ml

1.3 Pharmaceutical form:

Injection for I.M./I.V. OR S.C. use

2.0 Qualitative and quantitative composition

Each ml contains:
Pentazocine Lactate BP
eq. to Pentazocine ..... 30 mg
Water for injections BP q.s.

2.1 Qualitative declaration:
Pentazocine Lactate BP eq. to Pentazocine

2.3 Quantitative declaration:
Each ml contains:
Pentazocine Lactate BP
eq. to Pentazocine ..... 30 mg
Water for injections BP q.s

3. Pharmaceutical form
Solution for Injection for Intramuscular / Intravenous or Subcutaneous use only

4. Clinical particulars:
4.1 Therapeutic indications:
PENTAFORT INJECTION is indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. PENTAFORT 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 PENTAFORT 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 Injection than younger patients. Elderly patients generally should be started on low doses of 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 (see WARNINGS). 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 Injection should not be mixed in the same syringe with soluble barbiturates because precipitation will occur.

4.3 Contraindications

Pentazocine Injection is contraindicated in patients with:

• Significant respiratory depression [see Warnings and Precautions]

• Acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment [see Warnings and Precautions)]

• Known or suspected gastrointestinal obstruction, including paralytic ileus [see Warnings and Precautions]

• Hypersensitivity to pentazocine (e.g., anaphylaxis)

4.4 Special warnings and precautions for use:

WARNINGS

Drug Dependence

Special care should be exercised in prescribing pentazocine for emotionally unstable patients and for those with a history of drug misuse. Such patients should be closely supervised when greater than 4 or 5 days of therapy is contemplated. There have been instances of psychological and physical dependence on Pentazocine Injection in patients with such a history and, rarely, in patients without such a history. Extended use of parenteral Pentazocine Injection may lead to physical or psychological dependence in some patients. When Pentazocine Injection is abruptly discontinued, withdrawal symptoms such as abdominal cramps, elevated temperature, rhinorrhea, restlessness, anxiety, and lacrimation may occur. However, even when these have occurred, discontinuance has been accomplished with minimal difficulty. In the rare patient in whom more than minor difficulty has been encountered, reinstitution of parenteral

Pentazocine Injection with gradual withdrawal has ameliorated the patient's symptoms. Substituting methadone or other narcotics for Pentazocine Injection in the treatment of the pentazocine abstinence syndrome should be avoided. There have been rare reports of possible abstinence syndromes in newborns after prolonged use of Pentazocine Injection during pregnancy.

In prescribing parenteral Pentazocine Injection for chronic use, particularly if the drug is to be self-administered, the physician should take precautions to avoid increases in dose and frequency of injection by the patient.

Just as with all medication, the oral form of Pentazocine Injection is preferable for chronic administration.

Tissue Damage at Injection Sites

Severe sclerosis of the skin, subcutaneous tissues, and underlying muscle have occurred at the injection sites of patients who have received multiple doses of pentazocine lactate. Constant rotation of injection sites is, therefore, essential. In addition, animal studies have demonstrated that Pentazocine Injection is tolerated less well subcutaneously than intramuscularly.

Head Injury and Increased Intracranial Pressure

As in the case of other potent analgesics, the potential of Pentazocine Injection injection for elevating cerebrospinal fluid pressure may be attributed to CO_2 retention due to the respiratory depressant effects of the drug. These effects may be markedly exaggerated in the presence of head injury, other intracranial lesions, or a preexisting increase in intracranial pressure. Furthermore, Pentazocine Injection can produce effects which may obscure the clinical course of patients with head injuries. In such patients, Pentazocine Injection must be used with extreme caution and only if its use is deemed essential.

Acute CNS Manifestations

Patients receiving therapeutic doses of pentazocine have experienced hallucinations (usually visual), disorientation, and confusion which have cleared spontaneously within a period of hours. The mechanism of this reaction is not known. Such patients should be closely observed and vital signs checked. If the drug is reinstituted, it should be done with caution since these acute CNS manifestations may recur.

Due to the potential for increased CNS depressant effects, alcohol should be used with caution in patients who are currently receiving pentazocine.

Ambulatory Patients

Since sedation, dizziness, and occasional euphoria have been noted, ambulatory patients should be warned not to operate machinery, drive cars, or unnecessarily expose themselves to hazards.

Myocardial Infarction

Caution should be exercised in the intravenous use of pentazocine for patients with acute myocardial infarction accompanied by hypertension or left ventricular failure. Data suggest that intravenous administration of pentazocine increases systemic and pulmonary arterial pressure and systemic vascular resistance in patients with acute myocardial infarction.

PRECAUTIONS

Certain Respiratory Conditions

The possibility that Pentazocine Injection may cause respiratory depression should be considered in treatment of patients with bronchial asthma. Pentazocine Injection should be administered only with caution and in low dosage to patients with respiratory depression (e.g., from other medication, uremia, or severe infection), severely limited respiratory reserve, obstructive respiratory conditions, or cyanosis.

Impaired Renal or Hepatic Function

Although laboratory tests have not indicated that Pentazocine Injection causes or increases renal or hepatic impairment, the drug should be administered with caution to patients with such impairment. Extensive liver disease appears to predispose to greater side effects (e.g., marked apprehension, anxiety, dizziness, sleepiness) from the usual clinical dose, and may be the result of decreased metabolism of the drug by the liver.

Biliary Surgery

Narcotic drug products are generally considered to elevate biliary tract pressure for varying periods following their administration. Some evidence suggests that pentazocine may differ from other marketed narcotics in this respect (i.e., it causes little or no elevation in biliary tract pressures). The clinical significance of these findings, however, is not yet known.

Patients Receiving Narcotics

Pentazocine Injection is a mild narcotic antagonist. Some patients previously given narcotics, including methadone for the daily treatment of narcotic dependence, have experienced withdrawal symptoms after receiving Pentazocine Injection .

CNS Effect

Caution should be used when Pentazocine Injection is administered to patients prone to seizures; seizures have occurred in a few such patients in association with the use of Pentazocine Injection although no cause and effect relationship has been established.

Use in Anesthesia

Concomitant use of CNS depressants with parenteral Pentazocine Injection may produce additive CNS depression. Adequate equipment and facilities should be available to identify and treat systemic emergencies should they occur.

Usage in Pregnancy

Safe use of Pentazocine Injection during pregnancy (other than labor) has not been established. Animal reproduction studies have not demonstrated teratogenic or embryotoxic effects. However, Pentazocine Injection should be administered to pregnant patients (other than labor) only when, in the judgment of the physician, the potential benefits outweigh the possible hazards. Patients receiving Pentazocine Injection during labor have experienced no adverse effects other than those that occur with commonly used analgesics. Pentazocine Injection should be used with caution in women delivering premature infants.

Pediatric Use

The safety and efficacy of Pentazocine Injection as preoperative or preanesthetic medication have been established in pediatric patients 1 to 16 years of age. Use of Pentazocine Injection in

these age groups is supported by evidence from adequate and controlled studies in adults with additional data from published controlled trials in pediatric patients. The safety and efficacy of Pentazocine Injection as a premedication for sedation have not been established in pediatric patients less than one year old. Information on the safety profile of Pentazocine Injection as a postoperative analgesic in children less than 16 years is limited.

Geriatric Use
Elderly patients may be more sensitive to the analgesic effects of Pentazocine Injection than younger patients.

4.5 Interaction with other medicinal products and other forms of interaction

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 PENTAFORT INJECTION if serotonin syndrome is suspected.
Examples:	Selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), triptans, 5-HT3 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 PENTAFORT 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.
Intervention:	Monitor patients for signs of respiratory depression that may be greater than otherwise expected and decrease the dosage of PENTAFORT INJECTION and/or the muscle relaxant as necessary.
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.

Anticholinergic Drugs	
Clinical Impact:	The concomitant use of anticholinergic drugs may increase risk of urinary retention and/or severe constipation, which may lead to paralytic ileus.
Intervention:	Monitor patients for signs of urinary retention or reduced gastric motility when PENTAFORT INJECTION is used concomitantly with anticholinergic drugs.

4.6 Pregnancy and lactation

Safe use of Pentazocine Injection during pregnancy (other than labor) has not been established. Animal reproduction studies have not demonstrated teratogenic or embryotoxic effects. However, Pentazocine Injection should be administered to pregnant patients (other than labor) only when, in the judgment of the physician, the potential benefits outweigh the possible hazards. Patients receiving Pentazocine Injection during labor have experienced no adverse effects other than those that occur with commonly used analgesics. Pentazocine Injection should be used with caution in women delivering premature infants.

4.7 Effects on ability to drive and use machines:

Pentazocine 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 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 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

Acute overdose with PENTAFORT 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:

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 centers 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 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.

Effects on the Endocrine System

Opioids inhibit the secretion of adrenocorticotropic 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.

Concentration–Efficacy Relationships

PENTAFORT INJECTION is a potent analgesic and 30 mg is usually as effective an analgesic as morphine 10 mg or meperidine 75 mg to 100 mg; however, a few studies suggest the PENTAZOCINE INJECTION to morphine ratio may range from 20 mg to 40 mg PENTAFORT INJECTION to 10 mg morphine. The duration of analgesia may sometimes be less than that of morphine. Analgesia usually occurs within 15 to 20 minutes after intramuscular or subcutaneous injection and within 2 to 3 minutes after intravenous injection. PENTAFORT INJECTION weakly antagonizes the analgesic effects of morphine, meperidine, and phenazocine; in addition, it produces incomplete reversal of cardiovascular, respiratory, and behavioral depression induced by morphine and meperidine. PENTAFORT INJECTION has about 1/50 the antagonistic activity of nalorphine. It also has sedative activity. The minimum effective analgesic concentration will vary widely among patients, especially among patients who have been previously treated with potent agonist opioids. The minimum effective analgesic concentration of pentazocine for any individual patient may increase over time due to an increase in pain, the development of a new pain syndrome and/or the development of analgesic tolerance.

Concentration–Adverse Reaction Relationships

There is a relationship between increasing pentazocine plasma concentration and increasing frequency of dose-related opioid adverse reactions such as nausea, vomiting, CNS effects, and respiratory depression. In opioid-tolerant patients, the situation may be altered by the development of tolerance to opioid-related adverse reactions

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.

6. Pharmaceutical particulars

6.1 List of excipients

Water for Injections BP

6.2 Incompatibilities

None known

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store below 30°C.
Protect from light. Do not freeze
Keep medicine out of reach of childr

6.5 Nature and contents of container

1 ml glass ampoule. A plastic tray having 10 such ampoules with sticker label on it, placed in printed carton along with pack insert

6.6 Special precautions for disposal:

Needles and syringes must not be shared.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Registrant :

MARKETING AUTHORISATION HOLDER

PHARMABASE NIGERIA LIMITED

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MANUFACTURER

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