SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Pentazocine 25mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains pentazocine hydrochloride 25mg.

Excipients with known effect: Each film-coated tablet contains 169.6 mg lactose monohydrate.

Each film-coated tablet contains 20mg sodium.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film coated tablet
White film coated tablets embossed PZN 25 one side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Pentazocine is a strong analgesic for the relief of moderate to severe pain.

4.2 Posology and method of administration

Posology

The dosage is usually tailored to the individual patient and to the severity of the pain.

Adults
The usual initial dose is two 25mg tablets (50mg) every four hours after meals, followed by 25mg to 100mg of pentazocine every three to four hours.

Elderly

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

Paediatric Population
6-12 years: One 25mg tablet every three to four hours as necessary.

Pentazocine tablets are not recommended for children under 6 years of age. No data are available.

Method of administration
For oral use.

Prior to starting treatment with opioids, a discussion should be held with patients to put in place a strategy for ending treatment with pentazocine in order to minimise the risk of addiction and drug withdrawal syndrome (see section 4.4).

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Pentazocine should not be administered to patients with established respiratory depression, especially in the presence of cyanosis and excessive bronchial secretion
- Acute alcoholism
- Acute bronchial asthma
- Heart failure, secondary to chronic lung disease
- Porphyria
- Head injuries or conditions in which the intracranial pressure is raised or pathological brain conditions where clouding of the sensorium is undesirable

4.4 Special warnings and precautions for use

Pentazocine can both depress as well as elevate blood pressure possibly through the release of endogenous catecholamines. Particular caution should be observed therefore in using it in the presence of phaeochromocytoma, in the acute phase following myocardial infarction when it may increase pulmonary and systemic arterial pressure and vascular resistance, and in other clinical situations where alteration of vascular resistance and blood pressure might be particularly undesirable.

Caution should be observed in patients with severe renal or hepatic impairment and in elderly patients, who may additionally be especially sensitive to the effects of opioids, as both conditions may lead to an increase in bioavailability of pentazocine and call for a reduction in dosage.

Administer with caution to patients previously on large doses of narcotics.

Caution should be observed in patients who are prone to seizures and in the presence of other opioids or opioid-dependence since the weak opioid antagonistic effects of pentazocine may provoke withdrawal symptoms.

Caution should be observed in patients with hypothyroidism, adrenocortical insufficiency, prostatic hypertrophy and in patients with inflammatory or obstructive bowel disorders, cholecystitis, pancreatitis or other unidentified abdominal pain.

After long term treatment (> 3 months) with analgesics, with use every second day or more frequently, headache may develop or aggravate. Headache caused by overuse of analgesics (MOH - medication-overuse headache) should not be treated by increasing the dose. In such cases the use of analgesics should be discontinued in consultation with a doctor.

Risk from concomitant use of sedative medicines such as benzodiazepines or related drugs

Concomitant use of pentazocine and sedative medicines such as benzodiazepines or related drugs may result in sedation, respiratory depression, coma and death. Because of these risks, concomitant prescribing with these sedative medicines should be reserved for patients for whom alternative treatment options are not possible. If a decision is made to prescribe pentazocine concomitantly with sedative medicines, the lowest effective dose should be used, and the duration of treatment should be as short as possible.

The patients should be followed closely for signs and symptoms of respiratory depression and sedation. In this respect, it is strongly recommended to inform patients and their caregivers to be aware of these symptoms (see section 4.5).

Some opioids can cause CNS excitation or depression. Pentazocine, like most other strong analgesics, should not be used in patients who are receiving monoamine oxidase inhibitors or who have received them within the past 14 days (see section 4.5). Opioids can be taken after two weeks of MAOI's discontinuation.

Drug dependence, tolerance and potential for abuse

For all patients, prolonged use of this product may lead to drug dependence (addiction), even at therapeutic doses. The risks are increased in individuals with current or past history of substance misuse disorder (including alcohol misuse) or mental health disorder (e.g., major depression).

Additional support and monitoring may be necessary when prescribing for patients at risk of opioid misuse.

A comprehensive patient history should be taken to document concomitant medications, including over-the-counter medicines and medicines obtained on-line, and past and present medical and psychiatric conditions.

Patients may find that treatment is less effective with chronic use and express a need to increase the dose to obtain the same level of pain control as initially experienced. Patients may also supplement their treatment with additional pain relievers. These could be signs that the patient is developing tolerance. The risks of developing tolerance should be explained to the patient.

Overuse or misuse may result in overdose and/or death. It is important that patients only use medicines that are prescribed for them at the dose they have been prescribed and do not give this medicine to anyone else.

Patients should be closely monitored for signs of misuse, abuse, or addiction.

The clinical need for analgesic treatment should be reviewed regularly.

Drug withdrawal syndrome
Prior to starting treatment with any opioids, a discussion should be held with patients to put in place a withdrawal strategy for ending treatment with pentazocine.

Drug withdrawal syndrome may occur upon abrupt cessation of therapy or dose reduction. When a patient no longer requires therapy, it is advisable to taper the dose gradually to minimise symptoms of withdrawal. Tapering from a high dose may take weeks to months.

The opioid drug withdrawal syndrome is characterised by some or all of the following: restlessness, lacrimation, rhinorrhoea, yawning, perspiration, chills, myalgia, mydriasis and palpitations. Other symptoms may also develop including irritability, agitation, anxiety, hyperkinesia, tremor, weakness, insomnia, anorexia, abdominal cramps, nausea, vomiting, diarrhoea, increased blood pressure, increased respiratory rate or heart rate.

If women take this drug during pregnancy, there is a risk that their new-born infants will experience neonatal withdrawal syndrome.

Hyperalgesia
Hyperalgesia may be diagnosed if the patient on long-term opioid therapy presents with increased pain. This might be qualitatively and anatomically distinct from pain related to disease progression or to breakthrough pain resulting from development of opioid tolerance. Pain associated with hyperalgesia tends to be more diffuse than the pre-existing pain and less defined in quality. Symptoms of hyperalgesia may resolve with a reduction of opioid dose.

Excipients
Pentazocine contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

This medicine contains less than 1 mmol sodium (23 mg) per film-coated tablet, that is to say essentially ‘sodium-free’.

4.5 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.

Pentazocine should not be used in patients who are receiving monoamine oxidase inhibitors or who have received them within the past 14 days (see section 4.4).

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 of pentazocine.

Pentazocine can antagonise the effects of stronger opioid agonists such as diamorphine (heroin) and morphine and may provoke withdrawal symptoms if given to narcotic addicts. It is itself antagonised by naloxone.

Sedative medicines such as benzodiazepines or related drugs
The concomitant use of opioids with sedative medicines such as benzodiazepines or related drugs increases the risk of sedation, respiratory depression, coma and death because of additive CNS depressant effect. The dose and duration of concomitant use should be limited (see section 4.4).

4.6 Pregnancy and lactation

Pregnancy
Regular use during pregnancy may cause drug dependence in the foetus, leading to withdrawal symptoms in the neonate.

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.

Administration during labour may depress respiration in the neonate and an antidote for the child should be readily available.

Breast feeding
Administration to nursing women is not recommended as pentazocine may be secreted in breast milk and may cause respiratory depression in the infant.

4.7 Effects on ability to drive and use machines

Pentazocine may produce sedation, dizziness and occasionally euphoria, patients should be warned against the performance of potentially hazardous tasks such as driving a car or operating machinery. Alcohol may potentiate the sedative effect.

This medicine can impair cognitive function and can affect a patient's ability to drive safely. This class of medicine is in the list of drugs included in regulations under 5a of the Road Traffic Act 1988. When prescribing this medicine, patients should be told:

- The medicine is likely to affect your ability to drive
- Do not drive until you know how the medicine affects you
- It is an offence to drive while under the influence of this medicine
- However, you would not be committing an offence (called 'statutory defence') if:
  - The medicine has been prescribed to treat a medical or dental problem and
  - You have taken it according to the instructions given by the prescriber and in the information provided with the medicine and
  - It was not affecting your ability to drive safely

4.8 Undesirable effects

In chronic usage, care should be exercised to avoid any unnecessary increase in dosage since prolonged use of high dosage of pentazocine may produce dependence.

At normal therapeutic doses, side effects are generally of a minor nature. Sedation, the most common side effect, is less than that associated with morphine. The most frequent side effects are light-headedness, dizziness, nausea, vomiting and sweating.

The following side effects have also been reported:

Cardiac disorders: tachycardia, bradycardia, palpitations.

Vascular disorders: transient hypertension, hypotension, circulatory depression.

Nervous system disorders: hallucinations may occur occasionally, dysphoria, headache, disorientation, mood changes, nightmares, insomnia, paraesthesia, syncope, euphoria, grand mal convulsions, raised intracranial pressure, confusion, muscle tremor, thought disturbances.

Immune system disorders: oedema of the face, flushing of the skin including facial plethora, skin rashes, urticaria, dermatitis including pruritus, chills and allergic reactions.

Gastrointestinal disorders: constipation, dry mouth, biliary tract spasm.

Blood and lymphatic system disorders: transient eosinophilia, agranulocytosis, depression of white blood cell count.

Eye disorders: miosis, disturbances of vision.

Respiratory, thoracic and mediastinal disorders: respiratory depression.

Skin and subcutaneous system disorders: toxic epidermal necrolysis.

Renal and urinary disorders: urinary retention, ureteric tract spasm.

Pregnancy, puerperium and perinatal conditions: alterations in rate or strength of uterine contractions.

Reproductive system and breast disorders: decreased libido or potency.

General disorders and administration site conditions: hypothermia, drug withdrawal syndrome (uncommon).

Psychiatric disorders: drug dependence (see section 4.4).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

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, as may convulsions, 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 and consideration given to gastric lavage and gastric aspiration.

For respiratory depression due to overdosage or unusual sensitivity to pentazocine, parental naloxone is a specific and effective antagonist. Initial doses of 0.4 to 2mg of naloxone are recommended, repeated at 2-3 minute intervals if needed, up to a total of 10mg. Anti-convulsant therapy may be necessary.

Patients should be informed of the signs and symptoms of overdose and to ensure that family and friends are also aware of these signs and to seek immediate medical help if they occur.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Analgesics
ATC code: N02AD01

Pentazocine is an opioid benzomorphan derivative analgesic with actions and uses similar to those of morphine. Pentazocine has both agonist and antagonist action at opioid receptors. Pentazocine interrupts nociceptive input in the spinal cord. These analgesic effects are probably due to agonist actions at κ-receptors. Pentazocine is a weak antagonist at μ opioid receptors with about one fiftieth the potency of nalorphine.

Prolonged use of high doses of pentazocine may produce dependence. It is subject to abuse.

5.2 Pharmacokinetic properties

Absorption
Pentazocine is absorbed from the gastro-intestinal tract.

Distribution
Following administration by mouth, peak plasma concentrations are reached in 1 to 3 hours. After intramuscular injection, peak plasma concentrations are reached in 15 minutes to 1 hour.

Pentazocine diffuses across the placenta.

Biotransformation
Pentazocine is metabolised in the liver.

Elimination
Only a small proportion of the dose administered appears unchanged in the urine.

5.3 Preclinical safety data

There are no preclinical safety data of relevance to the prescriber which are additional to that already included in other sections of the SmPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core

Maize Starch
Lactose
Colloidal Anhydrous Silica
Magnesium Stearate
Sodium Starch Glycollate
Water

Coating
Hypromellose
Ethyl Cellulose
Diethyl Phthalate
Opaspray K-1-7000 White (E171)
Methanol
Dichloromethane

6.2 Incompatibilities

None known.

6.3 Shelf life

5 years

6.4 Special precautions for storage

Store in cool, dry place
Store in the original package in order to protect from light and moisture.

6.5 Nature and contents of container

Each container consists of a polypropylene tubular container with an open end equipped to accept a polyethylene closure, with a tamper-evident tear strip, and is of the appropriate size to accommodate 100, 250, 500 or 1,000 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Tillomed Laboratories Limited
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Great Marlings
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8 MARKETING AUTHORISATION NUMBER(S)

PL 11311/0529

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Date of latest renewal: 06/04/2009

10 DATE OF REVISION OF THE TEXT

20/12/2022