Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Meptid 100 mg/ml Solution for Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml of solution contains 100 mg of meptazinol (as hydrochloride).

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for Injection.
A clear colourless solution free from particulate matter.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the treatment of moderate to severe pain, including post-operative pain, obstetric pain and the pain of renal colic.

4.2 Posology and method of administration

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

Posology

Adults

Intramuscular dosage: 75 to 100 mg meptazinol. This injection may be repeated 2 to 4 hourly as required. For obstetric pain a dose of 100 to 150 mg should be used according to weight. This dose should approximate 2 mg/kg.

Intravenous dosage: 50 to 100 mg meptazinol by slow intravenous injection. The injection may be repeated 2 to 4 hourly as required. If vomiting occurs, a suitable antiemetic should be given.

Epidural/intrathecal use: this formulation is not suitable for these routes.

Elderly

The adult dosage schedule can be used in the elderly.

Paediatric population

No data are available

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Patients with the following conditions:

- acute alcoholism and where there is a risk of paralytic ileus
- raised intracranial pressure or head injury (in addition to interfering with respiration, affects pupillary responses vital for neurological assessment)

- phaeochromocytoma (risk of pressor response to histamine release)
- acute respiratory depression
- during an asthma attack
- patients on monoamine-oxidase inhibitors (MAOIs) and for 14 days after discontinuing an MAOI. (see section 4.5)

4.4 Special warnings and precautions for use

Caution should be exercised in patients whose respiratory system is already compromised.

Patients with moderate to severe renal impairment should be given a reduced dose as the effect in these patients may be prolonged and increased. Cerebral sensitivity may also be increased. Patients with hepatic impairment should be given a reduced dose as opioid analgesics may precipitate coma in these patients.

Since safety in long term use is not known it is recommended that this drug be used in the treatment of acute pain only, apart from appropriate therapy in malignant conditions. Repeated administration of opioid analgesics may cause dependence and tolerance (severe withdrawal symptoms if withdrawn abruptly).

Safety for use in myocardial infarction has not been established.

Meptazinol should also be used with caution in patients with the following conditions: hypotension, hypothyroidism, asthma (avoid during an attack), prostatic hypertrophy and convulsive disorders.

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 meptazinol.

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 newborn 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.

4.5 Interaction with other medicinal products and other forms of interactions

The following undesirable effects could occur as a result of possible interaction with meptazinol hydrochloride:

Antidepressants: CNS excitation or depression manifesting as hypertension or hypotension may occur if meptazinol is administered to patients receiving MAOIs (including moclobemide). Avoid concomitant use for 14 days after an MAOI is discontinued (see section 4.3). Possible increased sedation if meptazinol is used with tricyclic antidepressants.

Antipsychotics: enhanced sedative and hypotensive effect.

Antivirals: avoid concomitant use with ritonavir as plasma concentration of meptazinol may be increased.

Alcohol: enhanced sedative and hypotensive effect.

Quinolones (ciprofloxacin): avoid premedication with meptazinol as a reduced plasma-ciprofloxacin concentration may be experienced.

Anxiolytics and hypnotics: enhanced sedative effect.

Drugs used in nausea and vomiting: concomitant use of metoclopramide and domperidone may result in antagonism of gastrointestinal side-effects.

Ulcer healing drugs: cimetidine may inhibit metabolism of meptazinol resulting in increased plasma concentration.

4.6 Fertility, pregnancy and lactation

Pregnancy
No clinical data on exposed pregnancies are available.
Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development.

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.

Meptid injection is a useful analgesic in labour, however, it should not be given in other stages of pregnancy unless considered essential by the physician. Administration during labour may depress respiration in the neonate and an antidote for the child should be readily available.

Breast-feeding
Meptazinol may be secreted in breast milk and may cause respiratory depression in the infant.
Meptazinol should not be used during breast-feeding.

4.7 Effects on ability to drive and use machines

Since dizziness and occasionally drowsiness have been reported, patients should be cautioned against driving or operating machinery until it is established that they do not become dizzy or drowsy whilst taking meptazinol.

4.8 Undesirable effects

System Organ Class	Very Common (≥ 1/10)	Uncommon (≥ 1/1,000 to ≤ 1/100)	Unknown (frequency cannot be estimated from the available data)
Psychiatric disorders			Drug dependence (see section 4.4)
Nervous system disorders	dizziness, headache, vertigo, somnolence, drowsiness		
Vascular disorders		hypotension	
Respiratory, thoracic and mediastinal disorders		respiratory depression	
Gastrointestinal disorders	abdominal pain, constipation, diarrhoea, dyspepsia, nausea, vomiting		
Skin and subcutaneous tissue disorders	Increased sweating, rash		
General disorders and administration site conditions		Drug withdrawal syndrome	

For very rare reports of psychiatric disorders (hallucination, confusion, depression), causal relationship with meptazinol has not been established and therefore omitted from the above table.

Reactions not already stated which are attributable to opioid analgesics include difficulty with micturition, ureteric or biliary spasm, dry mouth, facial flushing, bradycardia, tachycardia, palpitations, hypothermia, dysphoria, mood changes, miosis, decreased libido or potency, urticaria and pruritus.

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 HPRA Pharmacovigilance, Website: www.hpra.ie

4.9 Overdose

Overdose with Meptid Injection has not been reported. Large doses, including seven times the recommended therapeutic dose, have been given in balanced and total intravenous anaesthesia without significant respiratory depressant effects.

In the event of cardiovascular and respiratory collapse, normal resuscitative procedures should be employed. Respiratory depression caused by overdosage with meptazinol may only be partially reversed with therapeutic doses of naloxone. Naloxone has a short duration of action in comparison with meptazinol. Repeated administration or administration by continuous intravenous infusion may be considered 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: Opioids; Other Opioids, ATC code: N02AX

Meptid (meptazinol) is a centrally acting analgesic belonging to the hexahydroazepine series, which has demonstrated mixed agonist and antagonist activity at opioid receptors.

Receptor binding studies have shown that although meptazinol displays only a low affinity for δ and κ opioid receptor sites, it has a somewhat higher affinity for a subpopulation of μ sites. These binding sites also display a high affinity for the endogenous opioid peptides, and are thought to be responsible for, among other things, analgesia, but not for the mediation of respiratory depression. A component of its analgesic action is also attributable, in mice at least, to an effect on central cholinergic transmission. In this respect it differs from all conventional analgesic drugs which have been examined.

5.2 Pharmacokinetic properties

After intramuscular administration, meptazinol is rapidly absorbed and peak plasma levels are reached within 30 minutes. The plasma half-life is approximately 2 hours. The peak analgesic effect is seen within 30-60 minutes and lasts about 3 - 4 hours. After intravenous administration, the onset of action is immediate, occurring within minutes, and lasts a minimum of one hour.

The major route of metabolism is via the glucuronidation pathway and excretion occurs mainly in the urine.

5.3 Preclinical safety data

Standard toxicity tests revealed no unexpected findings of clinical significance.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glucose anhydrous
Water for injections

6.2 Incompatibilities

Meptid Injection should not be mixed with other drugs in the same infusion solution or in the same syringe. Meptid Injection is an acidic solution of the hydrochloride salt of meptazinol and is therefore pharmaceutically incompatible with injection solutions known to be strongly basic (for example thiopentone) as precipitation of the meptazinol base may occur.

6.3 Shelf life

Unopened: 3 years
Once Opened: For single use only. Discard any unused contents.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

1 ml clear glass ampoules. The glass complies with the requirements of the European Pharmacopoeia Type 1. The ampoules will be packed in cartons of 10 and cartons of 1.

6.6 Special precautions for disposal

Single use only. Discard any unused contents.

7 MARKETING AUTHORISATION HOLDER

Almirall, S.A.
Ronda General Mitre, 151
Barcelona
08022
Spain

8 MARKETING AUTHORISATION NUMBER

PA0968/005/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 10th October 1983
Date of last renewal: 12th August 2008

10 DATE OF REVISION OF THE TEXT

July 2020