SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

NAVIDOXINE® 25 mg tablets (Meclozine hydrochloride)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains: meclozine hydrochloride 25 mg. For excipients, see 6.1

3. PHARMACEUTICAL FORM

Tablets.
White, oblong tablet with scored line on both sides, length 9 mm and width 5 mm. The tablet can be divided in two equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Meclozine is indicated in adult and adolescent over 12 years old, for the prevention and symptomatic treatment of nausea, vomiting and dizziness associated with travel sickness.

4.2 Posology and method of administration

Dosage adults and children over 12 years:
For motion sickness, the recommended initial dose is 25 to 50 mg taken one hour before departure and repeated every 24 hours during the journey.
Dosage in elderly subjects: Elderly subjects should start the treatment with fractionated doses (half doses), to be increased gradually according to tolerability and the clinical response.
Patients with renal impairment: As elimination is non-renal, the dosage remains the same and no special precautions are needed.

Dosage reduction may be required if NAVIDOXINE is used simultaneously with other central nervous system depressant drugs, with drugs having anticholinergic properties, or with MAO inhibitors (see Section 4.5).

4.3 Contraindications

NAVIDOXINE is contraindicated in subjects who have previously exhibited hypersensitivity to one of the ingredients of the drug or to piperazine derivatives. It is contraindicated in children under 12 years of age, in patients with prostatism and closed-angle glaucoma and in patients suffering from hepatic insufficiency.

4.4 Special warnings and special precautions for use

NAVIDOXINE should be used with caution in cases of urinary retention, digestive or urinary obstruction, myasthenia, decreased gastro-intestinal motility, in the event of treatment with MAOIs and with the concomitant ingestion of alcohol

Particular attention is recommended when NAVIDOXINE is administered to elderly subjects (sensitivity to adverse effects) and to subjects who will be required to drive a vehicle or use dangerous machinery (risk of sedation).

In addition:
- Use with caution when taking central nervous system depressants, hypnotics and tranquillisers concomitantly.
- To reduce the anticholinergic effects associated with meclozine, it is recommended that treatment in elderly subjects should be instituted at reduced doses and the duration of use of the product should be limited.
- In elderly subjects and in the case of dementia, the use of meclozine may engender or exacerbate the signs of confusion.
- Prolonged use of the drug may predispose to periodontal disease, caries and candidosis or cause sensations of oral discomfort (decreased production of saliva).

NAVIDOXINE should be used cautiously in patients suffering from epilepsy.
NAVIDOXINE treatment should be stopped four days before allergy testing to avoid effects on the test results.

Warning related to excipients
Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interactions with other medicinal products and other forms of interaction

NAVIDOXINE may potentiate the effects of central nervous system depressants (sedatives, hypnotics, alcohol), anticholinergic agents (tricyclic antidepressants, antihistamines, etc.) and MAOI. There is also a risk of interaction with medicines known to be hepatic enzyme inducers of inhibitors. Dosage should be adapted on an individual basis.

4.6 Pregnancy and lactation

Reproductive toxicology studies have shown the induction of cleft palate in the rat but not in other species at doses equivalent to 25-50 times the human dose.
Epidemiological studies in a large number of pregnant women have not shown that NAVIDOXINE increases the risk of malformation when administered during pregnancy. NAVIDOXINE should therefore only be administered to pregnant women if absolutely necessary for the shortest possible time and the dose should not exceed 50 mg daily.

NAVIDOXINE is excreted in the breast milk and should not be used during lactation.

4.7 Effects on ability to drive and use machines

Patients who drive or operate dangerous machines should be warned that NAVIDOXINE may cause drowsiness, particularly during the first few days of treatment, and should also be warned against the risks of potentiation with central nervous system depressant drugs: hypnotics, neuroleptics, anxiolytics and alcohol, simultaneous ingestion of which should be advised against.

4.8 Adverse effects

The undesirable effects reported vary with the individual sensitivity. The adverse effects are generally related to the CNS depressant effect or paradoxical stimulation of the CNS, the anticholinergic properties or hypersensitivity reactions.

The most common adverse effects include: drowsiness or sedation. A sensation of dry mouth is a frequent effect. Visual disorders, nausea and vomiting, and arthralgia are rare.

For the other adverse effects, the frequencies are not known:
Cardiovascular system: palpitations, tachycardia, hypotension.
Eyes, ENT system: tinnitus, auditory and visual hallucinations, diplopia, blurred vision, dry
nose, epistaxis.
Gastro-intestinal system: abdominal pain, constipation, diarrhoea, dry mouth, nausea, vomiting.
General disorders / unspecified sites: fatigue, weakness.
Immunological system: anaphylactic shock.
Metabolism and nutrition: anorexia, increased appetite and weight gain.
Nervous system: dizziness, headache, paraesthesia, somnolence, sedation, movement disorders
(including Parkinsonian syndrome), tremor, vertigo, headache.
Psychiatric disorders: anxiety, euphoria, excitability, hallucinations, insomnia, psychotic disorders.
Genito-urinary system: dysuria, polyuria, urinary retention.
Respiratory system: dry throat, dry nose, bronchospasm.
Skin and integument: rash and urticaria, photosensitivity, skin eruption.

In the presence of a non-serious adverse effect, the dose should be reduced at the expense of a reduction in activity, or administered in the evening at bedtime in the case of somnolence. If a serious effect occurs, treatment should be discontinued.

4.9 Overdose Symptoms

As with other antihistaminic drugs, overdosage may result in CNS depression and/or stimulation. Effects of anticholinergic overload are also observed such as fixed and dilated pupils, flushed face, dry mouth, excitation, hallucinations, and tonic-clonic seizures. Extrapyramidal syndrome has been reported. Other events such as ataxia, tremors, psychoses, hyperthermia, hypotension, hypertension, tachycardia, and arrhythmias have also been reported with antihistaminic drug overdoses.

Overdosage in adults may cause CNS depression with drowsiness, coma or excitement, seizures, and postictal depression. In young children, CNS stimulation is predominant. Severe toxicity in children and adults may result in cerebral edema, deep coma, respiratory depression, cardiorespiratory collapse, and death.

Management of overdose

There is no specific antidote. Treating poisoning by meclozine is basically supportive and symptomatic.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Meclozine is a derivative of benzhydrylpiperazine. It has anti-emetic, sedative, anticholinergic and H1 antihistamine properties.

5.2 Pharmacokinetic properties:

After administration of an oral dose, Meclozine appears rapidly in the systemic circulation and reaches its peak concentration after 2.2 hours. The plasma half-life is 5.7 to 11.1 hours. The bioavailability is variable because of extensive presystemic metabolisation. 10 metabolites have been detected, principally in the faeces. Meclozine is principally eliminated non-renally (less than 0.05% Meclozine is found in the urine after 72 hours).
The other pharmacokinetic parameters of Meclozine have not been established to date.

5.3 Preclinical safety data

Conventional acute and repeat dose toxicity studies in the rat and dog have not revealed any particular adverse effects in humans. Reproductive toxicity studies show teratogenicity in the rat but not in other species at doses equivalent to 20-50 times the maximum human dose. Antiarrhythmic activity and effects on cardiac conductivity have been observed during studies in animals exposed to doses exceeding the maximum exposure in humans and thus indicating the lack of clinical relevance.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

25 mg tablets: Anhydrous colloidal silica – Maize starch - Calcium stearate - Polyvidone. - Lactose - Talc q.s. one tablet

6.2 Incompatibilities

Not applicable

6.3 Shelf-life

5 years.

6.4 Special precautions for storage

Navidoxine 25 mg tablet: do not store above 25°C.
The medicinal product must be kept in the outer carton because of the potential sensitivity to moisture of meclozine hydrochloride.

6.5 Nature and contents of container

Box of 10 tablets.

6.6 Instructions for use and handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER
Gen.Orph SAS
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8. MARKETING AUTHORISATION NUMBERS
MA1263/00101

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1st June 2005

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13th January 2021