1. NAME OF THE MEDICINAL PRODUCT

DISFOR 500 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 500 mg of methocarbamol.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet.

White, biconvex, smooth, round tablets, scored on one side, without cracks and with even edges.

The score line is only so that the tablet can be broken to make swallowing easier, but not to divide it into equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Short-term symptomatic treatment of painful muscle spasms in acute musculoskeletal disorders.

4.2 Posology and method of administration

Posology

Treatment with methocarbamol should be kept as short as possible. The administration of methocarbamol should be discontinued as the painful symptoms subside.

Adults: 2-3 tablets four times a day (daily dose of 4 to 6 grams). In severe cases a higher dose may be necessary, the maximum recommended dose being 8 g per day for the first 48-72 hours.

Elderly patients: half the dose may be sufficient to achieve a therapeutic response. The recommended dose is 1 tablet 4 times a day.

Paediatric population: its use is not recommended in children under the age of 18 due to the lack of safety and efficacy data.

Patients with liver disease: since the elimination half-life of methocarbamol can be longer in these patients than in adults, the dose should be increased more gradually. A longer interval between successive doses may be required in such cases.

Method of administration

The tablets should be taken with a glass of water.

4.3 Contraindications

- Known hypersensitivity to methocarbamol or to any of the excipients listed in section 6.1.
- Coma or precoma.
- Known brain disease.

- History of seizures or epilepsy.
- Myasthenia gravis.

4.4 Special warnings and precautions for use

Methocarbamol should be administered with precaution in patients with impaired hepatic and renal function, avoiding prolonged treatments.

Interference with diagnostic tests:

Methocarbamol may interfere with the colour of certain analytical tests, such as the nitrosonaphthol test for 5-hydroxyindoleacetic acid or the Gitlow procedure for vanillylmandelic acid. It has also been reported that in some patients the colour of urine samples is altered during storage, turning brown, black, blue or green.

4.5 Interactions with other medicinal products and other forms of interaction

Methocarbamol can increase the effects of other central nervous system depressants or stimulants, including alcohol, barbiturates, anaesthetics and appetite suppressants.

It can also enhance the effects of anticholinergic agents such as atropine and certain psychotropic drugs.

Methocarbamol may inhibit the bromide effect of pyridostigmine. It should therefore be used with precaution in patients with myasthenia gravis who are treated with acetylcholinesterase inhibitors.

4.6 Fertility, pregnancy and lactation

Pregnancy

No studies have been carried out with methocarbamol on animal reproduction. It is not known whether methocarbamol may damage the foetus or affect reproductive capacity when administered to pregnant women.

The safety of methocarbamol with regard to possible adverse effects on foetal development has not been established. Isolated cases of foetal and congenital abnormalities after intrauterine exposure to methocarbamol have been described.

Methocarbamol is not recommended for pregnant women or women planning to become pregnant, particularly in the early stages of pregnancy, unless the doctor considers that the potential benefits outweigh the possible risks.

Breast-feeding

Methocarbamol and/or its metabolites have been detected in animal milk (dogs). However, it is not known whether methocarbamol or its metabolites are excreted in human milk. Accordingly, care should be taken when administering Disfor to breast-feeding women.

4.7 Effects on ability to drive and use machines

Disfor may cause drowsiness, so patients should not drive or operate machines unless they are sure that their mental capacity is not affected, especially if administered concomitantly with other medicines that can also cause drowsiness.

4.8 Adverse reactions

Adverse reactions described with the administration of methocarbamol are:

Blood and lymphatic system disorders: leukopenia.

Cardiac disorders: bradycardia, flushing, hypotension, syncope.

Eye disorders: diplopia, blurred vision, nystagmus.

Gastrointestinal disorders: dyspepsia, nausea and vomiting, dysgeusia.

General disorders and administration site conditions: angioneurotic oedema, anaphylactic reaction, fever, headache, conjunctivitis accompanied by nasal congestion, metallic taste.

Hepatobiliary disorders: jaundice (including cholestatic jaundice).

Nervous system disorders: nervousness, anxiety, tremor, amnesia, confusion, dizziness or lightheadedness, vertigo, drowsiness, insomnia, slight loss of muscle coordination, seizures (including epilepsy).

Skin and subcutaneous tissue disorders: pruritus, rash, urticaria.

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 Spanish Pharmacovigilance System for Medicinal Products for Human Use: https://www.notificaRAM.es/.

4.9 Overdose

Little information is available regarding acute methocarbamol toxicity. The cases of methocarbamol overdose on record occurred jointly with alcohol and other CNS depressants and include the following symptoms: nausea, dizziness, blurred vision, hypotension, seizures and coma. One adult survived a deliberate overdose of 22-30 grams of methocarbamol, without severe toxicity. Another adult survived a dose of 30-50 grams. In both cases, the main symptom was extreme drowsiness. Treatment was symptomatic and they recovered without other effects. However, cases of fatal overdose have been described.

The treatment of methocarbamol overdose includes symptomatic and support treatment. The support measures include keeping the airway open, monitoring urine output and vital signs and administering liquids intravenously, if necessary.
It is not known whether haemodialysis is of use in dealing with this overdose.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Muscle relaxants, centrally acting agents; Carbamic acid esters ATC code M03B A03.

Methocarbamol is a centrally acting muscle relaxant whose action could be due to a general depressant effect on the CNS. It exerts its muscle relaxant effect by inhibiting polysynaptic reflexes in the spinal cord and subcortical structures. At therapeutic doses it does not affect the physiological tone or contractility of skeletal muscles or the motility of smooth muscle.

5.2 Pharmacokinetic properties

Absorption
After oral administration, methocarbamol is absorbed rapidly and completely, reaching its maximum plasma levels after 1-3 hours. Its muscle relaxant effects become apparent 30 minutes after oral administration.

Distribution
Once in the systemic circulation, methocarbamol is widely distributed throughout the body and in healthy volunteers plasma protein binding ranges between 46 and 50%. In laboratory animals, the highest levels are detected in the liver and kidneys. The drug can pass through the placenta, although it is not known whether it is excreted in breast milk.

Metabolism
Methocarbamol is extensively metabolised in the liver by dealkylation and hydroxylation.

Clearance

In healthy volunteers, plasma clearance of methocarbamol varies from 0.2 to 0.8 l/h/kg, with an elimination half-life of 1-2 hours. Methocarbamol is mainly eliminated in the urine in the form of conjugated glucuronides and sulphates of its metabolites. A small proportion is excreted in the faeces.

Elderly patients:
In elderly patients, the elimination half-life of methocarbamol increases slightly in comparison to younger patients. Plasma protein binding is also slightly lower (41-43% compared with 46-50%).

Patients with hepatic impairment:
In 8 patients with hepatic impairment caused by alcoholic cirrhosis total methocarbamol clearance was reduced by approximately 70% with respect to the healthy population (11.9 l/h) and the half-life increased to 3.38 hours (± 1.62) compared with 1.11 hours (± 0.27) in healthy subjects. The fraction of bound methocarbamol was 40-50%, lower than the percentage observed in healthy subjects of the same age and weight (46-50%).

Patients with renal impairment:
In patients with renal insufficiency, methocarbamol clearance is also reduced.
In 8 patients with renal impairment on maintenance haemodialysis methocarbamol clearance was reduced by 40% with respect to the healthy population, although the elimination half-life was similar in both groups (1.2 versus 1.1 hours, respectively).

5.3. Preclinical safety data

The acute toxicity of methocarbamol is relatively low. In animal testing the following signs of intoxication were observed: ataxia, catalepsy, seizures and coma. No chronic toxicity studies have been carried out. The toxic effects on reproduction have not been evaluated. There are no long-term animal studies assessing the mutagenic potential of the product. No long-term studies have been carried out to determine its carcinogenic potential.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Corn starch
Magnesium stearate
Microcrystalline silica
Povidone
Sodium carboxymethyl potato starch (type A)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

No special storage precautions necessary.

6.5 Nature and contents of container

Pack of 20 and 50 tablets in a PVC-aluminium blister.

6.6 Special precautions for disposal and other handling

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

7. MARKETING AUTHORISATION HOLDER

FAES FARMA, S.A.
Máximo Aguirre, 14
48940 Leioa
Bizkaia, Spain

8. MARKETING AUTHORISATION NUMBER

Registered with the AEMPS under no. 32,899

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 23 November 1959.
Date of latest renewal: November 2009.

10. DATE OF REVISION OF THE TEXT

12/2015