SUMMARY OF PRODUCT CHARACTERISTICS
MYOXERIL® 10MG, Film-Coated tablets

1. NAME OF THE MEDICINAL PRODUCT:
MYOXERIL® 10MG

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains:

Cyclobenzaprine hydrochloride.....10mg

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Film-coated tablet

4. CLINICAL DATA

4.1. Therapeutic indications
MYOXERIL® is indicated for the treatment of muscle spasms associated with acute, non-central musculoskeletal pain.
MYOXERIL® reduces muscle spasm and associated signs, such as pain, motor limitations, and restrictions in activities of daily living.

4.2. Posology and method of administration
The recommended dose is one 10 mg tablet, three times a day.
The dose can range between 20 mg and 40 mg a day, in fractioned doses (2-4 tablets a day), up to a maximum dose of 60 mg a day (6 tablets a day).

The duration of treatment should not exceed 3 weeks.

4.3. Contraindications
- Known hypersensitivity to cyclobenzaprine or any of the excipients of the medicinal product.
- Heart problems, such as arrthymia, cardiac conduction abnormalities, congestive heart failure, or recent myocardial infarction.
- Thyroid disease called hyperthyroidism (overactive thyroid).
- MYOXERIL® should not be administered to patients who are receiving MAOIs (medications for depression or Parkinson's disease) or within 14 days of their withdrawal

SUMMARY OF PRODUCT CHARACTERISTICS
MYOXERIL® 10MG, Film-Coated tablets

4.4. Special warnings and precautions for use

MYOXERIL® should be used with caution in patient:

- taking other central nervous system depressants.
- with a history of urinary retention.
- with a history of increased intraocular pressure or angle-closure glaucoma.
- with epilepsy.
- with liver problems.
- with hypertension.
- in elderly person.

4.5. Interaction with other medicinal products and other forms of interaction

Medications that can cause hypertensive crisis or severe seizures if taken concomitantly with cyclobenzaprine:

- Anti-Parkinson's medications (MAOIs: rasagiline, selegiline)
- Antidepressants (MAOIs: tranylcypromine, moclobemide)
- Painkillers (tramadol)
- Antibacterial drugs (linezolide)

Medications that might cause tachycardia or arrhythmias if they are taken with cyclobenzaprine:

- Medications used for heart problems such as antiarrhythmics (dronedarone, Amiodarone, Disopyramide, Flecainide, Ranolazine), anti-angina medications (Ivabradine) and beta-blockers (sotalol);
- Anti-cancer drugs (medications used in the treatment of cancer: arsenic trioxide, lapatinib, nilotinib, pazopanib, sunitinib, vemurafenib, and vinflunine)
- Antibiotics (clarithromycin, eythromycin, telithromycin, levofloxacin, moxifloxacin).
- Antifungals (fluconazole, voriconazole).
- Antimalarials (lumefantrine).
- Antipsychotics (medications for treating schizophrenia: pimozide, asenapine, clozapine, droperidol, paliperidone, ziprasidone).
- Antidepressants (fluoxetine).
- Medications that act on the nervous system (methadone, tetrabenazine, pasireotide).
- Medications containing sodium phosphate.
- Anti-asthmatics (formoterol).

Medications that might increase the risk of serotonin symdrome such as anticancer drugs (procarbazine); anti-migraine and antidepressants (duloxetine, hydroxytryptophane, trazodone, desvenlafaxine, escitalopram).

Medications for treating arterial hypertension (guanethidine).

Cyclobenzaprine may reduce the depressor effect of alcohol and other medications that slow down the activity of the nervous system.

4.6. Pregnancy and breast-feeding

Pregnancy: Cyclobenzaprine, according to the category of medicines that can be used during pregnancy, belongs to category B.
There are no controlled studies in humans and studies in animals have not shown that cyclobenzaprine has any adverse effects on the fetus (see section 5.3).

Therefore, cyclobenzaprine should not be used during pregnancy, unless the potential benefit justifies the potential risks.

Breastfeeding: It is not known if cyclobenzaprine passes into breast milk. As cyclobenzaprine is similar to tricyclic antidepressants, some of which are excreted in breast milk, caution and monitoring is recommended when prescribing in breastfeeding women.

Fertility: Animal studies have not shown that cyclobenzaprine affects fertility (see section 5.3)

4.7. Effects on ability to drive and use machines

MYOXERIL® can cause sleepiness, vertigo, vision problems, clumsiness, or instability in some people. Caution is advised when using dangerous vehicles or machinery and when performing other activities requiring a special alert.

4.8. Undesirable effects

Like all medications, cyclobenzaprine can cause undesirable effects, but they do not occur systematically in everyone.
The most common effects are sleepiness, dry mouth, and dizziness.

Other undesirable effects described for cyclobenzaprine are:

- Immune system disorders: allergic reactions consisting of skin rash, urticaria, swelling of the face and tongue.
- Psychiatric disorders: confusion, nervousness, depression, sleeping problems, anxiety, agitation, abnormal thoughts, hallucinations, insomnia, disorientation, excitation, euphoria.

- Nervous system disorders: trembling, loss of motor coordination, disrupted speech, tingling, numbness, seizures, hypertonia (increased muscle tone or stiffness), dizziness.
- Eye disorders: blurred vision.
- Ear and labyrinth disorders: tinnitus.
- Heart and vascular disorders: tachycardia, syncope, arrhythmias, hypotension, palpitations, vasodilation.
- Gastrointestinal disorders: bad taste in the mouth, constipation, dyspepsia (poor digestion), nausea, vomiting, diarrhea, gastritis, anorexia, changes in taste, flatulence, abdominal pains, thirst, gastrointestinal pain.
- Hepatobiliary disorders: abnormal liver function, hepatitis, jaundice and cholestasis (blocking of the flow of bile).
- Musculoskeletal and connective tissue disorders: muscle contractions and local weakness.
- Kidney and urinary disorders: increased frequency of urination and/or urinary retention, reduced bladder tone.
- General problems: weakness, headache, asthenia (loss of strength), discomfort
- Endocrinal disorders: hypoglycemia
- Skin and subcutaneous tissue problems: sweating

4.9. Surdosage

The most common symptoms that accompany acute overdose are seizures, severe drowsiness, fast or irregular heartbeat, difficulty breathing, hallucinations, increased or decreased body temperature, and vomiting.

Symptomatic or supportive treatment recommended: stomach emptying by induction of emesis and gastric lavage. Administration of 20 to 30 grams of absorbent charcoal at 4 to 6-hour intervals for a period of 24 to 48 hours after ingestion. Perform an electrocardiogram (ECG) and monitor heart function for obvious signs of arrhythmia. Follow the patient carefully. Keep the airways open, maintain enough fluid intake, regulate body temperature.

To treat severe or life-threatening anticholinergic effects, administer Physostigmine Salicylate (1 to 3 mg intravenously). Repeat this if necessary if the life-threatening symptoms persist or recur, such as arrhythmias, seizures and deep coma. Physostigmine is recommended only in severe cases due to its toxicity.

Use standard medical measures to treat circulatory shock and metabolic acidosis. Cardiac arrhythmias can be treated with neostigmine, pyridostigmine or propanolol. When symptoms of heart failure appear, the administration of a short-acting digitalis preparation should be considered. Strict monitoring of heart function is recommended for at least five days.

Anticonvulsants can be used to treat seizures.

Dialysis is probably not effective due to the low plasma concentrations of the drug.

SUMMARY OF PRODUCT CHARACTERISTICS
MYOXERIL® 10MG, Film-Coated tablets

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Therapeutic class: Muscle relaxants, ATC code: M03B X08

Action mechanism

Cyclobenzaprine chloride is a muscle relaxant, related structurally and pharmacologically to the tricyclic antidepressants.

Cyclobenzaprine relieves muscle spasms by a central effect, mainly in the brainstem, while it lacks activity at the neuromuscular junction and has no direct effect on skeletal muscle. Nor is it a peripheral muscle blocker.

Studies in animals have shown that cyclobenzaprine has an influence both alpha and gamma motor neurons, reducing tonic somatic motor activity.
Cyclobenzaprine was found to be somewhat less potent in the spinal cord ischemia model, suggesting that the site of action of the drug is primarily supraspinal. However, it is postulated that it can also act on the spinal cord and exert a general relaxing activity of the skeletal muscle.

Cyclobenzaprine reduces the pain associated with muscle contractures and spasms and improves mobility. Cyclobenzaprine is ineffective in muscle spasm due to brain injury.

Cyclobenzaprine is structurally linked to tricyclic antidepressants and may have a similar action. These possible effects include central and peripheral anticholinergic actions, a sedative effect and an increase in heart rate.

The clinical responses observed include an improvement in muscle spasm proven by palpation, decreased pain and local hypersensitivity, increased range of motion and less restriction on daily activities.

MYOXERIL® has a rapid onset of action; clinical improvement was observed during the first day of treatment and independently of any sedative action.

5.2. Pharmacokinetic properties

Cyclobenzaprine hydrochloride is well absorbed in humans after oral administration, but plasma levels vary widely between one individual and another. Between 38% and 51% is excreted in the urine, and between 14% and 15% in feces. Oral absorption is almost complete. The half-life ranges from 1 to 3 days.

Cyclobenzaprine hydrochloride is extensively metabolized in humans. Oxidative N-demethylation, one of the metabolic pathways of cyclobenzaprine, is mediated by CYP3A4 and CYP1A2, and to a lesser extent, CYP2D6. Cyclobenzaprine is eliminated

quite slowly, with an effective half-life of 18 hours (range of 8 to 37 hours; n = 18); plasma clearance is 0.7 L/min.
Plasma concentrations of cyclobenzaprine are generally higher in the elderly and in patients with hepatic impairment.

5.3. Preclinical safety data

Non-clinical data on acute toxicity obtained from tests in mice have shown an LD50 of 163.9 mg / kg when cyclobenzaprine was administered orally and an LD50 of 19 mg / kg when administered intravenously.

In a 67-week toxicity study, conducted in rats, cyclobenzaprine administered at doses approximately 5-40 times the maximum recommended dose in humans, caused liver lipidosis. The animals' liver was whitish and in some cases hypertrophied. In the high dose groups, these microscopic alterations were observed after 26 weeks of treatment, being observed with greater anticipation in the animals that died before this period. In the lower dose groups, these changes in hepatocytes were observed after 26 weeks.

Preclinical data do not reveal a special risk in humans according to genotoxicity studies.

No evidence of carcinogenic potential was observed during an 81-week study with cyclobenzaprine in mice, nor in a 105-week study in rats.

Reprotoxicity studies in rat, mouse and rabbit have not shown that cyclobenzaprine produces adverse effects on the fetus or impaired fertility when doses up to 20 times higher than human are administered.

The excretion of cyclobenzaprine in milk has not been studied in animals.

6. PHARMACEUTICAL DATA

6.1. List of excipients

Microcrystalline cellulose, Lactose, Cornstarch, Croscarmellose sodium, colloidal anhydrous silica, Magnesium stearate, Instacoat, Yellow iron oxide

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

3 years

6.4. Special precautions for storage

Store MYOXERIL® in a dry place, protected from light, at a temperature below 30ºC

6.5. Nature and contents of container

MYOXERIL® is supplied in the form of yellow film-coated tablets. The tablets are packed in aluminum/aluminum blister packs of 10 tablets. Each box contains 20 tablets presented in two blisters.

Medication supplied under medical prescription.
Keep out of the sight and reach of children

6.6. Special precautions for disposal and other handling

No special requirements

7. MARKETING AUTHORIZATION HOLDER

CROSS PHARM S.A.
Quai des Bergues 23,
1201 Geneva
Switzerland

Manufactured by:
The Madras Pharmaceuticals
137-B, Old Mahabalipuram Road,
Karapakkam, Chennai 96 – Inde
Mfg. Lic. Nº : 110

8. MARKETING AUTHORIZATION NUMBER

Not applicable

9. DATE OF FIRST AUTHORIZATION / RENEWAL OF THE AUTHORIZATION

To be completed afterwards

10. DATE OF REVISION OF THE TEXT

January 2019.