SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

MYOXOL 4 mg/2 ml, solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Thiocolchicoside..... 4.0 mg
For a 2 ml ampoule

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection (IM) in ampoule.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Adjunctive treatment of painful muscle contractures in acute spinal pathology in adults and adolescents from 16 years of age.

4.2. Posology and method of administration

Posology

The recommended and maximum dose is 4 mg every 12 hours (i.e., 8 mg per day). The duration of treatment is limited to 5 consecutive days.
Doses higher than recommended or long-term use should be avoided (see section 4.4).

Pediatric population

MYOXOL should not be used in children and adolescents under the age of 16 years for safety reasons (see section 5.3).

Method of administration

Intramuscular route only.

4.3. Contraindications

This medication is contraindicated in the following cases:

- hypersensitivity to the active substance or to any of the excipients listed in section 6.1;
- hypersensitivity to colchicine;
- pregnancy and breastfeeding (see section 4.6);
- in women of childbearing age not using effective contraception during treatment with MYOXOL and for 1 month after stopping treatment (see sections 4.4 and 4.6);
- In men of childbearing age who are not using effective contraception during treatment with MYOXOL and for 3 months after stopping treatment (see sections 4.4 and 4.6);
- Hemostasis disorders or ongoing anticoagulant treatment (contraindication related to the intramuscular route).

4.4. Special warnings and precautions for use

Warnings

In patients with epilepsy or at risk of seizures, thiocolchicoside may increase the likelihood of seizures; therefore, it is recommended to assess the benefit-risk ratio of thiocolchicoside and to increase clinical monitoring. The occurrence of seizures requires discontinuation of treatment.
Cases of liver damage (e.g., cytolytic or cholestatic hepatitis) have been reported with thiocolchicoside since its marketing. Severe cases (fulminant hepatitis) have been reported in patients taking concomitant NSAIDs or paracetamol. Patients should stop treatment and contact their doctor if signs and symptoms of liver damage develop (see section 4.8).

Precautions for use

- Do not combine thiocolchicoside with other products in the same syringe.

- Cases of vasovagal syncope have been observed; therefore, avoid predisposing conditions and monitor for about ten minutes after injection (see section 4.8).

- This medicine contains sodium. The sodium content is less than 1 mmol per dose, i.e., "sodium-free".

Genotoxicity potential

Preclinical studies have shown that one of the metabolites of thiocolchicoside (SL59.0955) induces aneuploidy (an abnormal number of chromosomes in cells after cell division) at concentrations close to those observed in humans exposed to oral doses of 8 mg twice daily (see section 5.3). Aneuploidy is considered a risk factor for teratogenesis, embryo / fetotoxicity , spontaneous abortion, and impaired fertility in humans, as well as a potential risk factor for cancer.
As a precaution, use of the product at doses higher than the recommended dose or long-term use should be avoided (see section 4.2).
Patients (men and women) should be carefully informed of the potential risk of possible pregnancy and the effective contraceptive measures to follow (see sections 4.3 and 4.6).
This medicine contains sodium. The sodium content is less than 1 mmol (23 mg) per ampoule, i.e., "sodium-free".

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

Not applicable.

4.6. Fertility, pregnancy and breastfeeding

Contraception in women and men of reproductive age

MYOXOL is contraindicated in women and men of childbearing age who are not using effective contraception (see section 4.3).
Due to the aneugenic potential of thiocolchicoside and its metabolites, women of childbearing potential must use effective contraceptive methods during treatment with thiocolchicoside and for one month after stopping it (see section 5.3).
Men of childbearing age must use effective methods of contraception and not conceive a child during treatment with thiocolchicoside and for three months after stopping it (see section 4.3).

Pregnancy

Data on the use of thiocolchicoside in pregnant women are limited. Therefore, the potential risks to the embryo and fetus are unknown.
Animal studies have shown teratogenic effects (see section 5.3).
MYOXOL is contraindicated during pregnancy and in women of childbearing age not using contraception (see section 4.3).

Breastfeeding

Given that thiocolchicoside passes into breast milk, its use is contraindicated during breastfeeding (see section 4.3).

Fertility

In a rat fertility toxicity study, no impairment of fertility was observed at doses up to 12 mg/kg, corresponding to dose levels that did not induce any clinical effects. Thiocolchicoside and its metabolites exhibit aneugenic activity at various dose levels, which is a risk factor for impaired fertility in humans (see section 5.3).

4.7. Effects on the ability to drive vehicles and use machinery

Clinical studies have not shown any psychomotor alterations related to thiocolchicoside .
However, drowsiness can frequently occur; this must be taken into account by vehicle drivers and machine operators.

4.8. Undesirable effects

The classification of adverse events according to their frequency is as follows: very common (≥1/10), common (≥1/100 and <1/10), uncommon (≥1/1000 and <1/100), rare (≥1/10000 and <1/1000), very rare (<1/10000), not known (cannot be estimated from the available data).

General disorders and administration site abnormalities

- Frequency not known: injection site reactions, including pain, erythema, swelling around the injection site, embolia cutis medicamentosa (Nicolau syndrome).

Hypersensitivity reactions

- Rare: hypersensitivity reactions such as urticaria.
- Frequency not known: hypersensitivity reactions such as Quincke's edema and, exceptionally, anaphylactic shock.
- Frequency not known: anaphylactic reactions.

Skin reactions

- Uncommon: allergic skin reactions such as itching, erythema, maculopapular rashes, vesiculobullous rashes .

Gastrointestinal disorders

- Common: diarrhea (see section 4.4), stomach pain.
- Uncommon: nausea, vomiting.

Hepatobiliary disorders:

- Frequency not known: liver disorders (e.g. cytolytic or cholestatic hepatitis) (see section 4.4).

Neuropsychological disorders :

- Common: drowsiness.
- Rare: temporary excitement or confusion.
- Frequency not known: convulsions or recurrence of seizures in epileptic patients, vasovagal-type malaise reported almost exclusively within minutes following IM administration (see section 4.4).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals should report any suspected adverse reactions using the FRILAB reporting form available under the pharmacovigilance tab of the website: www.frilab.ch

4.9. Overdose

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic class: MYORELAXANT, ATC code: M03BX05.
(M: Muscle and Skeleton)
Thiocolchicoside , a synthetic sulfur analog of a natural colchicum glucoside, acts pharmacologically as a muscle relaxant in both humans and animals. It suppresses or significantly reduces centrally originating contractures: in spastic hypertonia, it decreases the passive resistance of the muscle to stretching and reduces or eliminates residual contractures. Its muscle-relaxant action is also evident in visceral muscles: it has been demonstrated, in particular, in the uterus.
However , thiocolchicoside has no curarizing effect: it acts via the central nervous system, not by paralyzing the motor endplate. Studies (1980) demonstrated a selective agonist-type affinity of thiocolchicoside for gamma-aminobutyric acid (GABA) receptors, as well as glycinergic agonist properties . Therefore, it does not impair voluntary movement, does not cause paralysis, and thus avoids any respiratory risk.
Finally, thiocolchicoside has no influence on the cardiovascular system.
Finally, thiocolchicoside also acts as an antagonist of $GABA_A$ type receptors (mainly located in the cerebral cortex), this pharmacological action being known to have convulsant or proconvulsant properties .

5.2. Pharmacokinetic properties

Absorption

Following intramuscular (IM) administration, the maximum plasma concentration (C_{max}) of thiocolchicoside occurs within 30 minutes and reaches values of 113 ng / mL after a 4 mg dose, and 175 ng / mL after an 8 mg dose. The corresponding AUC (area under the curve) values are 283 and 417 ng·h / mL , respectively .
The pharmacologically active metabolite of SL18.0740 is also observed at lower concentrations with a C_{max} of 11.7 ng / mL occurring 5 h after administration of thiocolchicoside and an AUC of 83 ng.h / mL .
There are no data available concerning the inactive metabolite SL59.0955.

Distribution

The apparent volume of distribution of thiocolchicoside is estimated to be approximately 42.7 L after an 8 mg IM administration. No data are available for the two metabolites.

Elimination

After IM administration, the apparent elimination half-life ($t_{1/2}$) of thiocolchicoside is 1.5 h and its plasma clearance is 19.2 L/h.

5.3. Preclinical safety data

The toxicological profile of thiocolchicoside was evaluated *in vitro* , and *in vivo* after parenteral and oral administration.
Thiocolchicoside is well tolerated after repeated oral administration for up to 6 months in rats and non-human primates at doses less than or equal to 2 mg/kg / day in rats and 2.5 mg/kg/day in non-human primates, and after repeated intramuscular administration for 4 weeks in primates at doses up to 0.5 mg/kg/day;
At high doses, after a single oral administration, thiocolchicoside causes vomiting in dogs, diarrhea in rats, and convulsions in rodents and non-rodents.
After repeated administration, thiocolchicoside caused gastrointestinal disturbances (enteritis, vomiting) when administered orally and vomiting when administered IM.
Thiocolchicoside itself does not induce gene mutation in bacteria (Ames test), chromosomal aberration in *vitro* (chromosomal aberration test on human lymphocytes) or chromosomal aberration *in vivo (in vivo* micronucleus test on mouse bone marrow after intraperitoneal administration).
The main glucuronide metabolite SL18.0740 does not induce gene mutations in bacteria (Ames test); however, it causes chromosomal aberrations *in vitro (in vitro* micronucleus test in human lymphocytes) and *in vivo (in vivo* micronucleus test in mouse bone marrow after oral administration). The micronuclei resulted primarily from chromosome loss (presence of centromeres in the micronuclei revealed by centromere-specific FISH staining), suggesting aneugenic properties. The aneugenic effect of SL18.0740 was observed at concentrations (in the *in vitro test*) and plasma exposures (in the *in vivo test*) higher (more than 10 times based on AUC) than those observed in human plasma at therapeutic doses.
The aglycone metabolite (3-desmethyl-thiocolchicine or SL59.0955), formed primarily after oral administration, induces chromosomal aberrations *in vitro (in vitro* micronucleus test on human lymphocytes) and *in vivo (in vivo* micronucleus test on rat bone marrow after oral administration). The micronuclei resulted mainly from chromosome loss (presence of centromeres in the micronuclei revealed by centromere-specific FISH or CREST staining), suggesting aneugenic properties. The aneugenic effect of SL59.0955 was observed at concentrations (in the *in vitro test*) and exposures (in the *in vivo test*) close to those observed in human plasma at therapeutic doses of 8 mg twice daily orally. The aneugenic

effect in dividing cells can lead to aneuploid cells. Aneuploidy is an alteration in chromosome number and a loss of heterozygosity, which is recognized as a risk factor for teratogenesis, embryotoxicity / spontaneous abortion, and impaired male fertility when it affects germ cells, and as a potential risk factor for cancer when it affects somatic cells. Since the presence of the aglycone metabolite (3- desmethyl-thiocolchicine or SL59.0955) after intramuscular administration has never been evaluated, its formation using this route of administration cannot be ruled out.
In rats, an oral dose of 12 mg/kg/day of thiocolchicoside resulted in major malformations and fetotoxicity (growth retardation, embryonic death, altered sex ratio). The no-observed-adverse-effect level (NOAEL) was 3 mg/kg/day.
In rabbits, thiocolchicoside showed maternal toxicity at doses of 24 mg/kg/day and above. In addition, minor abnormalities were observed (supernumerary ribs, delayed ossification).
In a rat fertility toxicity study, no impairment of fertility was observed at doses up to 12 mg/kg/day, which are doses that do not induce any clinical effects. Thiocolchicoside and its metabolites exhibit aneugenic activity at various dose levels, which is recognized as a risk factor for impaired human fertility.
The carcinogenic potential has not been evaluated.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Sodium chloride, hydrochloric acid, water for injections.

6.2. Incompatibilities

In the absence of compatibility studies, this medicine should not be mixed with other medicines.

6.3. Shelf life

2 years.

6.4. Special precautions for storage

Store at a temperature below 30°C and away from light.

6.5. Nature and contents of container

2ml glass ampoule, box of 5.

6.6. Special precautions for disposal and handling

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

7. MARKETING AUTHORISATION HOLDER AND OPERATOR

FRILAB SA
17 RUE DES PIERRES DU NITON
1207 GENEVA - SWITZERLAND

8. MANUFACTURER

MJ BIOPHARM PVT. LTD.
L-7 MIDC Industrial Area, Taloja
Dist. Raigad 410 208 Maharashtra
INDIA

9. DATE OF REVISION OF THE TEXT

February 2026.

10. DOSIMETRY

Not applicable.

11. INSTRUCTIONS FOR THE PREPARATION OF RADIOPHARMACEUTICALS

Not applicable.

CONDITIONS FOR PRESCRIPTION AND DISPENSING

Prescription-only medicine.
List I.