TECNICAL SPECIFICATIONS

MESENCHYMAL STEM CELLS

By Gencell Biotechnology

METFORMINA IA

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BIOTECHNOLOGY

MESENCHYMAL STEM CELLS

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Gencell® Mesenchymal Stem Cells

CTM METFORMIN IA

Mesenchymal Stem Cells.

PRODUCT NAME

CTM METFORMIN IA.

COMPOSITION

The solution contains Mesenchymal Stem Cells (MSCs) in the following presentations:
Células troncales mesenquimales pre-tratadas con metformina, en diferentes presentaciones:

7	Millon Cells
14	Millon Cells
21	Million Cells
28	Million Cells
42	Million Cells
49	Million Cells

PHARMACEUTICAL FORM AND USAGE CONSIDERATIONS

Injectable solution.

PRESENTATION

The plastic container protects the monovette containing 4 mL of product.

THERAPEUTIC PROPERTIES

Mechanism of Action

Mesenchymal stem cells (MSCs) play a key role in the repair of damaged joint tissues through multiple mechanisms of action. When administered intra-articularly, MSCs integrate into the joint environment, where cell adhesion molecules are increased, facilitating their attachment to the tissue and migration toward the injury site. The mechanisms through which MSCs contribute to joint repair include:

1. Modulation of Inflammation: MSCs secrete anti-inflammatory molecules that regulate the local immune response, reducing inflammation and pain in the affected joint.

2. Stimulation of the Immune System: They promote the proliferation and recruitment of regulatory T lymphocytes, which are essential for controlling and limiting disproportionate immune responses that may exacerbate joint damage.

3. Prevention of Apoptosis: They inhibit the apoptosis of endogenous cells in the cartilage and surrounding tissues, promoting cell survival and the integrity of the joint tissue.

4. Promotion of Cellular Regeneration: They stimulate the proliferation of cells in the cartilage and adjacent tissues, facilitating the regeneration and repair of damaged tissue.

5. Cellular Adaptation: They undergo transdifferentiation into the required cell type, such as chondrocytes or connective tissue cells, enabling more precise and effective repair of cartilage and other joint structures.

Pretreatment with metformin acts on the OCT-1 pathway, leading to increased expression of GLUT2 and GLUT4 transporters in bone tissues. This enhances glucose uptake and facilitates the energy metabolism required for bone formation. Additionally, metformin stimulates the differentiation of MSCs toward osteogenic lineages, promoting bone regeneration, aiding the consolidation of non-healed fractures, and improving bone density in osteoporosis.
Metformin also enhances the ability of MSCs to differentiate into chondrogenic and tendinogenic lineages. This pretreatment supports the regeneration of connective tissues and the repair of partial ligament tears and tendinitis by promoting collagen synthesis and the formation of new tissue in affected areas.
In the context of chondromalacia and osteoarthritis, metformin facilitates the transdifferentiation of MSCs into chondrogenic lineages, improving the repair of damaged cartilage. Pretreatment with metformin also reduces inflammation and improves the quality of articular cartilage, alleviating symptoms and promoting joint functionality.

CLINICAL DATA

a.Therapeutic Indications

CTM Metformin IA is indicated as an adjuvant therapy in the management of chronic metabolic diseases associated with insulin resistance, oxidative stress, and cellular dysfunction, including:

- Type 2 Diabetes Mellitus
- Metabolic Syndrome
- Non-alcoholic Fatty Liver Disease (NAFLD)
- Obesity with associated metabolic inflammation

This product assists in restoring tissue homeostasis, regulating inflammation, and improving glucose and lipid metabolism.

b.Dosage and Administration

Intravenous route.

Cannulate the patient with 100 mL of 0.9% saline solution and ensure correct placement of the venous line. Retrieve the content of the monovette and administer it through the Y-connector of the venoclysis set slowly (not as a bolus). Infuse the remaining saline solution over approximately 15 minutes.

c. Contraindications

Sensitivity or allergy to any component of the formula.
Diagnosis of neoplasia.
Renal or hepatic insufficiency.
Metabolic acidosis.

d. Warnings and Precautions

No evidence is available regarding safety in children under 12 years of age.
The product may contain traces of RPMI medium and metformin.
Administer only under the supervision of qualified healthcare professionals.

e. Interactions

To date, there are no extensive reports of severe adverse interactions between MSCs and specific drugs in the scientific literature. However, given their immunomodulatory profile, caution is advised when used concurrently with therapies that affect the immune or coagulation systems.

Immunosuppressants such as Methotrexate, Infliximab, or Tocilizumab may intensify immunosuppression, increasing infection risk or compromising immune response and MSC viability.
Anticoagulants and antiplatelet agents may increase bleeding risk.
Concomitant hypoglycemic agents (such as insulin, sulfonylureas, or other oral antidiabetics) may increase the risk of hypoglycemia.
Medical supervision is recommended during combined use.

f.Pregnancy and Lactation

The use of Mesenchymal Stem Cell-based therapies and metformin is contraindicated during pregnancy and lactation, as there are no research protocols or clinical studies supporting their safety under these conditions. It is unknown whether any component of the formulation or pre-stimulation process could cause harm during fetal development.

g.Adverse Effects

Possible side effects include dizziness, nausea, mild fever (<38°C), headache, or myalgia, which are self-limiting within 24–48 hours post-application.
Rare adverse reactions reported in the literature include hypersensitivity (such as urticaria), thromboembolism, chest pain, irregular heartbeat, shortness of breath, and numbness at the injection site or in extremities.
Metformin-related gastrointestinal symptoms, such as mild abdominal discomfort or diarrhea, may also occur. These effects are usually temporary and resolve without medical intervention.

ADDITIONAL DATA

a.Excipients

0.9% saline solution.

b.Shelf Life

After receipt, the product must be administered immediately or within no more than 24 hours.

c.Storage and Preservation Conditions

Store in a place protected from direct sunlight and refrigerated between 2 and 8 °C.
Do not expose to radiation or fire. Avoid freezing.
Keep out of reach of children and pets.

d.Waste Management

Dilute with 0.1% chlorine and dispose through the drain.
Freezing or refrigerating beyond the recommended period reduces product viability, which may increase the likelihood of side effects.

Marketing Authorization Holder

Gencell®