PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

MICRO MN

Manganese Sulfate Injection

Mn^{2+} 0.1 mg/mL
USP
Intravenous

Electrolyte

Sandoz Canada Inc.
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Boucherville, (Québec), Canada
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RECENT MAJOR LABEL CHANGES

4 DOSAGE AND ADMINISTRATION, 4.2 Recommended Dose and Dosage Adjustment (Pediatrics)	01/2022
7 WARNINGS AND PRECAUTIONS, Neurologic	01/2022

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Sections and Subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

MICRO MN (Manganese Sulfate Injection USP) is indicated for:

- use as a supplement to intravenous solutions given for total parenteral nutrition (TPN). Its administration in TPN solutions helps to maintain plasma manganese levels and to prevent depletion of endogenous stores of manganese and subsequent deficiency symptoms.

1.1 Pediatrics (≤ 18 years of age): MICRO MN is indicated for use in pediatric patients (see 4.2 Recommended Dose and Dose Adjustments).

1.2 Geriatrics (≥ 65 years of age): MICRO MN is indicated for use in geriatric patients. No dosage adjustments are required.

2 CONTRAINDICATIONS

MICRO MN is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

Periodic monitoring of manganese levels is suggested as a guideline for administration. The normal blood range for manganese is approximately 6 to 10 mcg/L.

4.2 Recommended Dose and Dosage Adjustment

Adults: For the metabolically stable adult receiving TPN, 0.15 to 0.8 mg/day is suggested as the additive dosage level for manganese.

Pediatrics (≤ 18 years of age): The following dosage levels of manganese are recommended:

Infants up to 10 kg:	≤ 1 mcg per kg/day
Children ≤ 15 kg:	1 mcg per kg/day, with a maximum daily dose of 15 mcg
Children 15.1 to 40 kg:	15 mcg per kg/day
Children and adolescents > 40 kg:	the adult preparations of trace elements should be prescribed.

See 7 WARNINGS AND PRECAUTIONS.

4.3 Reconstitution

Not applicable

4.4 Administration

MICRO MN is for intravenous use after dilution only.

Aseptic addition of MICRO MN to the amino acid/dextrose component of a TPN solution under a laminar flow hood is recommended. After dilution, the solution must be used within 24 hours, see 11 STORAGE, SATBILITY AND DISPOSAL.

Visually inspect parenteral drug products for particulate matter and discolouration prior to administration whenever container and solution permit.

5 OVERDOSAGE

Manganese toxicity (manganism), a rare central nervous system disease, can occur following chronic occupational exposure to the dust from manganese ore or fumes in steel processes. A metal fume fever syndrome can occur after exposure to high concentrations of manganese oxide; a few cases of pneumonitis have been associated with manganese exposure.

High doses of manganese can lead to deposition in the basal ganglia of the brain and cause toxic events that manifest symptomatically as Parkinson-like signs and symptoms, in addition to neuropsychiatric symptoms. If treatment lasts more than 4 weeks, manganese levels must be checked and if there is an excess of manganese, the administration of the parenteral nutrition should be stopped and corrective measures should be initiated.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table – Dosage Forms, Strengths, Composition and Packaging.

Route of Administration	Dosage Form/ Strength	Non-medicinal Ingredients
Intravenous	Solution / 0.1 mg/ mL	Sulfuric acid, water for injection.

COMPOSITION: MICRO MN contains 0.1 mg/mL of manganese as manganese sulfate monohydrate.

PACKAGING: Available in single use vials of 10 mL, boxes of 10.

The stopper is not made with natural rubber latex.

7 WARNINGS AND PRECAUTIONS

General
MICRO MN is a hypotonic solution which should be administered in admixtures only.

Do not give undiluted Micro Mn by direct injection into a peripheral vein because of the potential of infusion phlebitis.

Neurologic

Excess of manganese can lead to deposition in the basal ganglia of the brain and cause toxic events that manifest symptomatically as Parkinson-like signs and symptoms, in addition to neuropsychiatric symptoms.

If toxicity symptoms occur due to manganese, discontinue supplementation of TPN solutions immediately.

Hepatic / Biliary / Pancreatic
The possibility of manganese retention should be a consideration in patients with biliary obstruction and caution should be exercised since manganese is eliminated via the bile.

7.1 Special Populations

7.1.1 Pregnant Women
It is not known whether MICRO MN can cause fetal harm when administered to a pregnant woman or if it can affect reproductive capacity.

7.1.2 Breast-feeding
It is unknown if MICRO MN is excreted in human milk. Precaution should be exercised because many drugs can be excreted in human milk.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview
No adverse reactions have been reported for the amount of manganese present in this product. The amount is small and toxicity symptoms are not likely to occur at the suggested dosage level.

9 DRUG INTERACTIONS

9.2 Drug Interactions Overview
No drug interactions have been established.

9.4 Drug-Drug Interactions
Interactions with drugs have not been established.

9.5 Drug-Food Interactions
Interactions with food have not been established.

9.6 Drug-Herb Interactions
Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions
Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Manganese, an essential nutrient, is a component of several metalloenzymes, pyruvate carboxylase and superoxide dismutase, and a cofactor of a large number of enzyme systems including polymerase, galactotransferase, arginase and cholinesterase.

Manganese deficiency has been demonstrated in numerous animals and in one human subject with vitamin K deficiency whose symptoms included a delayed blood clotting response, mild evanescent dermatitis, reddening of hair and beard, slowed growth of hair, nails and beard, occasional nausea and vomiting, coincident decrease of serum phospholipids and triglycerides, and moderate weight loss.

10.2 Pharmacodynamics

Administration of manganese helps prevent deficiency symptoms such as nausea and vomiting, weight loss, reduced phospholipid and triglyceride plasma levels, dermatitis and changes in growth and colour of hair.

10.3 Pharmacokinetics

Absorption: Dietary manganese is poorly absorbed.

Distribution: It is estimated that the body of a normal 70 kg man contains 12 to 20 mg of manganese. This relatively small amount is widely distributed without notable concentration. However, manganese concentration tends to be higher in tissues rich in mitochondria (liver, kidney and pancreas). Reserve manganese stores do not normally occur.

Metabolism: Plasma manganese is bound to a β_1 globulin, transferrin. Normal whole blood levels of manganese range from 6 to 10 mcg/L.

Elimination: Bile is the major route of manganese excretion with the liver apparently maintaining manganese homeostasis. However, when the biliary route is blocked or overloaded, secretion from auxiliary routes (pancreatic juices and the walls of duodenum, jejunum and ileum) increases. Urinary excretion, which is negligible, can be increased by the administration of chelating agents.

11 STORAGE, STABILITY AND DISPOSAL

Store between 15 and 28ºC. Protect from freezing.

12 SPECIAL HANDLING INSTRUCTIONS

Not applicable

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name:	Manganese sulfate
Chemical name:	Manganese sulfate monohydrate
Molecular formula and molecular mass:	$MnSO_4 \cdot H_2O$, 169.01 g/mol
Physicochemical properties:	Manganese sulfate is a pale red, slightly efflorescent crystal or purple odourless powder. It is soluble in water and insoluble in alcohol.

14 CLINICAL TRIALS

This information was not available at the time of authorization.

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

This information was not available at the time of authorization.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE
MICRO MN
Manganese Sulfate Injection USP

Read this carefully before you start taking **MICRO MN** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **MICRO MN.**

What is MICRO MN used for?
MICRO MN is used with other nutrition products that are given to you through an infusion into your vein. It is given to you when you cannot eat normally. It helps maintain normal levels of the nutrient manganese in your blood.

How does MICRO MN work?
Manganese is an essential nutrient for your body. MICRO MN works by maintaining normal levels of manganese in your blood. This helps prevent problems when manganese levels are low.

What are the ingredients in MICRO MN?
Medicinal ingredient: manganese (as manganese sulfate monohydrate).

Non-medicinal ingredients: sulfuric acid, water for injection.

MICRO MN comes in the following dosage form: solution, 0.1 mg/mL

Do not use MICRO MN if you:
- are allergic to manganese or to any of the other ingredients of MICRO MN or to a component of the container.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take MICRO MN. Talk about any health conditions or problems you may have, including if you:
- have a liver condition where there is a blockage of the bile duct.
- are pregnant or plan to become pregnant.
- are breastfeeding or plan to breastfeed. It is not known if MICRO MN passes into breast milk.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

There are no known relevant interactions at this time.

How to take MICRO MN:
- MICRO MN will be given to you into your vein by a healthcare professional.
- Your healthcare professional will make sure that MICRO MN is prepared correctly before it is given to you.
- Your healthcare professional will routinely monitor the nutrient levels in your blood.

Usual dose:
Your healthcare professional will decide on the actual dose of MICRO MN that is right for you based on your age, body weight, and medical condition.

Overdose:

If you think you, or a person you are caring for, have taken too much **MICRO MN**, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

What are possible side effects from using MICRO MN?
There are no known side effects at this time. If you experience any side effects, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:
Your healthcare professional will store MICRO MN at 15 - 28°C. Protect from freezing.
Keep out of sight and reach of children.

If you want more information about MICRO MN:

- Talk to your healthcare professional.
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (https://health-products.canada.ca/dpd-bdpp/index-eng.jsp); the manufacturer's website www.sandoz.ca or by calling 1-800-361-3062.

This leaflet was prepared by Sandoz Canada Inc.

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