Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Tracutil, concentrate for solution for infusion.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

The concentrate for solution for infusion contains:

Active substance	per 1 ml
Ferrous chloride	695.8 Micrograms
Zinc chloride	681.5 Micrograms
Manganese chloride	197.9 Micrograms
Cupric chloride	204.6 Micrograms
Chromic chloride	5.3 Micrograms
Sodium selenite pentahydrate	7.89 Micrograms
Sodium molybdate dihydrate	2.42 Micrograms
Potassium iodide	16.6 Micrograms
Sodium fluoride	126.0 Micrograms

Trace element content	Micromoles /ampoule	Micrograms/ampoule
Iron	35.0 Micromoles	2000 Micrograms
Zinc	50.0 Micromoles	3300 Micrograms
Manganese	10.0 Micromoles	550 Micrograms
Copper	12.0 Micromoles	760 Micrograms
Chromium	0.2 Micromoles	10 Micrograms
Selenium	0.3 Micromoles	24 Micrograms
Molybdenum	0.1 Micromoles	10 Micrograms
Iodine	1.0 Micromoles	127 Micrograms
Fluorine	30.0 Micromoles	570 Micrograms

Maximum theoretical osmolarity: approx. 90 mOsm/l

pH: 1.7 – 2.3

For excipients see section 6.1.

3 PHARMACEUTICAL FORM

Concentrate for solution for infusion (A clear colourless aqueous solution).

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Tracutil is used as part of intravenous nutrition providing a source of trace elements for adult patients.

4.2 Posology and method of administration

For adults only.

Recommended dosage schedule

The recommended daily dose in patients with basal requirements is 10 ml (1 ampoule).

In patients with moderately increased requirements the daily dose may be up to 20 ml (2 ampoules), accompanied by monitoring of the trace element status.

In cases of significantly increased trace element requirements (such as extensive burns, severe hypercatabolic polytraumatic patients) higher doses may be necessary.

The doses for patients with impaired liver and/or kidney function should be determined individually. For these patients lower doses may be required.

Method of administration

Tracutil, which is a trace element concentrate, should only be administered intravenously after dilution with not less than 250 ml of a suitable solution for infusion, for example:

- Glucose solutions (5 % or 10 % w/v).
- Electrolyte solutions (e.g. sodium chloride 0.9%, Ringer's solution).

Compatibility must be tested before addition to other infusion solutions.

The infusion of the ready-to-use mixture should not take less than 6 hours and should be completed within 24 hours.

Administration can be continued for the duration of parenteral nutrition.

For incompatibilities and instructions for use please see sections 6.2. and 6.6.

Notes

Diarrhoea may lead to increased intestinal loss of zinc. The serum concentrations must be checked in this case.

Deficiencies of individual trace elements must be corrected by specific supplementation.

4.3 Contraindications

- Tracutil must not be administered to neonates, infants and children (due to lack of specific studies).
- Pronounced cholestasis (serum bilirubin > 140 mmol/l and elevated levels of gamma-glutamyltransferase and alkaline phosphatase).
- Hypersensitivity to any of the ingredients of Tracutil.
- Wilson's disease and disturbed iron storage (i.e. haemosiderosis or haemochromatosis).

4.4 Special warnings and precautions for use

Manganese blood levels should be regularly monitored in case of prolonged artificial nutrition. Dose reduction may be necessary, or Tracutil infusion should be stopped, if manganese accumulates.

Tracutil should be used with caution in case of impaired liver function, which may impair the biliary elimination of manganese, copper and zinc, leading to accumulation and overdose.

This trace element solution should be used with caution in case of impaired renal function, as excretion of some trace elements (selenium, fluoride, chromium, mobybdenum and zinc) may be significantly decreased.

To prevent iron overload, which is a risk mainly in patients with impaired liver function or those receiving blood transfusions, serum ferritin levels should be monitored at regular intervals.

In patients undergoing medium to long term parenteral nutrition, there is an increased frequency of zinc and selenium deficiency. In such circumstances, especially in the presence of hypercatabolism, e.g. after massive trauma, major surgery, burns etc., when necessary the dosage should be adapted and an extra supply of these elements should be provided.

Tracutil should be given with caution in cases of manifest hyperthyroidism or sensitivity to iodine if other iodine containing medicinal products (e.g. iodine antiseptics) are administered concomitantly.

Chromium deficiency leads to a decrease in glucose tolerance, which improves after chromium supplementation. Then in diabetic patients on insulin medication, relative overdose of insulin and consecutive hypoglycaemia may result. Therefore checks of the blood glucose levels are recommended. Re-adjustment of the insulin doses may become necessary.

4.5 Interaction with other medicinal products and other forms of interaction

For information on compatibility/incompatibility see sections 6.2 and 6.6.

4.6 Pregnancy and lactation

For Tracutil no clinical data on exposed pregnant and lactating women are available. Reproductive and developmental toxicity studies in animals have not been performed with Tracutil. Therefore, Tracutil should not be used during pregnancy and lactation except after careful consideration of its expected benefits and potential risks.

4.7 Effects on ability to drive and use machines

Not known.

4.8 Undesirable effects

There are isolated reports of anaphylactic reactions to parenterally administered iron with possible fatal outcome.

Iodine may cause allergic reactions.

4.9 Overdose

Overdose with Tracutil is extremely unlikely since the quantity of trace elements per ampoule is well below known toxic levels. If overdose is suspected, treatment with Tracutil should be discontinued. Overdose can be confirmed by appropriate laboratory tests.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Concentrate of trace elements for infusion.

ATC code: B05X

Tracutil is a balanced solution composed of all nine trace elements that are currently considered to be essential. They are necessary to maintain the organism's metabolic equilibrium.

The pharmacodynamic and pharmacokinetic properties of the ingredients resemble those of the naturally occurring substances.

During artificial nutrition, supply of trace elements is necessary since deficiencies can generate important metabolic and clinical disturbances.

Trace elements are normally derived from a balanced diet, but the need increases in case of hypercatabolism (e.g. due to surgery, polytrauma, burns), insufficient supply or abnormal loss and in cases of malabsorption (short bowel syndrome or Crohn's disease).

The composition of Tracutil is based on present international recommendations concerning the requirements for trace elements.

5.2 Pharmacokinetic properties

Elimination of individual trace elements takes place via different routes:

- Iron is eliminated via faeces and, to a minimal proportion, in urine.
- Zinc is predominantly excreted in the stool, and renal excretion is low.
- Manganese is predominantly excreted via the bile into the intestines and is partially re-absorbed from the intestines (enterohepatic circulation). The primary route of excretion is with the faeces; elimination with the urine or via sweat is insignificant.
- The main route of elimination of copper is in the bile, while only small amounts are excreted via the intestinal wall into the lumen or with the urine.
- Chromium and molybdenum are primarily excreted via the kidneys, and the remainder is eliminated via the intestines. Molybdenum is also known to be excreted in the bile and to be recycled via the enterohepatic circulation.
- Elimination of selenium is in the faeces or the urine, depending on the selenium status.
- Fluorine and iodine primarily undergo renal excretion.

5.3 Preclinical safety data

No preclinical studies have been conducted with Tracutil.

Since Tracutil is intended for replacement therapy, the risk for toxic effects is considered to be low at normal clinical use.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydrochloric acid
Water for injections

6.2 Incompatibilities

The product should not be added to alkaline solutions with marked buffer capacity, e.g. sodium bicarbonate solutions.

Do not add to fat emulsions.

The degradation of vitamin C in solutions for infusion is accelerated in the presence of trace elements.

Tracutil cannot be added directly to inorganic phosphate (additive) solutions.

It is not possible to present complete information about incompatibilities in this section.

Please refer to the marketing authorisation holder for further information.

6.3 Shelf Life

Shelf life in the unopened container
5 years

Shelf life after reconstitution
Chemical and physical in-use stability has been demonstrated for 24 hours at 25 ° C.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8 ° C, unless dilution has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

No special precautions for storage.

6.5 Nature and contents of container

Tracutil is supplied in 10 ml glass ampoules (glass type I).

Tracutil is available in packages containing 5 or 50 glass ampoules.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

Tracutil can be diluted in not less than 250 ml of 5 %, 10 %, 20 %, 40 % or 50 % glucose solutions or electrolyte solutions e.g. 0.9 sodium chloride or Ringer’s solution.

Addition to the diluent solution should be performed under strict aseptic conditions.

Tracutil must not be used as a diluent for other drugs.

The compatibility with solutions administered simultaneously via a common inlet cannula must be ensured.

Administration should be completed within 24 hours.

The product should be inspected visually for particulate matter, damage of container or any visible signs of deterioration prior to dilution and administration. Solution where such defects are observed have to be discarded.

7 MARKETING AUTHORISATION HOLDER

Braun Melsungen AG
Carl-Braun-Sraße 1
34212 Melsungen
Germany

8 MARKETING AUTHORISATION NUMBER

PA 0736/019/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorization: 24th November 2000

Date of last renewal: 18th July 2005

10 DATE OF REVISION OF THE TEXT

August 2007