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

Trace element content	***Micromoles /ampoule***	***Micrograms/ampoule***
Iron	35	2,000
Zinc	50	3,300
Manganese	10	550
Copper	12	760
Chromium	0.2	10
Selenium	0.3	24
Molybdenum	0.1	10
Iodine	1.0	127
Fluorine	30	570

Excipients with known effect:
Each 10 ml ampoule contains 147 micromoles (or 3.4 mg) of sodium.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Concentrate for solution for infusion.
Clear colourless aqueous solution

pH 1.7 – 2.3

Theoretical osmolarity 90 mOsm/l

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

Posology
Adults
The recommended daily dose in adult 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.

Paediatric population
Tracutil is contraindicated in neonates, infants and children (see section 4.3).
Tracutil is not recommended in adolescents (see section 4.4).

Renal and hepatic impairment
The doses for patients with impaired hepatic and/or renal 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 % w/v or 10 % w/v)
– electrolyte solutions (e.g. sodium chloride 0.9% w/v, 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 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

- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1
- Pronounced cholestasis (serum bilirubin > 140 mmol/l and elevated levels of gamma-glutamyltransferase and alkaline phosphatase)
- Wilson's disease and disturbed iron storage (i.e. haemosiderosis or haemochromatosis).

Tracutil is contraindicated in neonates, infants and children as its composition is not suitable for this age group.

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 hepatic 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, molybdenum and zinc) may be significantly decreased.

To prevent iron overload, which is a risk mainly in patients with impaired hepatic 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 dose 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.

Paediatric population
Tracutil is not recommended in adolescents due to lack of specific studies.

This medicinal product contains less than 1 mmol sodium (23 mg) per 10 ml dose; i.e. essentially 'sodium-free'.

4.5 Interactions with other Medicinal Products and other Forms of Interaction

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

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no or limited amount of data from the use of Tracutil in pregnant women. Animal studies are insufficient with respect to reproductive toxicity (see section 5.3). Tracutil should not be used during pregnancy unless the clinical condition of the woman requires treatment with Tracutil.

Breastfeeding
It is unknown whether the active substances/metabolites of Tracutil are excreted in human milk.
Tracutil should not be used during lactation except after careful consideration of its expected benefits to mother and potential risks to the child.

Fertility
No data available.

4.7 Effects on ability to drive and use machines

Not relevant

4.8 Undesirable effects

Immune system disorder:
Not known: Anaphylactic reactions to parenterally administered iron, with possible fatal outcome.

Iodine may cause allergic reactions.

Reporting of suspected adverse reactions
Reporting of adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the following:

United Kingdom
Yellow Card Scheme
www.mhra.gov.uk/yellowcard

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

Pharmacotherapeutic group:. Blood substitutes and perfusion solutions i.v. solution additives,; ATC code: B05X

Pharmacodynamic effects
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
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 renally, 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 conventional non-clinical studies on safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential and toxicity to reproduction and development 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 (for pH-adjustment)
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 should not 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.

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

unopened: 5 years

after dilution: 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

This medicinal product does not require any special storage conditions.

For storage conditions after dilution of the medicinal product, see section 6.3.

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.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused medicinal product or waste should be disposed of in accordance with local requirements.

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

Administration should be completed within 24 hours.

Tracutil can be diluted in not less than 250 ml of 5% w/v, 10% w/v, 20% w/v, 40% w/v or 50% w/v glucose solutions or electrolyte solutions e.g. 0.9 w/v 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 medicinal products.

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

7 MARKETING AUTHORISATION HOLDER

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8 Marketing Authorisation Number

03551/0056

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 18 July 1995
Date of last renewal: 07 November 2012

10 DATE OF REVISION OF THE TEXT

11/12/2013