ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

TOT'HEMA, oral solution in ampoule

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Iron .....50.00 mg
Corresponding to ferrous gluconate .....399.73 mg

Manganese.....1.33 mg
Corresponding to manganese gluconate.....10.78 mg

Copper .....0.70 mg
Corresponding to copper gluconate .....……5.00 mg
For a 10 mL ampoule.

Excipients with known effect: glucose (80 mg/10 mL), sucrose (3000 mg/10 mL), ethanol.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral solution in ampoule.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Curative treatment of iron deficiency anaemia in adults, children and infants.
Preventive and curative treatment of iron deficiency in pregnant women, premature infants, twins or babies born to a mother with iron deficiency, when an adequate dietary iron intake cannot be ensured.

4.2 Posology and method of administration

Posology

Curative treatment of iron deficiency and iron deficiency anaemia:
Adults: 100 to 200 mg of elemental iron per day, i.e. 2 to 4 ampoules per day.
Infants from 1 month and children: 5 to 10 mg of elemental iron/kg/day.

Preventive treatment of iron deficiency:
Pregnant women: 50 mg of elemental iron per day, i.e. 1 ampoule per day during the last 2 trimesters of pregnancy (or from the 4th month).

Treatment duration
Treatment must last long enough to cure anaemia and restore iron stocks, which, in adults, are 600 mg for women and 1200 mg for men.
Anaemia due to iron deficiency: 3 to 6 months depending on the depletion of iron stocks, to be eventually prolonged if the cause of anaemia is not under control.

Testing treatment efficacy is only useful following at least 3 months of treatment: it should check that anaemia is cured (Hb, MCV) and that iron stocks are restored.

Method of administration
Oral use.
Shake the ampoule before use.
Content of ampoule should be diluted in water (sweetened or not), or in any other non-alcoholic drink.
Take preferably before meals, but the time of administration and sometimes the dose can be adapted according to digestive tolerance.
One ampoule contains 50 mg of elemental iron.

4.3 Contraindications

- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.
- Iron overload, in particular normal or hypersideremic anaemia such as thalassemia, refractory anaemia, anaemia due to medullary insufficiency and inflammatory anaemia.

4.4 Special warnings and precautions for use

- The prevention of infantile deficiency is based on the early introduction of a diversified diet.
- This medicine is not recommended as a treatment for hyposideremia associated to inflammatory syndromes.
- Iron supplementation should be carried out along with treatment of iron loss cause, whenever it can.
- This medicine contains 3 g of sucrose per ampoule. This should be taken into account in the daily intakes in case of a low-sugar diet or diabetes. This medicine is not recommended in patients with fructose intolerance, glucose-galactose malabsorption syndrome or sucrase-isomaltase deficiency.
- This medicine contains 0.08 g of glucose per ampoule. This should be taken into account in the daily intakes in case of a low-sugar diet or diabetes. This medicine is not recommended in patients with glucose-galactose malabsorption syndrome.
- The presence of glucose and of sucrose may be harmful to the teeth in case of prolonged use (at least 2 weeks).
- This medicine contains small amounts of ethanol (alcohol), less than 100 mg per ampoule.

4.5 Interaction with other medicinal products and other forms of interaction

Combinations not recommended
+ Iron (salts) (injectable route):
Lipothymia or shock due to rapid iron release from its complex form and to siderophylin saturation.

Combinations with precaution for use
+ Cyclines (oral route):
Reduced digestive absorption of cyclines (creation of complex form).
Take iron salts at least 2 hours before or after taking cyclines.

+ Fluoroquinolones:
Reduced digestive absorption of fluoroquinolones (creation of complex form).
Take iron salts at least 2 hours before or after taking fluoroquinolones.

+ Salts, oxides and hydroxides of magnesium, aluminium and calcium (local gastro-intestinal medication):
Reduced digestive absorption of iron salts.
Take local gastrointestinal medication at least 2 hours before or after taking iron salts.

+ Diphosphonates (oral use):
Reduced absorption of diphosphonates.
Take iron salts at least 2 hours before or after taking diphosphonates.

+ Penicillamine:
Reduced digestive absorption of penicillamine.
Take iron salts at least 2 hours before or after taking penicillamine.

+ Thyroxin (oral use):
Reduced digestive absorption of thyroxin.
Take iron salts at least 2 hours before or after taking thyroxin.

+ Food
Drinking a lot of tea inhibits absorption of iron. Avoid drinking tea before or after taking iron salts.

4.6 Fertility, pregnancy and lactation

Pregnancy
Available data concerning a limited number of pregnancies did not reveal any particular risk to pregnant women, nor foetus, nor new-born. Therefore, under normal conditions of use, this medicinal product can be prescribed during pregnancy.

Breastfeeding
Excretion of this medicinal product into maternal milk has not been assessed. Therefore, its use during lactation may only be considered if necessary.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

The adverse reactions observed during clinical studies conducted with TOT'HEMA, oral solution in ampoule, are listed following the MedDRA system organ class and by frequency using the following categories: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1 000 to < 1/100), rare (≥ 1/10 000 to < 1/1 000), very rare (< 1/10 000), unknown (cannot be estimated from the available data).

- Gastrointestinal disorders:

Uncommon: nausea, vomiting, heartburn, constipation, diarrhoea, black stools (usual color), stained teeth (exceptional brown or black stains that disappear once treatment is ended).

In addition, the following post-marketing adverse reactions have been reported (frequency unknown):
- Immune system disorders:

Possible allergic reactions.

Reporting of suspected adverse reactions
Reporting suspected 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 national reporting system: Agence nationale de sécurité du médicament et des produits de santé (ANSM - French Health Products Safety Agency) and Regional Pharmacovigilance Centers - Website: www.signalement-sante.gouv.fr.

4.9 Overdose

Following massive ingestion, cases of overdose with iron salts have been reported, particularly in children less than 2 years old: symptoms included signs of irritation and gastro-intestinal necrosis associated with nausea, vomiting and a state of shock, in most cases.
Treatment should be provided as early as possible by pumping stomach using a 1% solution of sodium bicarbonate.
The use of a chelating agent is efficient, the most specific being deferoxamine, mainly when the serum iron concentration is higher than 5 µg/mL. State of shock, dehydration and acido-basic disturbances are treated following the standard practice.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: COMBINATION, ANTIANAEMIC, MINERAL SUPPLEMENT, OLIGOELEMENT, ATC code: B03AE10: ANTIANEMIC PREPARATIONS, IRON IN OTHER COMBINATIONS, VARIOUS COMBINATIONS.

Ferrous iron supplement (50 mg of iron element per ampoule of 10 mL).

5.2 Pharmacokinetic properties

Absorption takes place mainly in the duodenum and the proximal part of the jejunum.
Ferrous salts are usually poorly absorbed (10 to 20% of the ingested dose). This absorption is increased when iron stocks are low.

5.3 Preclinical safety data

Not documented.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycerol, liquid glucose, sucrose, anhydrous citric acid, sodium citrate, sodium benzoate, polysorbate 80, caramel colouring agent (E150c)*, tutti frutti flavour**, demineralised water.

*Composition of caramel colouring agent (E150c): glucose, ammonium hydroxide.
**Composition of tutti frutti flavour: isoamyl acetate, isoamyl butyrate, benzaldehyde, ethyl methylphenylglycidate, gamma undecalactone, ethylvanilline, alcohol, water.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Oral solution in 10 mL ampoule (brown glass).
Box of 20 ampoules.

6.6 Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

LABORATOIRE INNOTECH INTERNATIONAL
22 AVENUE ARISTIDE BRIAND
94110 ARCUEIL

8. MARKETING AUTHORISATION NUMBER(S)

- 34009 310 731 3 0: 10 mL in an ampoule (brown glass); box of 20 ampoules.

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 11 February 1993
Date of latest renewal: 11 February 2013

10. DATE OF REVISION OF THE TEXT

28 December 2018

11. DOSIMETRY

Not applicable.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Not applicable.

GENERAL CLASSIFICATION FOR SUPPLY
Medicinal product not subject to medical prescription.