SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Addaven concentrate for solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Addaven contains:	1 ml	1 ampoule (10 ml)
Chromic chloride hexahydrate	5.33 microgram	53.3 microgram
Copper chloride dihydrate	0.10 mg	1.02 mg
Ferric chloride hexahydrate	0.54 mg	5.40 mg
Manganese chloride tetrahydrate	19.8 microgram	198 microgram
Potassium iodide	16.6 microgram	166 microgram
Sodium fluoride	0.21 mg	2.10 mg
Sodium molybdate dihydrate	4.85 microgram	48.5 microgram
Sodium selenite anhydrous	17.3 microgram	173 microgram
Zinc chloride	1.05 mg	10.5 mg

The active ingredients in 1 ml of Addaven correspond to:

Cr	0.020 micromol	1.0 microgram
Cu	0.60 micromol	38 microgram
Fe	2.0 micromol	110 microgram
Mn	0.10 micromol	5.5 microgram
I	0.10 micromol	13 microgram
F	5.0 micromol	95 microgram
Mo	0.020 micromol	1.9 microgram (as Mo^{6+})
Se	0.10 micromol	7.9 microgram (as Se^{4+})
Zn	7.7 micromol	500 microgram

The content of sodium and potassium correspond to

Sodium	120 microgram	5.2 micromol
Potassium	3.9 microgram	0.1 micromol

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Concentrate for solution for infusion.
Clear solution, almost colourless.

- Osmolality: approx. 3100 mosm/kg water
- pH: 2.5

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

To meet basal to moderately increased requirements of trace elements in intravenous nutrition.

4.2 Posology and method of administration

Posology

Adults: The recommended daily dose of Addaven in adult patients with basal to moderately increased requirements is 10 ml (one ampoule).

In patients with renal or hepatic impairments, or mild cholestasis the dose should be adapted.

Children ≥15 kg: 0.1 ml Addaven is given per kg body weight and day.

Method of administration

Addaven must not be given undiluted. Addaven shall be given as an intravenous infusion, diluted in a parenteral nutrition solution/emulsion.
For instructions on dilution of the medicinal product before administration, see section 6.6.

4.3 Contraindications

- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.
- Conditions with total biliary obstruction.
- Wilson's disease, hemochromatosis.
- Children less than 15 kg body weight.

4.4 Special warnings and precautions for use

Parenterally administered iron or iodine preparations can cause hypersensitivity reactions on rare occasions, including serious and potentially fatal anaphylactic reactions.
Patients should be clinically observed for signs and symptoms of hypersensitivity reactions. In case of hypersensitivity reactions, the infusion should be stopped immediately and appropriate measures performed.

If iron is taken orally in parallel with infusion of Addaven, the total intake of iron should be determined to ensure that there is no iron accumulation.

Addaven should be used with caution in patients with liver dysfunction. Liver dysfunction, including impaired biliary excretion, may interfere with excretion of trace elements from Addaven, leading to a risk of accumulation.

Addaven should be used with caution in patients with impaired renal function as excretion of some trace elements in urine may be significantly decreased.

If the treatment is continued for more than 4 weeks, checking trace element levels in plasma, especially manganese, is required.

If an individual patient has a markedly increased requirement for any of the trace elements, the regimen can be adjusted using separate supplements.

4.5 Interaction with other medicinal products and other forms of interaction

No interactions with other drugs have been observed.

4.6 Fertility, pregnancy and lactation

Pregnancy
Animal reproduction studies or clinical investigations during pregnancy have not been carried out with Addaven. However, the requirements of trace elements in a pregnant woman are slightly increased compared to non-pregnant women.
No adverse events are to be expected when Addaven is administered during pregnancy.

Breast-feeding
The active substances in Addaven are secreted in human milk and effects have been shown in breastfed newborns/infants of treated women. These effects are desirable and anticipated.

4.7 Effects on ability to drive and use machines

Addaven has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

No adverse effects related to the trace elements in Addaven, following intravenous administration according to recommendations, have been reported.

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 listed in Appendix V*.

4.9 Overdose

In patients with impaired renal or biliary function, there is an increased risk for accumulation of trace elements. In case of a chronic overload of iron there is a risk of haemosiderosis, which in severe and rare cases can be treated by venesection.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Electrolytes in combination with other drugs, ATC code: B05X A31

Addaven is a mixture of trace elements in amounts normally absorbed from the oral diet and should have no pharmacodynamic effect besides maintaining or repleting the nutritional status.

5.2 Pharmacokinetic properties

When infused intravenously, the trace elements in Addaven are handled in a similar way to trace elements from an oral diet. Individual trace elements will be taken up by tissues to

different extents, depending on the requirements within each tissue to maintain or restore the concentration of each element for the metabolic requirements of that tissue.

Copper and manganese are normally excreted via the bile, whereas selenium, zinc and chromium (especially in patients receiving intravenous nutrition) are mainly excreted via the urine.

The main route of molybdenum excretion is the urine, although small amounts are excreted in the bile.

Iron is eliminated in small amounts by superficial loss and desquamation of gut cells. Premenopausal women can lose 30-150 mg of iron in the monthly blood loss.

5.3 Preclinical safety data

There are no preclinical data of relevance to the safety evaluation beyond those already included in the SmPC.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Xylitol
Hydrochloric acid, concentrated (for pH adjustment)
Water for injections

6.2 Incompatibilities

This medicinal product must only be mixed with other medicinal products for which compatibility has been documented.

6.3 Shelf life

Shelf life of the medicinal product as packed for sale
3 years

Shelf life after mixing
Chemical and physical in-use stability after dilution 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 2-8°C, unless mixing has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

No special precautions for storage.

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

6.5 Nature and contents of container

Ampoule (polypropylene) 20 x 10 ml

6.6 Special precautions for disposal and other handling

Compatibility
Addaven may only be added to medicinal or nutrition solutions for which compatibility has been documented. Compatibility with different products and the storage time of the different admixtures will be available upon request.

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

7. MARKETING AUTHORISATION HOLDER

To be completed nationally

8. MARKETING AUTHORISATION NUMBER(S)

To be completed nationally

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

To be completed nationally

10. DATE OF REVISION OF THE TEXT

22 February 2015