PROFESSIONAL INFORMATION

SCHEDULING STATUS: **S3**

1. NAME OF THE MEDICINE

ADDAVEN® concentrate for solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

	1 mL contains	10 mL contains
Chromium (3+) chloride $6H_2O$	5,33 µg (microgram)	53,33 µg (microgram)
Cupric chloride dihydrate	0,10 mg	1,02 mg
Ferric chloride hexahydrate	0,54 mg	5,40 mg
Manganese chloride tetrahydrate	19,80 µg (microgram)	198 µg (microgram)
Sodium molybdate dihydrate	4,85 µg (microgram)	48,5 µg (microgram)
Sodium selenite anhydrous	17,30 µg (microgram)	173 µg (microgram)
Zinc chloride	1,05 mg	10,5 mg
Potassium iodide	16,60 µg (microgram)	166 µg (microgram)
Sodium fluoride	0,21 mg	2,10 mg

The active ingredients in ADDAVEN correspond to:

	µmoL/1 mL	**1 mL contains**	**10 mL contains**
Fe^{3+}	2,0 µmoL	110 µg (microgram)	1,1 mg
Zn^{2+}	7,7 µmoL	500 µg (microgram)	5,0 mg
Mn^{2+}	0,10 µmoL	5,5 µg (microgram)	55 µg
Cu^{2+}	0,60 µmoL	38 µg (microgram)	380 µg
Cr^{3+}	0,02 µmoL	1,0 µg (microgram)	10 µg
Se^{4+}	0,10 µmoL	7,9 µg (microgram) (as Se^{4+})	79 µg

	µmoL/1 mL	**1 mL contains**	**10 mL contains**
Mo^{6+}	0,02 µmoL	1,9 µg (microgram) (as $Mo^{6+)}$	19 µg
F^-	5,0 µmoL	95 µg (microgram)	950 µg
I^-	0,10 µmoL	13 µg (microgram)	130,0 µg

The content of sodium and potassium correspond to:

Sodium 1,20 mg/10 mL 52 µmoL

Potassium 39 µg/10 mL 1 µmoL

Excipients with known effect:

Contains sugar alcohol, xylitol (3 g/10 mL)

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

ADDAVEN is a concentrated trace element solution for infusion which is clear and colourless to slightly yellow.

Osmolality: 3 100 mOsm/kg water

pH: 2,5

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ADDAVEN is indicated as a trace element supplement to be used during total parenteral nutrition in adults.

4.2 Posology and method of administration

Posology

Adults: The recommended daily dosage of ADDAVEN in adult patients with basic to moderately increased requirements is 10 mL (one ampoule), diluted as described under “Method of administration”.

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

Method of administration

ADDAVEN must not be given undiluted. ADDAVEN is to be diluted in a parenteral nutrition solution/emulsion before being given as an intravenous infusion.

Up to 20 mL ADDAVEN can be added aseptically to 1 000 mL Vamin 18 Electrolyte Free, glucose solution 55 mg/mL - 600 mg/mL in glass bottles or glucose solution 55 mg/mL - 500 mg/mL in plastic containers.

The addition of ADDAVEN should be performed aseptically.

Longer infusion periods are desirable, as this will minimise renal losses. The typical minimum infusion time when ADDAVEN is administered as part of parenteral nutrition is 8 hours.

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

Additions of other medicines should be avoided due to the risk of incompatibilities.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage must not be longer than 24 hours at 2 - 8 °C.

ADDAVEN is for single use in one patient only. Discard any residue.

Compatibility

Only medicines and nutrition solutions where compatibility has been documented may be added to ADDAVEN. ADDAVEN is used as an additive to parenteral nutrition admixtures in compounded bags where data are available. Compatibility data are available for the addition of 10 mL ADDAVEN to the named branded products SMOFlipid, Intralipid 20 %, Aminoven 10 %, Vamin 18 Electrolyte Free, Dipeptiven, Soluvit Novum, Vitalipid Novum Adult and Glycophos in defined amounts, and generics of glucose and electrolytes in

defined concentrations. 10 mL of ADDAVEN can also be added to the SmofKabiven range of products.

NOTE: ADDAVEN should never be added directly to a lipid emulsion because of the destabilising effects of trace elements. It is recommended that the macronutrients (amino acid solution and glucose with or without lipid emulsion) are mixed first, before adding the ADDAVEN and any further additions, e.g. vitamins or electrolytes. Additions should be made aseptically.

Special populations

No specific data are available. See “Posology” above.

4.3 Contraindications

- Hypersensitivity to the active substances or to any of the excipients of ADDAVEN listed in section 6.1.
- Conditions with total biliary obstruction.
- Wilson’s disease, haemochromatosis.

4.4 Special warnings and precautions for use

To be used as intravenous infusion only.

ADDAVEN must not be given undiluted. See section 4.2.

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.

Peripheral infusion of ADDAVEN diluted in saline or glucose instead of a parenteral nutrition solution may result in local intolerability due to low pH. Osmolarity also

needs to be considered. See section 4.2 "Method of administration" for dilution instructions.

ADDAVEN should be used with caution in patients with liver dysfunction (especially cholestasis). 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.

Monitoring of trace element levels, especially manganese, is recommended. If the treatment is continued for more than 4 weeks, checking of manganese levels in blood 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.

Laboratory and some animal studies indicate that vitamin B6 deficiency can increase the production of oxalate from xylitol. Adequate levels of vitamin B6 should be maintained.

Use in the elderly

Because of the increased likelihood of impaired renal or hepatic function or concomitant disorders and their treatment, ADDAVEN should be used with cautious monitoring in the elderly.

Paediatric use

ADDAVEN is not recommended for use in children.

Effects on laboratory tests

No effects on laboratory tests have been identified. ADDAVEN is administered as part of parenteral nutrition.

No other additions should be made to solutions containing ADDAVEN unless compatibility is known.

4.5 Interactions with other medicines and other forms of interaction

No interactions with other medicines have been recorded.

Molybdenum interacts with copper to form complexes that increase urinary elimination of copper.

Amino acids, which are present in all total intravenous nutrition (IVN) mixtures, could complex with zinc and copper and the complex could be excreted in urine. However, amino acid loss in urine is usually small.

Interactions of copper with ascorbic acid from vitamin supplementation of the parenteral nutrition mixture may occur, resulting in oxidative loss of ascorbic acid, which can be limited by use of oxygen impermeable bags.

4.6 Fertility, pregnancy and lactation

Fertility

The potential effects of ADDAVEN on fertility and general reproductive performance have not been determined.

Pregnancy

Safety during pregnancy has not been established.

Animal reproduction studies or clinical investigations during pregnancy have not been carried out with ADDAVEN.

Breastfeeding

The active substances in ADDAVEN are secreted in human milk and effects have been shown in breastfed newborns/infants of treated women.

Safety during breastfeeding has not been established.

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

There have been no clinical trials of ADDAVEN. As a component of the parenteral nutrition administered, it would be extremely difficult to identify adverse reactions that could be attributed directly to ADDAVEN.

Allergic reactions to iodine may occur following topical application.

No adverse reactions are known to occur as a consequence of using the recommended intravenous iodide dosage levels.

A minimum infusion time of 8 hours will minimise the risk of oxalosis associated with the infusion of xylitol (see Section 4.2 “Posology and method of administration”).

System Organ Class	**Frequency**	**Undesirable Effects**
Nervous system disorders	Frequency not known(1)	Headache
Gastrointestinal disorders	Frequency not known	Nausea, vomiting
General disorders and administration conditions	Frequency not known	Chills, pyrexia

(1) Post-marketing data. Frequency cannot be estimated from the available data

<u>Reporting of suspected adverse reactions</u>

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on the SAHPRA website.

Healthcare providers are asked to report any suspected adverse drug reactions to the Holder of the Certificate of Registration at the following email address: safety.fksa@fresenius-kabi.com and to the relevant medicines regulatory authority in the country where the product is marketed.

4.9 Overdose

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.

In overdose, side effects can be precipitated and/or be of increased severity (see section 4.8).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A.24 Mineral substitutes, electrolytes

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

ADDAVEN is a sterile concentrated solution containing a mixture of trace elements in amounts normally absorbed from the oral diet.

The contents of one ampoule will meet the daily requirements of chromium, copper, iron, manganese, molybdenum, selenium, zinc, fluoride and iodide in adults with basic to moderately increased requirements.

5.2 Pharmacokinetic properties

Absorption

For intravenous infusions, absorption of this nutrition is not a pharmacokinetic factor.

Distribution and metabolism

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 metabolic requirements.

Excretion

Copper and manganese are normally excreted via the bile, whereas selenium, zinc and chromium (especially in patients receiving IVN) 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. Iron excretion occurs with all kinds of bleeding e.g. menstrual bleeding.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Xylitol

Hydrochloric acid (for pH adjustment)

Water for injections

6.2 Incompatibilities

ADDAVEN may only be added to medicinal or nutritional solutions for which compatibility has been documented. For compatibility information, please refer to section 4.2 “Posology and method of administration”.

6.3 Shelf life

Shelf life of the medicine as packed for sale

36 months

Shelf life after mixing with additives

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 must not be longer than 24 hours at 2 - 8 °C.

6.4 Special precautions for storage

Store at or below 30 °C.

6.5 Nature and contents of container

10 mL polypropylene ampoule

Cartons: 1 x 10 mL polypropylene ampoule, 20 x 10 mL polypropylene ampoules

6.6 Special precautions for disposal and other handling

Handling

Do not use if ADDAVEN is cloudy or contains sediment.

Additions of ADDAVEN should be made aseptically within one hour prior to infusion start.

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 medicine or waste material should be disposed of in accordance with local requirements.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION

FRESENIUS KABI SOUTH AFRICA (PTY) LTD

Stand 7, Growthpoint Business Park

162 Tonetti Street

Halfway House extension 7

Midrand

Gauteng

1685

8. REGISTRATION NUMBER

49/24/0996

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

Date of registration: 26 July 2022

10. DATE OF REVISION OF THE TEXT

22 October 2025