

**Directions for Use**

B. Braun Medical SA, 1023 Crissier, Switzerland

**Nutriflex® plus**  
Solution for Infusionنیوٹری فلیکس پلس  
انفیوژن کیلئے محلول**Composition**

Amounts of active ingredients in both the 1000 ml and 2000 ml sizes of the product before and after mixing of the two chambers are given below.

Composition	Before Mixing		After Mixing	Before Mixing		After Mixing
	Lower Com- partment 600 ml	Upper Com- partment 400 ml	1000 ml	Lower Com- partment 1200 ml	Upper Com- partment 800ml	2000 ml
Isoleucine		2.82 g	2.82 g		5.64 g	5.64 g
Leucine		3.76 g	3.76 g		7.52 g	7.52 g
Lysine		2.73 g	2.73 g		5.46 g	5.46 g
(as Lysine Hydrochloride)		(3.41g)	(3.41g)		(6.82 g)	(6.82 g)
Methionine		2.35 g	2.35 g		4.70 g	4.70 g
Phenylalanine		4.21 g	4.21 g		8.42 g	8.42 g
Threonine		2.18 g	2.18 g		4.36 g	4.36 g
Tryptophan		0.68 g	0.68 g		1.36 g	1.36 g
Valine		3.12 g	3.12 g		6.24 g	6.24 g
Arginine Monoglutamate		5.98 g	5.98 g		11.96 g	11.96 g
(eq. to Arginine)		(3.24 g)	(3.24 g)		(6.48 g)	(6.48 g)
(eq. to Glutamic Acid)		(2.74 g)	(2.74 g)		(5.48 g)	(5.48 g)
Histidine		1.50 g	1.50 g		3.00 g	3.00 g
(as Histidine Hydrochloride Monohydrate)		(2.03 g)	(2.03 g)		(4.06 g)	(4.06 g)
Alanine		5.82 g	5.82 g		11.64 g	11.64 g
Aspartic Acid		1.80 g	1.80 g		3.60 g	3.60 g
Glutamic Acid		1.47 g	1.47 g		2.94 g	2.94 g
Glycine		1.98 g	1.98 g		3.96 g	3.96 g
Proline		4.08 g	4.08 g		8.16 g	8.16 g
Serine		3.60 g	3.60 g		7.20 g	7.20 g
Magnesium Acetate Tetrahydrate		1.23 g	1.23 g		2.46 g	2.46 g
Sodium Acetate Trihydrate		1.56 g	1.56 g		3.12 g	3.12 g
Sodium Dihydrogen Phosphate Dihydrate		3.12 g	3.12 g		6.24 g	6.24 g
Potassium Hydroxide		1.40 g	1.40 g		2.80 g	2.80 g
Sodium Hydroxide		0.23 g	0.23 g		0.46 g	0.46 g
Glucose	150.0 g		150.0 g	300.0 g		300.0 g
(as Glucose Monohydrate)	(165.0 g)		(165.0 g)	(330.0 g)		(330.0 g)
Calcium Chloride Dihydrate	0.53 g		0.53 g	1.06 g		1.06 g
<i>Electrolytes:</i>						
Sodium		37.2 mmol	37.2 mmol		74.4 mmol	74.4 mmol
Potassium		25.0 mmol	25.0 mmol		50.0 mmol	50.0 mmol
Calcium	3.6 mmol		3.6 mmol	7.2 mmol		7.2 mmol
Magnesium		5.7 mmol	5.7 mmol		11.4 mmol	11.4 mmol
Chloride	7.2 mmol	28.3 mmol	35.5 mmol	14.4 mmol	56.6 mmol	71.0 mmol
Dihydrogen phosphate		20.0 mmol	20.0 mmol		40.0 mmol	40.0 mmol
Acetate		22.9 mmol	22.9 mmol		45.8 mmol	45.8 mmol
Total amino acids		48 g	48 g		96 g	96 g
Nitrogen		6.8 g	6.8 g		13.6 g	13.6 g
Non-protein energy	[kJ (kcal)]	2510 (600)	2510 (600)	5025 (1200)		5025 (1200)
Total energy	[kJ (kcal)]	2510 (600)	795 (190)	3310 (790)	5025 (1200)	1590 (380)
					1590 (380)	6615 (1580)

**Excipients**

Citric acid, water for injections.

**Pharmaceutical form**

Solution for infusion

clear, colourless or slightly yellowish aqueous solutions

Osmolarity: 1400 mOsm/l

**Indications**

Supply of amino acids, energy, electrolytes and fluids during parenteral nutrition to patients in states of moderately severe catabolism when oral or enteral nutrition is impossible, insufficient or contraindicated.

**Contraindications***Related to the product:*

- congenital abnormalities of amino acid metabolism
- unstable metabolism (e.g. decompensated diabetes mellitus, metabolic acidosis)
- hyperglycaemia not responding to insulin doses of up to 6 units insulin/hour
- pathologically elevated serum electrolyte values
- intracranial or intraspinal haemorrhage
- known hypersensitivity to any of the ingredients

On account of its composition the product should not be administered to neonates, infants and children under 2 years of age.

*Related to parenteral nutrition:*

- unstable circulatory status with vital threat (states of collapse and shock)
- cellular hypoxia, acidosis
- coma of unknown origin
- severe hepatic insufficiency
- severe renal insufficiency (oligo- or anuria) without renal replacement therapy

*Related to infusion therapy in general:*

- hyperhydration
- acute pulmonary oedema
- decompensated cardiac insufficiency

**Special warnings and precautions for use**

Caution should be exercised in cases of increased serum osmolarity.

As for all large-volume infusion solutions Nutriflex plus should be administered with caution to patients with impaired cardiac or renal function.

Disturbances of fluid and electrolyte metabolism (e.g. hypotonic dehydration, hyponatremia, hypokalaemia) should be corrected prior to the administration of Nutriflex plus.

Solutions containing sodium salts should be used with caution in patients with sodium retention (see section 'Interactions').

In patients with renal insufficiency, the dose must be carefully adjusted according to individual needs, severity of organ insufficiency and the kind of instituted renal replacement therapy (haemodialysis, haemofiltration etc.).

Likewise in patients with insufficiencies of liver, adrenal glands, heart and lungs the dose must be carefully adjusted according to individual needs and the severity of organ insufficiency.

Too rapid infusion can lead to fluid overload with pathological serum electrolyte concentrations, hyperhydration and pulmonary oedema.

As with all solutions containing carbohydrates the administration of Nutriflex plus can lead to hyperglycaemia. The blood glucose level should be monitored. If there is hyperglycaemia the rate of infusion should be reduced or insulin should be administered.

To avoid occurrence of a re-feeding syndrome in malnourished or depleted patients (see section 'Undesirable effects'), parenteral nutrition should be built up gradually with great caution. Adequate substitution of potassium, magnesium and phosphate must be ensured.

Intravenous infusion of amino acids is accompanied by increased urinary excretion of the

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trace elements, especially copper and, in particular, zinc. This should be considered in the dosing of trace elements, especially during long-term intravenous nutrition.

Clinical monitoring should include fluid balance, serum electrolyte concentrations, acid-base balance, blood glucose, BUN. Hepatic function should be monitored as well. Frequency and kind of laboratory testing should be adapted to the overall condition of the patient.

During long-term administration also blood cell counts and blood coagulation should be monitored carefully.

Substitution of additional energy in form of lipids may be necessary, as well as an adequate supply of essential fatty acids, electrolytes, vitamins and trace elements.

Nutriflex plus should not be given simultaneously with blood in the same infusion set due to the risk of pseudoagglutination.

As with all intravenous solutions strict aseptic precautions are necessary for the infusion of Nutriflex plus.

Nutriflex plus is a preparation of complex composition. If the product is mixed with other solutions or emulsions, compatibility must be ensured.

#### Interactions

Corticosteroids and ACTH are associated with sodium and fluid retention.

Solutions containing potassium should be used with caution in patients receiving medicinal products that increase the serum potassium concentration, such as potassium sparing diuretics (triamterene, amiloride), ACE inhibitors, cyclosporine and tacrolimus.

#### Pregnancy and lactation

For Nutriflex plus no clinical data on exposed pregnancies are available. Preclinical studies with respect to effects on pregnancy, embryonal/foetal development, parturition and/or postnatal development have not been performed with Nutriflex plus. The prescriber should consider the benefit / risk relationship before administering Nutriflex plus to pregnant women.

Breast-feeding is not recommended if women need parenteral nutrition in that time.

#### Dosage

The dosage is adjusted individually according to the patients' requirements and clinical status.

*Adolescents from 15<sup>th</sup> year of life onward and adults*

Up to 40 ml per kg body weight per day, corresponding to:

- 1.92 g amino acids per kg body weight per day
- 6.0 g glucose per kg body weight per day

If the oxidative metabolism of glucose is impaired, which may be the case in the post-operative or post-traumatic phase or in the presence of hypoxia or organ failure, glucose intake should be limited to 2 - 4 g of glucose per kg body weight per day. The blood glucose level should not exceed 6.1 mmol/l (110 mg/100 ml).

It is recommended that Nutriflex plus be administered continuously, if feasible.

The infusion rate should be adjusted individually according to the patient's metabolic and clinical status. It may be:

Up to 1.7 ml per kg body weight per hour, corresponding to:

- 0.082 g amino acids per kg body weight per hour
- 0.26 g glucose per kg body weight per hour.

Corresponding drop rate: up to 0.6 drops per kg body weight per min.

Thus, for a patient weighing 70 kg the maximum infusion rate is 119 ml per hour (40 drops per min.), corresponding to 5.7 g of amino acids and 17.85 g of glucose per hour. In special clinical settings, e.g. haemodialysis, higher infusion rates may have to be applied.

#### Paediatric patients

The dosages for this age group as stated below are average values for guidance. The exact dosage should be adjusted individually according to age, developmental stage and prevailing disease. The calorie supply should be adapted individually according to the energy requirements during the respective growth period. If necessary, additional glucose or lipid infusions may be given.

Daily dose for 3<sup>rd</sup> to 5<sup>th</sup> year of life: 31 ml per kg body weight, corresponding to 1.49 g amino acids per kg body weight and 4.65 g glucose per kg body weight

Daily dose for 6<sup>th</sup> to 14<sup>th</sup> year of life: 21 ml per kg body weight, corresponding to 1.0 g amino acids per kg body weight and 3.51 g glucose per kg body weight

Infusion rate: Up to 1.7 ml per kg BW per hour, corresponding to 0.082 g amino acids per kg body weight per hour and 0.26 g glucose per kg body weight per hour

Corresponding drop rate: up to 0.6 drops per kg body weight per min.

If higher doses are necessary, account should be taken of the following limits of the total daily fluid intake:

- 3<sup>rd</sup> - 5<sup>th</sup> year: 80 - 100 ml per kg body weight
- 6<sup>th</sup> - 10<sup>th</sup> year: 60 - 80 ml per kg body weight
- 11<sup>th</sup> - 14<sup>th</sup> year: 50 - 70 ml per kg body weight

#### Duration of use

The duration of treatment for the indications stated is not limited. During long-term administration of Nutriflex plus it is necessary to provide for appropriate supply of additional energy (preferably in the form of lipids), essential fatty acids, trace elements and vitamins.

#### Method of administration

Intravenous use. For central venous infusion only.

#### Overdose

Overdose of Nutriflex plus is not to be expected on proper administration.

#### Symptoms of fluid and electrolyte overdose

Hypertonic hyperhydration, electrolyte imbalances and pulmonary oedema.

#### Symptoms of amino acid overdose:

Renal amino acid losses with consecutive amino acid imbalances, nausea, vomiting and shivering.

#### Symptoms of glucose overdose:

Hyperglycaemia, glucosuria, dehydration, hyperosmolality, hyperglycaemic and hyperosmolar coma.

#### Emergency treatment, antidotes

Immediate stop of infusion is indicated for overdose.

Further therapeutic measures depend on the particular symptoms and their severity. When infusion is recommenced after the symptoms have declined it is recommended that the infusion rate be raised gradually with monitoring at frequent intervals.

#### Undesirable effects

Undesirable effects with the components of Nutriflex plus are rare ( $\geq 1/10000$  to  $< 1/1000$ ) and usually related to inadequate dosage and/or infusion rate. Those that do occur are usually reversible and regress when therapy is discontinued.

#### Metabolism and nutrition disorders

Parenteral nutrition in malnourished or depleted patients with full doses and infusion rates from the very beginning and without adequate substitution of potassium, magnesium and phosphate may lead to the re-feeding syndrome, characterised by hypokalaemia, hypophosphataemia and hypomagnesaemia. Clinical manifestations may develop within a few days of starting parenteral nutrition and may include haemolytic anaemia due to hypophosphataemia and somnolence. See also section 'Special warnings and precautions for use'.

#### Gastrointestinal disorders

Nausea or vomiting may occur.

#### Renal and urinary disorders

In the event of a forced infusion osmotically induced polyuria might occur as a result of the high osmolality.

If these side effects occur the infusion should be discontinued or, if appropriate, the infusion should be continued at a lower dose level.

#### Undesirable effect after abruptly stopping administration

Abrupt discontinuation of high glucose infusion rates during parenteral nutrition may lead to hypoglycaemia, especially in children less than 3 years of age and in patients with disturbed glucose metabolism. Tapering glucose administration off is recommended.

#### Note:

Patients are advised to inform their doctor or pharmacist if they notice any adverse effect not mentioned in this leaflet.

#### Expiry date

The product must not be used after the expiry date printed on the container.

#### Instructions for storage / use / handling

Do not store above 25 °C

Keep bag in the outer carton in order to protect from light.

Immediately before use the internal peel seam between the two compartments must be opened allowing the respective contents to be aseptically mixed.

Remove the bag from its protective pack and proceed as follows :

- open out the bag and lay on a solid surface
- open the peel seam by using pressure with both hands
- briefly mix the contents of the bag together

An additive port is provided for admixing of supplements to Nutriflex plus.

Only mixtures of known compatibility should be prepared. Information on compatibility of specified mixtures is available from the manufacturer.

When admixing other solutions or fat emulsions to Nutriflex plus, aseptic precautions must be strictly observed. Fat emulsions can be easily admixed by means of a special transfer set.

Ideally after mixing the two solutions, Nutriflex plus should be administered immediately but it can in special circumstances be stored for up to 7 days at room temperature and up to 14 days if stored in a refrigerator (including administration time).

After infusion, any remaining solution should never be stored for later use. Only completely clear solutions from undamaged containers are to be used. Any unused product or waste material should be disposed of in accordance with local requirements.

Date of last revision

10.2008

خانے میں موجود اجزاء کو اپنے وزن سے پیچھے رکھیں۔ 25°C سے زیادہ درجہ حرارت پر نہ رکھیں۔ ٹھنڈ نہ کریں۔ اگر ششلی سے ٹھنڈ ہو جائے تو ٹیکہ خالص کریں۔ ٹیکہ کو باہر والے کارٹن میں رکھیں تاکہ روشنی سے بچایا جاسکے۔ بچوں کی تیق سے دور رکھیں۔

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