715/NP71578/0416

Directions for Use

B. Braun Medical SA, 1023 Crissier, Switzerland

Nutriflex® plus

Composition	Before mixing: Lower chamber contains 600 ml	Before mixing: Upper chamber contains 400 ml	After mixing: Lower chamber contains 1000 ml
Isoleucine		2.82 g	2.82 g
Leucine		3.76 g	3.76 g
Lysine Hydrochloride ≙ Lysine 2.73 g		3.41 g	3.41 g
Methionine		2.35 g	2.35 g
Phenylalanine		4.21 g	4.21 g
Threonine		2.18 g	2.18 g
Tryptophan		0.68 g	0.68 g
Valine		3.12 g	3.12 g
Arginine Monoglutamate ≙ Arginine 3.24 g and Glutamic Acid 2.74 g		5.98 g	5.98 g
Histidine Hydrochloride Monohydrate ≙ Histidine 1.50 g		2.03 g	2.03 g
Alanine		5.82 g	5.82 g
Aspartic Acid		1.80 g	1.80 g
Glutamic Acid		1.47 g	1.47 g
Glycine		1.98 g	1.98 g
Proline		4.08 g	4.08 g
Serine		3.60 g	3.60 g
Magnesium Acetate Tetrahydrate		1.23 g	1.23 g
Sodium Acetate Trihydrate		1.56 g	1.56 g
Sodium Dihydrogen Phosphate Dihydrate		3.12 g	3.12 g
Potassium Hydroxide		1.40 g	1.40 g
Sodium Hydroxide		0.23 g	0.23 g
Glucose Monohydrate ≙ Glucose 150 g	165 g		165 g
Calcium Chloride Dihydrate	0.53 g		0.53 g
Water for Injections	490 g	360 g	850 g
Excipient: Citric Acid Monohydrate			
Electrolytes:			
Na^+		37.2 mmol	37.2 mmol
K^+		25.0 mmol	25.0 mmol
Ca^{++}	3.6 mmol		3.6 mmol
Mg^{++}		5.7 mmol	5.7 mmol
Cl^-	7.2 mmol	28.3 mmol	35.5 mmol
$H_2PO_4^-$		20.0 mmol	20.0 mmol
$Acetate^-$		22.9 mmol	22.9 mmol
Total Aminoacids		48.1 g	48.1 g
Nitrogen (N)		6.8 g	6.8 g
kJ (kcal)	2510 (600)	795 (190)	3310 (790)
Osmolarity (mosm/l)			1400

Composition	Before mixing: Lower chamber contains 1200 ml	Before mixing: Upper chamber contains 800 ml	After mixing: Lower chamber contains 2000 ml
Isoleucine		5.64 g	5.64 g
Leucine		7.52 g	7.52 g
Lysine Hydrochloride ≙ Lysine 5.46 g		6.82 g	6.82 g
Methionine		4.70 g	4.70 g
Phenylalanine		8.42 g	8.42 g
Threonine		4.36 g	4.36 g
Tryptophan		1.36 g	1.36 g
Valine		6.24 g	6.24 g
Arginine Monoglutamate ≙ Arginine 6.48 g and Glutamic Acid 5.48 g		11.96 g	11.96 g
Histidine Hydrochloride Monohydrate ≙ Histidine 3.00 g		4.06 g	4.06 g
Alanine		11.64 g	11.64 g
Aspartic Acid		3.60 g	3.60 g
Glutamic Acid		2.94 g	2.94 g
Glycine		3.96 g	3.96 g
Proline		8.16 g	8.16 g
Serine		7.20 g	7.20 g
Magnesium Acetate Tetrahydrate		2.46 g	2.46 g
Sodium Acetate Trihydrate		3.12 g	3.12 g
Sodium Dihydrogen Phosphate Dihydrate		6.24 g	6.24 g
Potassium Hydroxide		2.80 g	2.80 g
Sodium Hydroxide		0.46 g	0.46 g
Glucose Monohydrate ≙ Glucose 300 g	330 g		330 g
Calcium Chloride Dihydrate	1.06 g		1.06 g
Water for Injections	980 g	720 g	1700 g
Excipient: Citric Acid Monohydrate			
Electrolytes:			
Na^+		74.4 mmol	74.4 mmol
K^+		50.0 mmol	50.0 mmol
Ca^{++}	7.2 mmol		7.2 mmol
Mg^{++}		11.4 mmol	11.4 mmol
Cl^-	14.4 mmol	56.6 mmol	71.0 mmol
$H_2PO_4^-$		40.0 mmol	40.0 mmol
$Acetate^-$		45.8 mmol	45.8 mmol
Total Aminoacids		96.2 g	96.2 g
Nitrogen (N)		13.6 g	13.6 g
kJ (kcal)	5025 (1200)	1590 (380)	6615 (1580)
Osmolarity (mosm/l)			1400

Product Description
Glucose solution - Clear, faintly yellowish solution
Aminoacids solution - Clear, faintly yellowish solution

Pharmaceutical form
Intravenous infusion solution for parenteral nutrition.

Pharmacological properties
Nutriflex® plus is a parenteral nutrition solution, intended for patients who cannot be fed either orally or through a nasogastric tube.
Parenteral nutrition must supply the body with all the components necessary for growth and tissue regeneration. The aminoacids play a prominent role, being the building blocks for protein synthesis.

In order to ensure a specific utilisation of the aminoacids, the administration of the following components is necessary:
- Energy sources:
Since glucose is employed directly as an energy source, it appears to be the best choice of carbohydrate.
- Electrolytes:
Magnesium, sodium, potassium, calcium, phosphate. Magnesium is involved in numerous biological processes. Its role as enzyme activator is of considerable significance in lipid, phosphate and glucose metabolism.
Calcium also activates enzymes, and in the reduction of cell membrane permeability it is of great importance.
Phosphate is involved in almost all energy transfer reactions.

The number of components to be infused and the known incompatibilities between particular substances pose numerous problems in the manufacture of parenteral nutrition solutions.

Pharmacokinetic properties
Following intravenous infusion, the constituents of Nutriflex® solutions are immediately available for metabolism. A portion of the aminoacids is used for protein synthesis, the rest being broken down as follows: the amino groups are separated by transamination and the carbon moiety is either oxidised to CO_2 in the citric acid cycle or utilised in the liver as a substrate for gluconeogenesis. The amino groups resulting from protein breakdown in muscle tissue are transported to the liver, where urea is synthesised. As a matter of principle the protein intake regarding nitrogen should exceed the urinary nitrogen excretion.

Indications
Parenteral nutrition in whom an enteral nutrition, orally or via a nasogastric tube is impossible, inadequate or undesirable.
Parenteral nutrition with Nutriflex® plus is particularly appropriate for overcoming the intense catabolic processes in patients in the postoperative phase or following *trauma*, e.g.:
- after surgical procedures
- following multiple injuries
- after severe burns
- in cases of sepsis (the treatment of sepsis should begin before the catheter is inserted).

In *Medicine*, e.g.:
- malabsorption syndrome
- exudative and inflammatory bowel disease
- Whipple's disease, Crohn's disease, ulcerative colitis
- acute pancreatitis
- severe diarrhoea or emesis.

For patients with a higher requirement of energy the addition of a lipid emulsion is possible.

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Contra-indications
- severe haemodynamic disturbances (shock, cardiac failure)
- metabolic acidosis
- severe renal failure
- advanced liver disease
- overhydration
- hyperkalaemia
- disorders of aminoacid metabolism
- untreated diabetes insipidus
- complication of diabetes mellitus, with the exception of hypoglycaemia
- treatment with high dosis of cardiac glycosides.

Special warnings and special precautions for use
Since Nutriflex® plus solution is hyperosmolar (1400 mosm/l), it must be infused via a central venous catheter. Monitor electrolyte and blood glucose levels. If hyperglycemia occurs, adjust the infusion rate.
Only completely clear solutions from undamaged containers are to be used.
The contents of the two containers should be mixed immediately before use and administered thereafter. Previously opened containers should never be used. Any residual solution should be discarded.
Conventional aseptic precautions during the administration of aminoacids must be strictly observed.
The Nutriflex® solutions are not indicated for babys and infants because of their different requirements regarding the balance of the ingredients.

Pregnancy and lactation
Pregnancy category C:
controlled studies in man and animals are not available.
For this reason Nutriflex® solutions should only be prescribed when the potential benefits outweigh the potential risks to the foetus.

Interaction with other medicaments and other forms of interaction
Because of the potassium content the efficacy of cardiac glycosides can be reduced.

Posology and method of administration
Since the osmolarity of Nutriflex® plus is approximately 1400 mosm/l, it must be given via a central venous catheter. It is recommended that Nutriflex® plus should be given as a continuous infusion over 24 hours. The aseptic precautions necessary when administering aminoacids should be closely observed.
The dosage must be adjusted according to the patient's individual needs but 1000-2000 ml Nutriflex® plus per day may be regarded as a normal dose, and should suffice for the majority of circumstances. If there are no contraindications the dose may be in the range of 0.8 - 1.4 g aminoacids per kg body weight per day. 2000 ml Nutriflex® plus, containing 96 g aminoacids and 300 g glucose, may well be given if necessary. However, in liver failure these doses should be reduced.
The time taken to infuse 1000 ml Nutriflex® plus should not be less than 10 hours (33 drops/min).

Overdose
A daily dose of 2000 ml Nutriflex® plus should not be exceeded.
Signs of overdosage: an osmotic diuresis with a simultaneous loss of aminoacids, together with dizziness and nausea. Gross overdose may lead to acidosis, hyperosmolar coma, hyperammonaemia.
Treatment: stop the infusion; in severe cases peritoneal dialysis or haemodialysis.

Undesirable effects
Nausea and vomiting are possible during the infusion.
Acidosis has been observed with the use of concentrated aminoacid solutions.
As a result of the high osmolarity an osmotic diuresis may ensue.

Incompatibilities
Nutritional supplements such as fat emulsions and concentrated solutions of vitamins, trace elements or electrolytes (NaCl, KCl) may be added via the medication port provided for that purpose. The exceptions are calcium, phosphate and bicarbonate, which may produce precipitations. The addition of Insuline is possible.
All additions should be made with the usual aseptic precautions, following the recommendations of the manufacturer. Check the clarity of the solution following the addition.

Shelf life
The shelf life is 2 years.

Special precautions of storage
Nutriflex® should be stored in the original packaging, below 30° C. Nutriflex® should not be used after the date printed on the container.
Nutriflex® should be administered immediately after mixing the two solutions (upper and lower chambers) but the bag can also be stored for 7 days between +2°C and +8°C in darkness and 2 days at room temperature and daylight but without exposure to direct sunlight.

Container
Nutriflex® plus : 1000 ml x 5
Nutriflex® plus : 2000 ml x 5
Twin-Flex® : a flexible bag with 2 chambers separated by a peel seam.

Date
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Product Registration Holder:
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Penang, Malaysia

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