Directions for Use
B. Braun Medical SA · 1023 Crissier, Switzerland

Combiflex® peri

Amino Acids + Electrolytes
Solution for Infusion

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 Compartment 600 ml	Upper Compartment 400 ml	1000 ml	Lower Compartment 1200 ml	Upper Compartment 800 ml	2000 ml
Isoleucine		2.34 g	2.34 g		4.68 g	4.68 g
Leucine		3.13 g	3.13 g		6.26 g	6.26 g
Lysine Hydrochloride		2.84 g	2.84 g		5.68 g	5.68 g
≙ Lysine		(2.27 g)	(2.27 g)		(4.54 g)	(4.54 g)
Methionine		1.96 g	1.96 g		3.92 g	3.92 g
Phenylalanine		3.51 g	3.51 g		7.02 g	7.02 g
Threonine		1.82 g	1.82 g		3.64 g	3.64 g
Tryptophan		0.57 g	0.57 g		1.14 g	1.14 g
Valine		2.60 g	2.60 g		5.20 g	5.20 g
Arginine Monoglutamate		4.98 g	4.98 g		9.96 g	9.96 g
≙ Arginine		(2.70 g)	(2.70 g)		(5.40 g)	(5.40 g)
≙ Glutamic Acid		(2.28 g)	(2.28 g)		(4.56 g)	(4.56 g)
Histidine Hydrochloride Monohydrate		1.69 g	1.69 g		3.38 g	3.38 g
≙ Histidine		(1.25 g)	(1.25 g)		(2.50 g)	(2.50 g)
Alanine		4.85 g	4.85 g		9.70 g	9.70 g
Aspartic Acid		1.50 g	1.50 g		3.00 g	3.00 g
Glutamic Acid		1.22 g	1.22 g		2.44 g	2.44 g
Glycine		1.65 g	1.65 g		3.30 g	3.30 g
Proline		3.40 g	3.40 g		6.80 g	6.80 g
Serine		3.00 g	3.00 g		6.00 g	6.00 g
Magnesium Acetate Tetrahydrate		0.86 g	0.86 g		1.72 g	1.72 g
Sodium Acetate Trihydrate		1.56 g	1.56 g		3.12 g	3.12 g
Potassium Dihydrogen Phosphate		0.78 g	0.78 g		1.56 g	1.56 g
Potassium Hydroxide		0.52 g	0.52 g		1.04 g	1.04 g
Sodium Hydroxide		0.50 g	0.50 g		1.00 g	1.00 g
Glucose Monohydrate	88.0 g		88.0 g	176.0 g		176.0 g
≙ Anhydrous Glucose	(80.0 g)		(80.0 g)	(160.0 g)		(160.0 g)
Sodium Chloride	0.17 g		0.17 g	0.34 g		0.34 g
Calcium Chloride Dihydrate	0.37 g		0.37 g	0.74 g		0.74 g
Electrolytes:						
Sodium	3.0 mmol	24.0 mmol	27.0 mmol	6.0 mmol	48.0 mmol	54.0 mmol
Potassium		15.0 mmol	15.0 mmol		30.0 mmol	30.0 mmol
Calcium	2.5 mmol		2.5 mmol	5.0 mmol		5.0 mmol
Magnesium		4.0 mmol	4.0 mmol		8.0 mmol	8.0 mmol
Chloride	8.0 mmol	23.6 mmol	31.6 mmol	16.0 mmol	47.2 mmol	63.2 mmol
Dihydrogen phosphate		5.7 mmol	5.7 mmol		11.4 mmol	11.4 mmol
Acetate		19.5 mmol	19.5 mmol		39.0 mmol	39.0 mmol
Total Amino Acids		40 g	40 g		80 g	80 g
Nitrogen		5.7 g	5.7 g		11.4 g	11.4 g
Non-protein energy kJ (kcal)	1340 (320)		1340 (320)	2680 (640)		2680 (640)
kJ (kcal), total	1340 (320)	670 (160)	2010 (480)	2680 (640)	1340 (320)	4020 (960)
Osmolarity (mOsm/l)			900			900

Excipients
Citric acid, water for injections.

Pharmaceutical form
Solution for infusion.

Indications
Supply of the daily requirements of energy, amino acids, electrolytes and fluids during parenteral nutrition to patients with mild to moderately severe catabolism when oral or enteral nutrition is impossible, insufficient or contraindicated.

Contraindications
This product must not be administered in the following conditions
- inborn errors of amino acid metabolism,
- pathologically elevated serum electrolyte values,
- unstable metabolism (e.g. decompensated diabetes mellitus, metabolic acidosis),
- coma of unknown origin,
- hyperglycaemia not responding to insulin doses of up to 6 units insulin/hour,
- severe hepatic insufficiency,
- severe renal insufficiency without renal replacement therapy,
- known hypersensivity 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.
General contra-indications to parenteral nutrition are:
- unstable circulatory status with vital threat (states of collapse and shock),
- cellular hypoxia,
- 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 Combiflex® peri should be administered with caution to patients with impaired cardiac or renal function.

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Disturbances of fluid and electrolyte metabolism (e.g. hypotonic dedration, hyponatremia) should be corrected prior to the administration of Combiflex® peri.
Too rapid infusion can lead to fluid overload with pathological serum electrolyte concentrations, hyperhydration and pulmonary oedema.
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 hepatic insufficiency the dose must be carefully adjusted according to individual needs and the severity of organ insufficiency.
As with all solutions containing carbohydrates the administration of Combiflex® peri 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 trace elements, especially copper and, in particular, zinc. This should be considered in the dosing of trace elements, especially during long-term intravenous nutrition.
Combiflex® peri should not be given simultaneously with blood in the same infusion set due to the risk of pseudoagglutination.
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.
Substitution of additional energy in form of lipids may be necessary, as well an adequate supply of essential fatty acids, electrolytes, vitamins and trace elements.
As with all intravenous solutions strict aseptic precautions are necessary for the infusion of Combiflex® peri.
Combiflex® peri is a preparation of complex composition. If the product is mixed with other solutions or emulsions, compatibility must be ensured.
As Combiflex® peri can be administered peripherally the state of the veins should be taken into account. It is recommended to change the vein regularly.

Interactions
None known.

Pregnancy and lactation
For Combiflex® peri 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 Combiflex® peri. The prescriber should consider the benefit/risk relationship before administering Combiflex® peri to pregnant women.
Breast-feeding is not recommended if women need parenteral nutrition in that time.

Dosage
The dosage is adapted to the patients' individual requirements.
The maximum daily dose amounts to 40 ml/kg body weight, corresponding to
– 1.6 g amino acids /kg body weight per day
– 3.2 g glucose /kg body weight per day
It is recommended that Combiflex® peri be administered continuously.
The maximum rate of infusion is 2.0 ml/kg body weight per hour, corresponding to
– 0.08 g amino acids /kg body weight per hour
– 0.16 g glucose/kg body weight per hour.
For a patient weighing 70 kg this corresponds to an infusion rate of 140 ml per hour. The amount of amino acid administered is then 5.6 g/hour and of glucose 11.2 g/hour.
An individual adjustment of the dosage is necessary in liver and renal insufficiency (see also section **"Special warnings and precautions for use"**).

Duration of use
Parenteral nutrition with this solution only can be performed for one week max.
If used for supplementary parenteral nutrition in combination with oral or enteral food intake or further intravenous nutrients, the duration of its use is not generally limited.

Method of administration
For intravenous use. Especially qualified for infusion in peripheral veins.

Instructions for use/handling
Immediately before use the internal peal 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 seal by using pressure with both hands
– briefly mix the contents of the bag together.
After infusion, any remaining solution should never be stored for later use. Only completely clear solutions from undamaged containers are to be used.
The construction of the dual chamber bag permits the mixing of amino acids, glucose and optional fat in the lower chamber. The addition of further electrolytes is possible if required. Conventional aseptic precautions during the admixing of solutions or fat emulsions to Combiflex® peri must be strictly observed. Fat emulsions can be easily admixed by means of a special transfer set.

Overdose
Overdose of Combiflex® peri is not to be expected on proper administration.

Symptoms of fluid and electrolyte overdose:
Hypertonic hyperhydration, electrolyte imbalance and pulmonary oedema.

Symptoms of amino acid overdose:
Renal amino acid losses with consecutive amino acid imbalances, sickness, vomiting and shivering.

Symptoms of glucose overdose:
Hyperglycaemia, glucosuria, dehydration, hyperosmolality, hyperglycaemic and hyperosmolar coma.

Treatment:
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 Combiflex® peri are rare and usually related to inadequate dosage and/or infusion rate. Those that do occur are usually reversible and regress when therapy is discontinued. Nausea or vomiting may occasionally occur. In the event of a forced infusion an osmotically induced polyuria might occur as a result of the high osmolarity.
If these side effects occur the infusion should be discontinued or, if appropriate, the infusion should be continued at a lower dose level.
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".**

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
To protect from light, keep containers in the outer carton.
Ideally after mixing the two solutions, Combiflex® peri should be administered immediately but in special circumstances it can be stored for up to 7 days at room temperature and up to 14 days if stored in a refrigerator (including administration time).

Date of last revision
11.2005

Presentation:
Combiflex® peri 1000 ml, 2000 ml bags
Reg. No.: DKI1296900949A1
Harus dengan resep dokter

Manufactured by:
B. Braun Medical SA
1023 Crissier
Switzerland

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PT. Phapros Tbk., Indonesia

Imported by:
PT. B. Braun Medical Indonesia
Jakarta-Indonesia

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