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Direction for Use

B. Braun Medical Ltd. · 6204 Sempach, Switzerland

Combiflex® peri

Amino Acids + Electrolytes Solution for Infusion

Combiflex Peri is presented in a double chambered bag, separated by an internal seal peel seam. By pressing on the peel seam the contents of the two chambers can be aseptically mixed before use

Composition

Active ingredients

The active ingredients in each chamber of the bag and the amounts after mixing in the ready to use solution are given for both sizes of Combiflex peri below :

Excipients

Citric Acid Monohydrate, water for injection

Pharmaceutical Form

Solution for Infusion

Pharmaco-therapeutic Group

Parenteral nutrition

Pharmacological Properties

Pharmacodinamic Properties

Parenteral nutrition must supply the body with all components necessary for growth and tissue generation. The Aminoacid play the prominent role, being the building blocks for protein synthesis. However in order to ensure optimal utilization of amino acids the administration of an energy is required. This can be fulfilled partly in the form of carbohydrates. As glucose can be employed directly, it is the carbohydrate of choice. Additional energy, ideally supplemented in the form of fat. Electrolyte are administered for the maintenance of metabolic and physiological functions. The ensure are complete parenteral nutrition regime with Combiflex® peri.

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:						
Na^+	3.0 mmol	24.0 mmol	27.0 mmol	6.0 mmol	48.0 mmol	54.0 mmol
K^+		15.0 mmol	15.0 mmol		30.0 mmol	30.0 mmol
Ca^{2+}	2.5 mmol		2.5 mmol	5.0 mmol		5.0 mmol
Mg^{2+}		4.0 mmol	4.0 mmol		8.0 mmol	8.0 mmol
Cl^-	8.0 mmol	23.6 mmol	31.6 mmol	16.0 mmol	47.2 mmol	63.2 mmol
$H_2PO_4^-$		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

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Pharmacokinetic Properties
Following intravenous infusion, the constituents of Combiflex peri are immediately available for metabolism. Electrolytes are available in sufficient amounts to sustain the numerous biological processes that they are required for. A portion of the amino acids is used for protein synthesis, the rest being broken down as follow; the amino groups are separated by transamination and the carbon moiety is either oxidized to CO_2 in the citric acid cycle or utilized in the liver as a substrate for gluconeogenesis. The amino groups resulting from protein breakdown in muscle tissue are transported to the liver, where they are used to synthesis urea or non essential amino acids.
Glucose is metabolized to CO_2 and H_2O

Therapeutic Indications
Parenteral nutrition

Contra indications
Combiflex® peri may be contra indicated in acute shock, in born errors of amino metabolism, irreversible liver damage and severe uraemia when dialysis facilities are not available.
Combiflex® peri is contra-indicated and infants up to the age of 24 months because of their different nutritional requirements.

Precautions for Use
Fluid, electrolytes and acid-base balance should be monitored.
As with other solutions containing glucose, administration of Combiflex® peri may lead to hyperglycemia. Blood glucose levels should be monitor and the rate of infusion adjusted.
As with all large volume infusion fluids, Combiflex® peri should be administered with caution to patients with cardiac or renal dysfunction. Care should be exercised in the administration of parenteral nutrition solutions containing amino acids to patients with altered amino acid metabolism, or with hepatic dysfunction.
Monitoring of nutritional and electrolyte status should be performed and trace element and vitamin levels should be assessed, particularly in the critically ill or those patients receiving prolonged parenteral nutrition
Administration of amino acid solutions may cause acute folate deficiency and supplementary folic acid should be administered. Vitamin B12 status should be monitored and supplementation giver if necessary

Form of Interaction with Other Medicinal products
None Known

Special Warnings
Use in pregnancy and lactation :
Animal reproduction studies have not been performed with Combiflex® peri. There are however, published report of successful and save administration of its components during pregnancy in the human.

Dosage
The dosage must be adjusted according to individual patient needs but 1000 ml – 2000 ml Combiflex® peri per day is regarded as a normal dose, sufficient for the majority of circumstances providing 0,6 – 1,2 g amino acids per kg body weight per day. For example, 2000 ml provide a 70 kg patient with 1.2 g amino acids (o.17 g N) and 2.3 g glucose per kg BW and day.
Combiflex® peri is should be administered by continues infusion at maximum rate of 2.0 ml (= 40 drops) per kg BW per hour up to a maximum dosage of 40 ml per kg BW per day.
An individual adjustment of the dosage is necessary in liver insufficiency.
Combiflex has an osmolarity of about 900 mOsm/l and as such can be given via a peripheral vein.
Combiflex® peri can be supplemented with trace elements, vitamins and electrolytes according to individual patient requirements and known compatibility.

Instruction for Use
Immediately before use the internal peel seam between the two compartments must be broken allowing the respective contents to be aseptically mixed. The vertical positioning of the two chambers permits that the nutrients will flow under gravity into the lower chamber. After that the bag should be inverted a few times to ensure homogeneous mixing.
After infusion, any remaining solution should never be stored for later use. Only completely clear solutions from undamaged containers are to be used.
Conventional special aseptic precautions during the admixing of solutions or fat emulsions to Combiflex® peri must be strictly observed. Only mixtures of known compatibility should be prepared. Information on compatibility is available from the manufacturer. Fat emulsion can be easily admixed by means of special transfer set.

Overdose
In general, significant over dosage due to Combiflex® peri is unlikely to occur. Over dosage would arise from fluid overload with symptoms such as nausea, vomiting, flushing and sweating being observed.
In case of suspicion of over dosage, the infusion speed should be reduced or in severe cases the infusion stopped. The infusion can be restarted after cessation of the symptoms.
Gross overdosage during total parenteral nutrition may lead to complications such as acidosis, hyperosmolar coma, hyperamonaemia.
If Combiflex® peri is administered at the recommended rated no such problems are to be anticipated.

Undesirable Effects
Undesirable effects with the components of Combiflex® peri are rare. 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 osmotic diuresis might occur as a result of the high osmolarity.
Patients are encouraged to report any adverse reactions they experience which are not mentioned in this leaflet to the doctor or the pharmacist.
Abnormal results of liver function tests and cholestasis have been reported in some patients receiving parenteral nutrition

Expiry date
Store Combiflex® peri at room temperature, in the original packaging, protected from light. It must not be used after the expiry date printed on the container.
Ideally after mixing the solutions, Combiflex® peri 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 refrigerator (including administration time).

Do not store above 25° C

Presentation
Combiflex® peri 1000 ml
Reg No : DKI2496901349A1

Harus Dengan Resep Dokter

Manufactured by :
B. Braun Medical SA
Route de sorge 9
CH-1023 Crissier
Switzerland

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Karawang - Indonesia

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