PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S3

TRIOMEL N4-600E,

TRIOMEL N5-860E,

TRIOMEL N7-960E,

TRIOMEL N9-840E

(Emulsion for infusion)

Refined olive oil, refined soya-bean oil, alanine, arginine, aspartic acid, glutamic acid, glycine, histidine. isoleucine, leucine, lysine acetate (equiv to lysine), methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, valine, sodium acetate 3H2O, potassium chloride, magnesium chloride 6H2O, sodium glycerophosphate hydrated, calcium chloride 2H2O.

Read all of this leaflet carefully before you are given TRIOMEL

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- TRIOMEL has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What TRIOMEL is and what it is used for

TRIOMEL is an emulsion for infusion.

TRIOMEL is used to provide nutrition in adults and children greater than two years of age by a tube into a vein when normal feeding by mouth is not suitable.

TRIOMEL must only be used under medical supervision.

2. What you need to know before you receive TRIOMEL

Do not receive TRIOMEL, emulsion for infusion in the following cases:

- For premature neonates, infants and children less than 2 years old
- If you are hypersensitive (allergic) to egg proteins, soybean, peanuts or to any other ingredient
- If you have a severe kidney problem and you are not on dialysis or another form of blood filtration treatment
- If your body has problems using certain amino acids e.g. phenylketonuria
- If you have especially high level of fats in your blood
- If you have severe hyperglycaemia (too much sugar in your blood)
- If you have an abnormally high amount in the blood of sodium, potassium, magnesium, calcium and/or phosphorous

Treatment with TRIOMEL is not suitable if you have:

- Acute pulmonary oedema (infiltration of serum into the lung tissue), hyperhydration (accumulation of water), heart failure, dehydration, or in unstable situation such as

those following severe injuries, untreated diabetes mellitus, shock due to a sudden heart failure, heart attack, severe metabolic acidosis (when the blood is excessively acid), septicaemia (generalised infection) and coma.

In all cases, your doctor will base his/her decision on whether you should receive TRIOMEL on factors such as your age, weight and clinical condition, together with the results of any test performed.

Warnings and precautions

Take special care with TRIOMEL in the following instances:

The infusion must be stopped immediately if any signs or symptoms of an allergic reaction (such as sweating, fever, chills, headache, skin rashes or breathing difficulty) develop. This medicine contains soybean oil, and egg phosphatide. Soybean and egg proteins may cause hypersensitivity reactions. Cross-allergic reactions between soybean and peanut proteins have been observed.

Difficulty breathing could also be a sign that small particles have formed, blocking blood vessels in the lungs (pulmonary vascular precipitates). If you experience any difficulty breathing, tell your doctor or nurse. They will decide a course of action to be taken.

The antibiotic named ceftriaxone must not be mixed or given simultaneously with these TRIOMEL formulations given to you by a drip into your vein.
These drugs must not be given to you together even via different infusion lines or different infusion sites.

However, you may be given TRIOMEL and ceftriaxone sequentially one after another if infusion lines at different sites are used or if the infusion lines are replaced or were thoroughly

flushed with physiological salt solution between the infusions to avoid precipitation (formation of particles of ceftriaxone-calcium salt).

Certain medications and illnesses can increase the risk of developing infection or sepsis (bacteria in the blood). There is a particular risk of infection or sepsis when a tube (intravenous catheter) is placed in your vein. Your doctor will carefully watch you for any signs of infection. Patients who require parenteral nutrition (giving nutrition through a tube in your vein) may be more likely to develop infections from their medical conditions. Using aseptic (“germ-free”) techniques when placing and caring for the catheter and when making the nutritional formula (TPN) can reduce the risk of infection.

The balance of water and salt in your body and metabolic disorders will be corrected before starting the infusion. Your doctor will monitor your condition while you receive TRIOMEL and may change the dosage or give you additional nutrients such as vitamins, electrolytes and trace elements if he/she feels it is appropriate.

Caution should be exercised in administering TRIOMEL to patients with liver or kidney problems, blood clotting problems, anaemia, increased serum osmolarity, adrenal insufficiency, heart failure, diabetes, high cholestrol or pulmonary dysfunction.

During the infusion if you notice pain, burning or swelling at the infusion site, or leakage of the infusion, tell your doctor or nurse. The administration will be stopped immediately and restarted in another vein.

Reduced ability of the body to remove the fats contained in this medicine may result in a "fat overload syndrome" (See Possible Side Effects).

If your blood sugar gets too high, your doctor should adjust the rate of TRIOMEL delivery or give you medication to control your blood sugar (insulin).

Other medicines and TRIOMEL

Always tell your health care provider if you are taking any other medicine.
(This includes complementary or traditional medicines.)

TRIOMEL must not be administered simultaneously with blood through the same infusion tubing.

TRIOMEL contains calcium. It should not be given together or through the same tube with the antibiotic ceftriaxone because particles may form. If the same device is used to give you successively these medicines, it should be thoroughly rinsed.

The olive and soybean oils present in TRIOMEL contain vitamin K. This does not normally affect blood thinning medicines (anticoagulants). However, if you take anticoagulant medicines you should tell your doctor.

TRIOMEL contains potassium. Special care should be taken in patients taking diuretics, ACE inhibitors, angiotensin II receptor antagonists (medicines for high blood pressure), or immunosuppressants. These types of medicines may increase potassium levels in your blood.

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before taking this medicine.

Driving and using machines

TRIOMEL is not expected to affect your ability to drive or use machines.

3. How to receive TRIOMEL

TRIOMEL should only be given in adults and children greater than two years of age.

TRIOMEL may only be administered via a plastic tube into a large vein.

Dosage – Adults

Your doctor will specify a flow rate corresponding to your needs and clinical condition.

Dosage – Children greater than two years of age and adolescents

Your doctor will decide the dose the child will need and for how long it will be given. This will depend on age, weight and height, clinical condition, daily fluid volume, energy and nitrogen requirements.

If you receive more TRIOMEL than you should

Since a healthcare professional will administer this medicine, he/she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

4. Possible side effects

TRIOMEL**,** emulsion for infusion can cause side effects**.**

If you notice any changes in the way you feel during or after the treatment, tell your doctor or nurse straight away.

If any abnormal signs or symptoms of an allergic reaction develop, such as sweating, fever, shivering, headache, skin rashes or breathing difficulties, the infusion will be stopped immediately.

The following side –effects have been reported with TRIOMEL**:**

Frequency - Common: may affect up to 1 in 10 people

- Fast heart rate (tachycardia)
- Loss of appetite (anorexia)
- Increased level of fat in the blood (hypertriglyceridemia)
- Abdominal pain
- Diarrhea
- Nausea
- Increased blood pressure (hypertension)

Frequency - Not known:

- Leakage of the infusion to the surrounding tissue (extravasation) which may result at infusion site level in pain, irritation, swelling/oedema, redness (erythema)/warmth, death of the tissue cells (skin necrosis) or blisters

Other side effects of unknown frequency are:

- Vomiting
- Rash
- Fever
- Chills
- Abnormal blood test results for liver function.
- Increase in the size of the liver (hepatomegaly).
- Icterus (jaundice).
- Decrease in the number of platelets.

- Problems with the elimination of bile (cholestasis)
- Increased nitrogen levels in the blood (azotemia)
- Elevated liver enzymes
- Formation of small particles which may lead to blockage of blood vessels in the lungs (pulmonary vascular precipitates) resulting in pulmonary vascular embolism and difficulty breathing (respiratory distress).
- Reduced ability to remove the lipids contained in TRIOMEL may result in a "fat overload syndrome" which may be caused by overdose but may also occur at the start of an infusion, even according to instructions, and is associated with a sudden deterioration in the patient's clinical condition. It is characterised by excessive lipids in blood (hyperlipidaemia), fever, liver fatty infiltration, increase of liver size (hepatomegaly), anaemia, a fall in white blood cells and blood platelets, problem with your blood clotting and coma. All of these symptoms are usually reversible when the lipid emulsion infusion is stopped.

If any side effect gets serious, or if you notice any side effect not listed in this leaflet, please tell your doctor or pharmacist.

Not all side-effects reported for TRIOMEL are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking this medicine, please consult your doctor, pharmacist or other health care professional for advice.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist. You can also report side effects to SAHPRA via the “6.04 Adverse Drug Reaction Reporting Form”, found online under SAHPRA’s publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of TRIOMEL.

For reporting of side effects directly to the HCR, contact +27 11 635 0134 or email Adcock.aereports@adcock.com

5. How to store TRIOMEL

Before Reconstitution:

Store at or below 30 °C. Do not freeze. Store in the overpouch. Keep container in the outer carton.

After Reconstitution:

It is recommended that the product be used immediately after the peel seals have been broken any unused portion of the reconstituted product must be discarded in accordance with local requirements.

The reconstituted emulsion, is stable for a maximum of 7 days at between 2 °C to 8 °C followed by a maximum of 48 hours at temperatures not exceeding 25 °C.

After addition of supplements (electrolytes, organic phosphates, trace elements, vitamins):

For specific admixtures, chemical and physical in-use stability has been demonstrated for 7 days at 2 °C to 8 °C followed by 48 hours at or below 25 °C. From a microbiological point of view, any admixture should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 °C to 8 °C, unless addition of supplements has taken place in controlled and validated aseptic conditions.

Do not receive TRIOMEL after the expiry date stated on the container.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

Store all medicines out of reach of children.

6. Contents of the pack and other information

What TRIOMEL contains

Per 1,5 litre Bag of solution

Active Substances	**Lipid emulsion compartment (300 ml)**				**Amino Acid with electrolytes solution compartment (600 ml)**				**Glucose with calcium solution compartment (600 ml)**			
	N4-600E	**N5-860E**	**N7-960E**	**N9-840E**	**N4-600E**	**N5-860E**	**N7-960E**	**N9-840E**	**N4-600E**	**N5-860E**	**N7-960E**	**N9-840E**
Refined Olive Oil + Refined Soya-bean Oil*	45 g	60 g	60 g	60 g								
Alanine					5,50 g	7,14 g	9,61 g	12,36 g				
Arginine					3,72 g	4,84 g	6,51 g	8,37 g				
Aspartic acid					1,10 g	1,43 g	1,92 g	2,47 g				
Glutamic acid					1,90 g	2,47 g	3,32 g	4,27 g				
Glycine					2,63 g	3,42 g	4,60 g	5,92 g				
Histidine					2,26 g	2,95 g	3,97 g	5,09 g				

Isoleucine					1,90 g	2,47 g	3,32 g	4,27 g				
Leucine					2,63 g	3,42 g	4,60 g	5,92 g				
Lysine acetate (equiv to Lysine)					4,21 g *2,99 g*	5,48 g *3,88 g*	*7,31 g* *5,23 g*	*9,48 g* *6,72 g*				
Methionine					1,90 g	2,47 g	3,32 g	4,27 g				
Phenylalanine					2,63 g	3,42 g	4,60 g	5,92 g				
Proline					2,26 g	2,95 g	3,97 g	5,09 g				
Serine					1,50 g	1,95 g	2,62 g	3,37 g				
Threonine					1,90 g	2,47 g	3,32 g	4,27 g				
Tryptophan					0,64 g	0,82 g	1,10 g	1,42 g				
Tyrosine					0,10 g	0,13 g	0,17 g	0,22 g				
Valine					2,43 g	3,16 g	4,25 g	5,47 g				
Sodium Acetate, $3H_2O$					1,73 g	2,24 g	2,24 g	2,24 g				
Potassium Chloride					1,79 g	3,35 g	3,35 g	3,35 g				

Magnesium Chloride, $6H_2O$					0,67 g	1,22 g	1,22 g	1,22 g				
Sodium Glycerophosphate, hydrated					2,87 g	5,51 g	5,51 g	5,51 g				
Glucose Monohydrate (equiv to glucose anhydrous)									123,75 g *112,50 g*	189,75 g *172,50 g*	*231,00 g* *210,00 g*	*181,50 g* *165,00 g*
Calcium Chloride, $2H_2O$									0,44 g	0,77 g	0,77 g	0,77 g

* A mixture of refined olive oil (approximately 80 % m/v) and refined soya-bean oil (approximately 20 % m/v), is calculated to reach an essential fatty acids content of 20 % of total fatty acids.

After the contents of the three compartments have been mixed, the ternary mixture for each of the bag presentations provides the following:-

Per bag	**1 litre**				**1,5 litre**				**2 litre**			
	N4-600E	**N5-860E**	**N7-960E**	**N9-840E**	**N4-600E**	**N5-860E**	**N7-960E**	**N9-840E**	**N4-600E**	**N5-860E**	**N7-960E**	**N9-840E**
Nitrogen (g)	4,0	—	7,0	9,0	6,0	7,8	10,5	13,5	8,0	10,4	14,0	18,0
Amino Acids (g)	25,3	—	44,3	56,9	38,0	49,4	66,4	85,4	50,6	65,8	88,6	113,9
Glucose (g)	75,0	—	140	110	112,5	172,5	210	165	150,0	230,0	280	220
Lipids (g)	30,0	—	40	40	45.0	60	60	60	60,0	80	80	80
Energy:		—										
Total calories (Kcal)	700	—	1140	1070	1050	1490	1710	1600	1400	1980	2270	2140
Non-protein calories (Kcal)	600	—	960	840	900	1290	1440	1260	1200	1720	1920	1680
Glucose calories (Kcal)	300	—	560	440	450	690	840	660	600	920	1120	880
Lipid calories (Kcal)**	300	—	400	400	450	600	600	600	600	800	800	800

Non-protein calories/nitrogen ratio (Kcal/g)	150	—	137	93	150	165	137	93	150	165	137	93
Glucose/lipid calories ratio	50/50	—	58/42	52/48	50/50	53/47	58/42	52/48	50/50	53/47	58/42	52/48
Lipid/total calories (%)	43	—	35	37	43	40	35	37	43	40	35	37
Electrolytes:		—										
Sodium (mmol)	21,0	—	35,0	35,0	31,5	52,5	52,5	52,5	42,0	70,0	70,0	70,0
Potassium (mmol)	16,0	—	30,0	30,0	24,0	45,0	45,0	45,0	32,0	60,0	60,0	60,0
Magnesium (mmol)	2,2	—	4,0	4,0	3,3	6,0	6,0	6,0	4,4	8,0	8,0	8,0
Calcium (mmol)	2,0	—	3,5	3,5	3,0	5,3	5,3	5,3	4,0	7,0	7,0	7,0
Phosphate (mmol)***	8,5	—	15,0	15,0	12,7	22,5	22,5	22,5	17,0	30,0	30,0	30,0
Acetate (mmol)	27	—	45	54	41	55	67	80	55	73	89	107
Chloride (mmol)	24	—	45	45	37	68	68	68	49	90	90	90
pH	6,4	—	6,4	6,4	6,4	6,4	6,4	6,4	6,4	6,4	6,4	6,4
Osmolarity (mosm/l)	760	—	1360	1310	760	1120	1360	1310	760	1120	1360	1310

**Includes calories from purified egg phosphatides

*** Includes phosphate provided by the lipid emulsion

Per bag	**2,5 litre**	
	N4-600E	**N5-860E**
Nitrogen (g)	10,0	13,0
Amino Acids (g)	63,3	82,3
Glucose (g)	187,5	287,5
Lipids (g)	75	100
Energy:		
Total calories (Kcal)	1750	2480
Non-protein calories (Kcal)	1500	2150
Glucose calories (Kcal)	750	1150
Lipid calories (Kcal)**	750	1000
Non-protein calories/nitrogen ratio (Kcal/g)	150	165
Glucose/lipid calories ratio	50/50	53/47
Lipid/total calories (%)	43	40
Electrolytes:		

Sodium (mmol)	52,5	87,5
Potassium (mmol)	40,0	75,0
Magnesium (mmol)	5,5	10,0
Calcium (mmol)	5,0	8,8
Phosphate (mmol)***	21,2	37,5
Acetate (mmol)	69	91
Chloride (mmol)	61	113
pH	6.4	6,4
Osmolarity (mosm/l)	760	1120

**Includes calories from purified egg phosphatides

*** Includes phosphate provided by the lipid emulsion

The active substances are refined olive oil, refined soya-bean oil, alanine, arginine, aspartic acid, glutamic acid, glycine, histidine. isoleucine, leucine, lysine acetate (equiv to lysine), methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, valine, sodium acetate 3H2O, potassium chloride, magnesium chloride 6H2O, sodium glycerophosphate hydrated, calcium chloride 2H2O.

The other ingredients are purified egg phosphatide, glycerol, sodium oleate, water for injection, glacial acetic acid (for pH adjustment), hydrochloric acid (for pH adjustment) and sodium hydroxide (for pH adjustment).

What TRIOMEL looks like and contents of the pack

Identification prior to reconstitution:

The lipid compartment contains the lipid emulsion which is a homogenous liquid with a milky appearance.

The amino acids and glucose compartments consist of solutions which are clear and colourless or slightly yellow and practically free from particles.

Identification after reconstitution:

Homogenous liquid with a milky appearance

TRIOMEL is packed into a three-compartment bag. The triple-compartment bag is a multi-layer, clear and colourless plastic container packaged into an overpouch (silver, aluminium foil, or clear, colourless laminated plastic). The inner contact layer of the bag material is made of blend of polyolefinic copolymers and is compatible with amino acid solution, glucose solution and lipid emulsions. Other layers are made of polyethylene vinyl acetate (EVA), and of copolyster. One compartment contains a lipid emulsion, the second compartment contains

an amino acid solution with electrolytes and the third compartment contains a glucose solution with calcium.

The glucose compartment is fitted with an injection site to be used for addition of supplements.
The amino acids compartment is fitted with an administration site for insertion of the spike of the infusion set.
The bag is packaged in an oxygen barrier overpouch with an oxygen absorber sachet.
TRIOMEL is available in pack sizes of 1 l, 1,5 l, 2 l and 2,5 l.

Holder of Certificate of Registration

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