Package leaflet: Information for the user

Numeta G13%E Preterm, emulsion for infusion

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your child's doctor, pharmacist, or nurse.
- If your child gets any side effects, talk to your child's doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Numeta G13%E Preterm is and what it is used for

Numeta G13%E Preterm is a specialised nutrition emulsion designed for preterm newborns. It is given through a tube which is placed in your child's vein, when your child is not able to eat all of his or her nutrition by mouth.

Numeta is presented in the form of a three chamber bag in which the separate chambers contain:
a 50 % glucose solution
a 5.9% paediatric amino acid solution, with electrolytes
a 12.5% lipid (fat) emulsion

Depending on your child's needs, two or three of these solutions are mixed together in the bag before it is given to your child.

Numeta G13%E Preterm must only be used under medical supervision.

2. What you need to know before your child is given Numeta G13%E Preterm

Your child should not be given Numeta G13%E Preterm, in the following cases:

With the glucose and amino acid/electrolyte solutions mixed together in the bag ("2 in 1"):
- If your child is allergic to egg, soya, peanuts or to any ingredient of this medicine or component of the container (listed in section 6).

- If your child's body has problems using building blocks of protein.
- If your child has high concentrations of any of the electrolytes included in Numeta G13%E Preterm in their blood.
- Numeta G13%E Preterm (or other calcium containing solutions) must not be given at the same time as ceftriaxone (an antibiotic), even if separate infusion lines are used. There is a risk of particle formation in the newborn´s bloodstream which may be fatal.
- If your child has hyperglycaemia (especially high levels of sugar in his/her blood).

With the glucose, amino acid/electrolyte and lipid solutionsmixed together in the bag ("3 in 1").
All of the above situations mentioned for the "2 in 1" plus the following:
- If your child has especially high level of fats in his/her blood.

In all cases, the doctor will base their decision on whether your child should receive this medicine on factors such as age, weight and clinical condition. The doctor will also consider the results of any tests performed.

Warnings and precautions

Talk to your child's doctor or nurse before they are given Numeta G13%E Preterm.

When used in neonates and children below 2 years, the solution (in bags and administration sets) should be protected from light exposure until administration is completed. Exposure of Numeta G13%E Preterm to ambient light, especially after admixtures with trace elements and/or vitamins, generates peroxides and other degradation products that can be reduced by protection from light exposure.

Allergic reactions:
The infusion must be stopped immediately if any signs or symptoms of an allergic reaction (such as fever, sweating, shivering, headache, skin rashes, or difficulty breathing) develop. This medicinal product contains soybean oil, which may rarely cause hypersensitivity reactions. Uncommonly, it has been observed that some people who are allergic to peanut proteins are also allergic to soybean proteins.

Numeta G13%E Preterm contains glucose produced from cornstarch. Therefore, Numeta G13%E Preterm should be used with caution in patients with known allergy to corn or corn products.

Risk of particle formation with ceftriaxone (antibiotic):
A certain antibiotic named ceftriaxone must not be mixed or given simultaneously with any calcium containing solutions (including Numeta G13%E Preterm) given to you by a drip into your vein.
Your doctor knows this and will not give you them together even via different infusion lines or different infusion sites.

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

Infection and sepsis:
The doctor will carefully watch your child for any signs of infection. An “aseptic technique” (i.e., germ free technique) when placing and maintaining the catheter as well as when making the nutritional formula can reduce the risk of infection.

Occasionally, children can develop infection and sepsis (bacteria in the blood) when they have a tube in their vein (intravenous catheter). Certain medications and illnesses can increase the risk of developing infection or sepsis. Patients who require parenteral nutrition (giving nutrition through a tube in your child’s vein) can be more likely to develop infection from their medical conditions.

Fat overload syndrome:
Fat overload syndrome has been reported with similar products. The reduced or limited ability of the body to remove the fats contained in Numeta G13%E Preterm may result in a "fat overload syndrome" (see section 4 – Possible Side Effects).

Changes in blood chemistry levels:
The doctor will check and monitor your child’s fluids, blood chemistries and other blood values during treatement with Numeta G13%E Preterm. Occasionally refeeding someone who is severely undernourished can result in major changes in blood chemistry levels that may need to be corrected. Extra fluid in the tissues and swelling can also develop. It is recommended that parenteral nutrition is started slowly and carefully.

Monitoring and adjustment:
The doctor will be closely monitoring and adjusting Numeta G13%E Preterm to meet your child’s individual needs especially if they have the following conditions:

- severe post-traumatic conditions
- severe diabetes mellitus
- shock
- heart attack
- severe infection
- certain types of coma

Use with caution:
Numeta G13%E Preterm should be used with caution if your child has:

- pulmonary oedema (fluid in the lungs) or heart failure.
- severe liver problems.
- problems in using nutrients correctly.
- high blood sugar.
- kidney problems.
- severe metabolic disorders (when the body cannot break down substances in a normal way).
- blood clotting disorders.

Your child´s body fluid status, liver test values and/or other blood values will be closely monitored.

There is limited information on giving this medicine in preterm (premature) infants less than 28-week gestational age.

Other medicines and Numeta G13%E Preterm

Tell the doctor if your child is taking or using, has recently taken or used or might take or use any other medicines.

Numeta G13%E Preterm must not be given at the same time as:

- **ceftriaxone** (an antibiotic) not even in separate infusion lines because of the risk of particle formation.
- **blood** through the same infusion tubing due to the risk of pseudoagglutination (red blood cells becoming stuck together in a stack).
- **Ampicillin, fosphenytoin or furosemide** through the same infusion line because of the risk of particle formation

Coumarin and warfarin (Anticoagulants):
The doctor will carefully watch your child if they are taking coumarin or warfarin. These medicines are anticoagulants used to prevent clotting of the blood. Olive and soybean oil have a natural content of vitamin K1. Vitamin K1 may interfere with medicines such as coumarin and warfarin.

Laboratory tests:
The lipids contained in this emulsion may interfere with the results of certain laboratory tests. Laboratory tests may be performed after a period of 5 to 6 hours following the use of lipids or when no additional lipids are administered.

Interactions of Numeta G13%E Preterm with medicines that may affect potassium levels/metabolism:
Numeta G13%E Preterm contains potassium. High levels of blood potassium may cause abnormal heart rhythm. Special care should be taken in patients taking diuretics (medicines to reduce fluid retention) or ACE inhibitors (medicines for high blood pressure) or angiotensin II receptor antagonists (medicines for high blood pressure) or immunosuppressants (medicines that may lower the body's normal immune defences). These types of medicines may increase potassium levels.

3. How Numeta G13%E Preterm is given

Your child should always be given Numeta G13%E Preterm exactly as the doctor has indicated. Check with your doctor if you are not sure.

Age group
Numeta G13%E Preterm has been designed to meet the nutritional needs of preterm newborns.

Numeta G13%E Preterm may not be appropriate for some preterm infants, as their condition may require individualised formulations to meet their specific nutritional needs. The doctor will decide if this medicine is suitable for your child.

Administration
This medicine is an emulsion for infusion. It is given through a plastic tube in a vein in your child's arm or in a large vein in your child's chest.

The doctor may choose not to give lipids to your child. The design of the Numeta G13%E Preterm bag allows only the peel seal between the amino acids/electrolyte and glucose chambers to be broken if necessary. The peel seal between the amino acids and lipid chambers remains intact in this case. The content of the bag can then be infused without lipids.

When used in neonates and children below 2 years, the solution (in bags and administration sets) should be protected from light exposure until administration is completed (see section 2).

Dosage and duration of treatment

The doctor will decide the dose and for how long it will be given. The dosage depends on the nutrition needs of your child. The dosage will be based on your child's weight, medical condition, and on their body's ability to break down and use the ingredients in Numeta G13%E Preterm. Additional nutrition or proteins given orally/enterally may also be given.

If your child is given too much Numeta G13%E Preterm

Symptoms
Too much of this medicine, or giving it too quickly may result in the following:

- nausea (feeling sick)
- vomiting
- shivering
- electrolyte disturbances (improper amounts of electrolytes in the blood)
- signs of hypervolemia (increase of circulating blood volume, too much fluid in the blood vessels)
- acidosis (increased acidity of the blood)

In such situations, the infusion must be stopped immediately. The doctor will decide if additional actions are required.

To prevent these events occurring, the doctor will regularly monitor your child's condition and test their blood levels during treatment.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not every child gets them.

If you notice any changes in the way your child feels during or after the treatment, tell the doctor or nurse immediately.

The tests the doctor will perform while your child is taking the medicine should minimise the risk of side effects.

If signs of an allergic reaction occur, the infusion shall be stopped and a doctor contacted immediately. This can be serious and the signs may include:

- sweating
- shivering
- headache
- skin rashes

– breathing difficulties

Other side effects that have been noticed are:

Common: may affect up to 1 in 10 people
- Low phosphate level in the blood (hypophosphataemia)
- High sugar level in the blood (hyperglycaemia)
- High calcium level in the blood (hypercalcaemia)
- High triglycerides level in the blood (hypertriglyceridaemia)
- Electrolyte disturbance (hyponatraemia)

Uncommon: may affect up to 1 in 100 people
- High lipid level in the blood (hyperlipidaemia)
- Condition where bile cannot flow from the liver to the duodenum (cholestasis). The duodenum is a part of the intestines.

*Not known: frequency cannot be estimated from the available data (*These adverse reactions have been reported only for Numeta G13%E Preterm and G16E when peripherally administered with insufficient dilution).
- Skin necrosis
- Soft tissue injury
- Extravasation

The following side effects have been reported with other parenteral nutrition products:
- The reduced or limited ability to remove the lipids contained in Numeta may result in a " fat overload syndrome". The following signs and symptoms of this syndrome are usually reversible when the infusion of the lipid emulsion is stopped:
    - Sudden and abrupt worsening of the patient's medical condition
    - High levels of fats in the blood (hyperlipidaemia)
    - Fever
    - Liver fatty infiltration (hepatomegaly)
    - Worsening liver function
    - Reduction in red blood cells which can make the skin pale and cause weakness or breathlessness (anaemia)
    - Low white blood cell count, which can increase the risk of infection (leukopenia)
    - Low platelet count which can increase the risk of bruising and/or bleeding (thrombocytopenia)
    - Coagulation disorders which effect the ability of the blood to clot
    - Coma, requiring hospitalisation.
- Formation of small particles which may lead to blockage of blood vessels in the lungs (pulmonary vascular precipitates) or difficulty breathing

Reporting of side effects
If your child gets any side effects talk to the doctor or nurse. This includes any possible side effects not listed in this leaflet.

You can also report side effects directly (see details below). By reporting side effects you can help provide more information on the safety of this medicine.
[to be completed nationally according to the national reporting system listed in Appendix V]

5. How to store Numeta G13%E Preterm

Keep this medicine out of the sight and reach of children when not being administered.

When used in neonates and children below 2 years, the solution (in bags and administration sets) should be protected from light exposure until administration is completed (see section 2).

Do not use this medicine after the expiry date which is stated on the bag and the outer packaging (MM/YYYY). The expiry date refers to the last day of that month.

Do not freeze.
Store in the overpouch.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Numeta G13%E Preterm looks like and contents of the pack

Numeta G13%E Preterm is presented in the form of a triple-chamber bag. Each bag contains a sterile combination of a glucose solution, an amino acid solution for children, with electrolytes, and a lipid emulsion, as described below.

Container size	50% glucose solution	5.9% amino acid solution with electrolytes	12.5% lipid emulsion
300 mL	80 mL	160 mL	60 mL

Appearance before reconstitution:

- The solutions in the amino acid and glucose chambers are clear, colorless or slightly yellow
- The lipid emulsion chamber is a uniform and milky-white liquid

Appearance after reconstitution:

- "2 in 1" solution (amino acids/electrolytes and glucose) for infusion is clear, colorless or slightly yellow
- "3 in 1" emulsion for infusion is uniform and milky-white

The three-compartment bag is a multi-layer plastic bag.

To prevent air contact, Numeta G13%E Preterm is packaged in an oxygen barrier overpouch that also contains an oxygen absorber and an oxygen indicator.

<u>Pack sizes</u>

300 mL bag: 10 units per cardboard box
1 bag of 300 mL

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

United Kingdom:
Baxter Healthcare Ltd
Caxton Way
Thetford
Norfolk
IP24 3SE
United Kingdom

Ireland & Malta:
Baxter Holding B.V.
Kobaltweg 49
3542CE Utrecht
Netherlands

Manufacturer

BAXTER S.A.
BOULEVARD RENE BRANQUART, 80
7860 LESSINES
BELGIUM

This medicinal product is authorised in the Member States of the EEA under the following names:

Country	Name
Austria Germany	**Numeta G 13 % E Emulsion zur Infusion**
Belgium Luxembourg	**NUMETZAH G13%E, émulsion pour perfusion**
France	**NUMETAH G13%E PREMATURES, emulsion pour perfusion**
Denmark Norway Sweden	**Numeta G13E**
Czech Republic	**NUMETA G 13 % E**
Greece	**NUMETA Preterm G 13 E**
Netherlands	**NUMETA G13%E emulsie voor infusie**
Ireland Malta United Kingdom	**Numeta G13%E Preterm, Emulsion for Infusion**
Italy	**NUMETA G13E emulsione per infusione**
Finland	**Numeta G13E infuusioneste, emulsio**
Poland	**NUMETA G 13 % E Preterm**
Portugal	**Numeta G13%E**
Spain	**NUMETA G13%E, emulsión para perfusión**

This leaflet was last revised August 2020

The following information is intended for medical or healthcare professionals only*

*Please observe that in certain cases this product may be administered at home by parents or other caregivers. In such cases parents/caregivers should read the following information.

No additions to the bag should be made without first checking the compatibility. Formation of particles or breaking down of the lipid emulsion could result. This can lead to blockage of the blood vessels.

Numeta G13%E Preterm should be at room temperature before use.

Before using Numeta G13%E Preterm, the bag will be prepared as shown below.

Confirm that the bag is not damaged. Use the bag only if it is not damaged. An undamaged bag looks like this:

- The non-permanent seals are intact. This is indicated by no mixture of any of the three chambers
- The amino acid solution and the glucose solution are clear, colorless, or slightly yellow without visible particles
- The lipid emulsion is a uniform liquid with a milky white appearance.

Before opening the overpouch, check the colour of the oxygen indicator.

- Compare it to the reference colour printed next to the OK symbol and shown in the printed area of the indicator label.
- Do not use the product if the colour of the oxygen indicator does not correspond to the reference color printed next to the OK symbol.

Figures 1 and 2 illustrate how to remove the protective overpouch. Discard the overpouch, oxygen indicator and oxygen absorber.

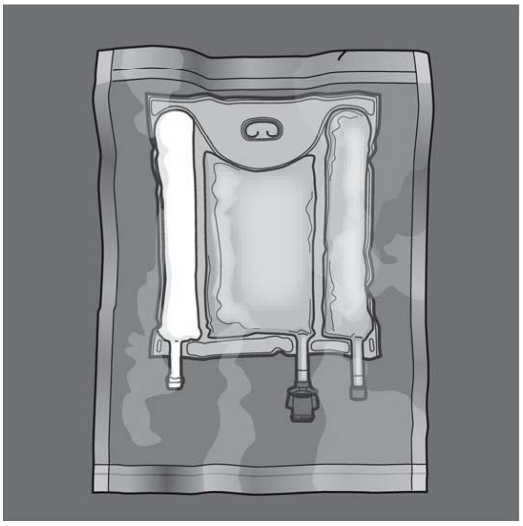


Figure 1

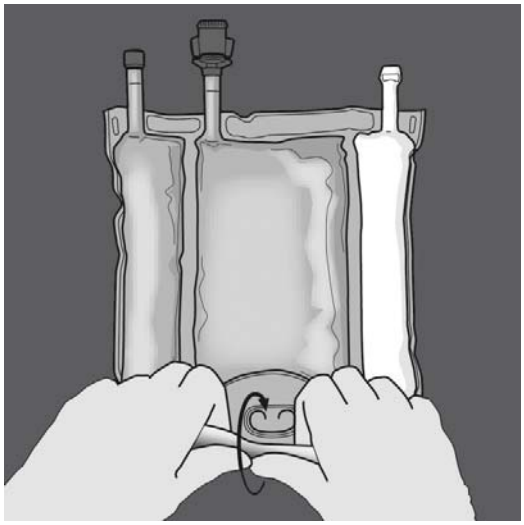
Figure 2

Preparation of the mixed emulsion:

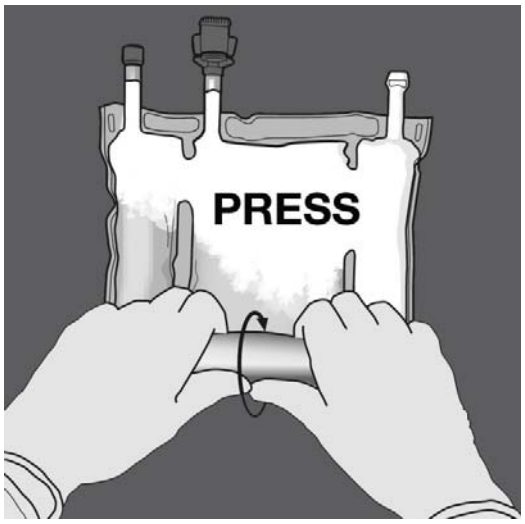
- Ensure that the product is at room temperature when breaking the non-permanent seals.
- Place bag onto a flat clean surface.

Activation of the 3 chambers (mixing of 3 solutions by breaking two non-permanent seals)

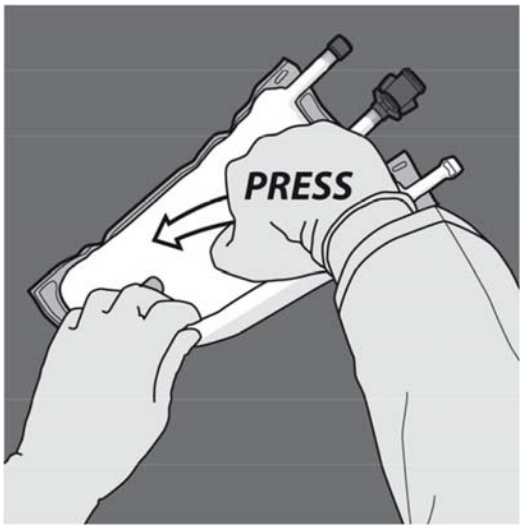
Step 1: Start rolling the bag from the D-hanger side.



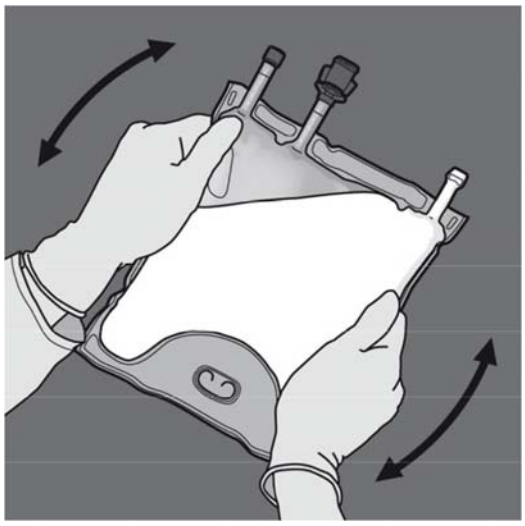
Step 2: Apply pressure until peal seals open.



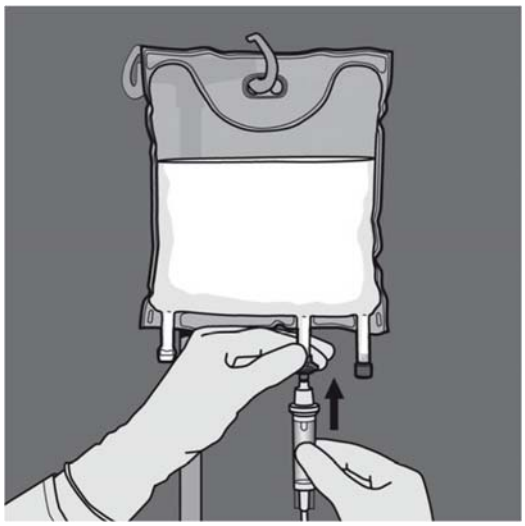
Step 3: Change direction by rolling the bag towards the D-hanger.
Continue until the seal is completely opened.
Proceed the same way to complete the opening of the second peel seal.



Step 4: Turn the bag over at least three times to mix the content thoroughly.
The appearance of the mixed solution should be a milky-white emulsion.

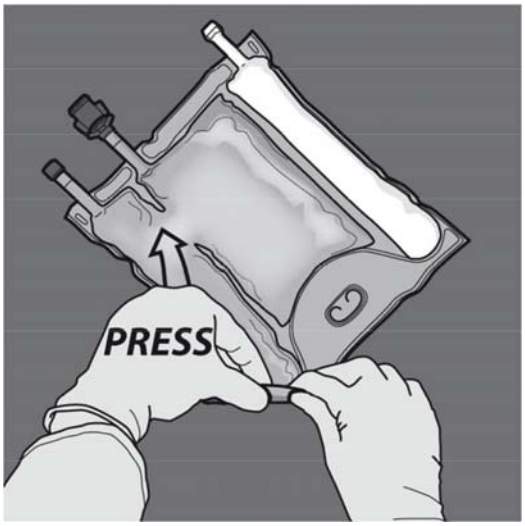


Step 5: Remove the protective cap from the administration site and insert the IV administration set.

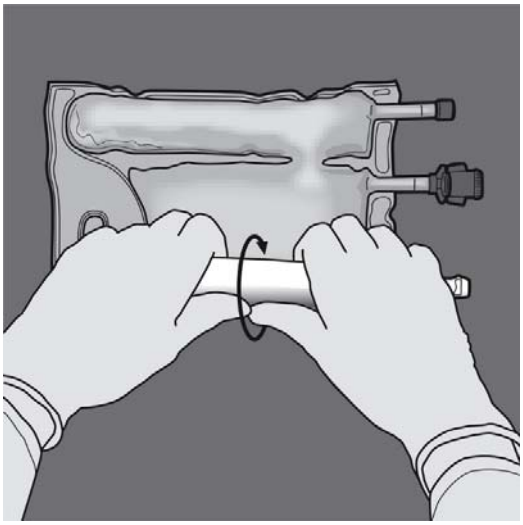


Activating the 2 chambers (mixing of 2 solutions by breaking the non-permanent seal between the amino acid and glucose chambers)

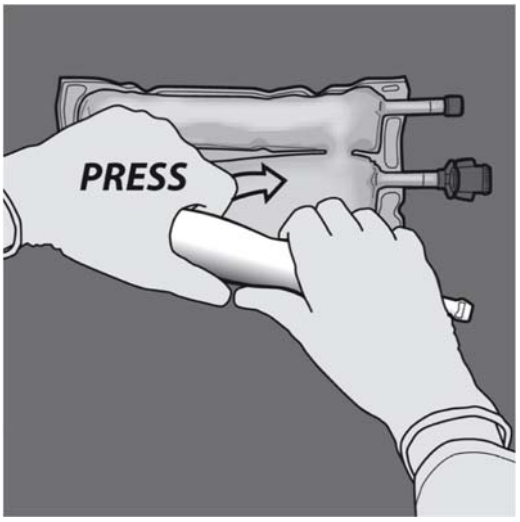
Step 1: To mix only 2 solutions, roll the bag from the top (hanger end) corner of the seal separating the solutions.
Apply pressure to open the seal separating the glucose and amino acid compartments.



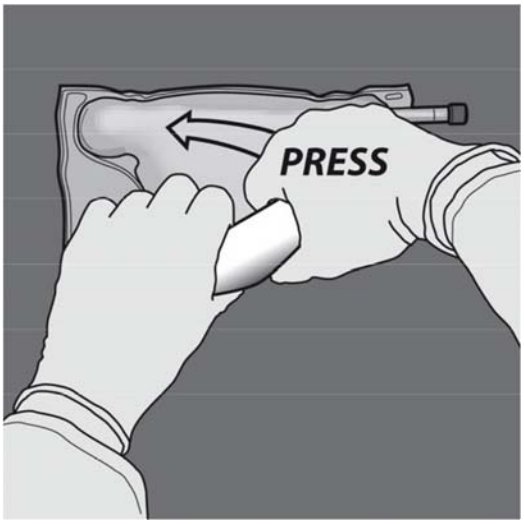
Step 2: Place the bag such that the lipid emulsion compartment is nearest to the operator.
Roll the bag while protecting the lipid emulsion compartment in the palms of the hands.



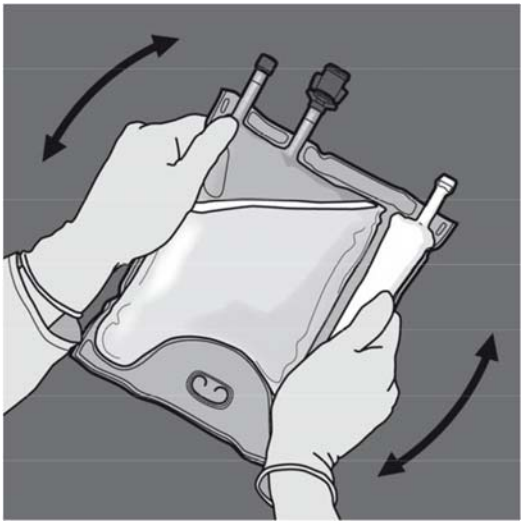
Step 3: Apply pressure with one hand and roll the bag toward the tubes.



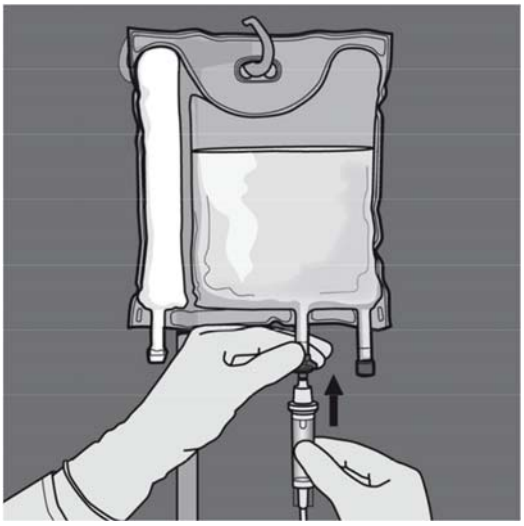
Step 4: Change direction by rolling the bag towards the top (hanger end).
Press with the other hand, continuing until the seal separating the amino acid and glucose solutions is completely opened.



Step 5: Turn the bag over at least three times to mix the content thoroughly.
The appearance of the mixed solution should be clear, colorless or slightly yellow.



Step 6: Remove the protective cap from the administration site and insert the IV administration set.



The flow rate should be increased gradually during the first hour. The administration flow rate must be adjusted based on the following factors:

- the dose being administered
- the daily volume intake
- the duration of the infusion.

Method of administration:

When used in neonates and children below 2 years, the solution (in bags and administration sets) should be protected from light exposure until administration is completed.

Due to its high osmolarity, undiluted Numeta G13%E Preterm can only be administered through a central vein; however, sufficient dilution of Numeta G13%E Preterm with water for injection lowers the osmolarity and allows peripheral infusion. The formula below indicates how the dilution impacts osmolarity of the bags:

$$Final\ osmolarity = \frac{Volume\ of\ bag * Initial\ osmolarity}{Water\ added + Volume\ of\ bag}$$

The table below shows examples of osmolarity for activated 2CB and activated 3CB admixtures after addition of water for injection:

	Amino Acids and Glucose (Activated 2CB)	**Amino Acids, Glucose, and Lipids (Activated 3CB)**
Initial volume in the bag (mL)	240	300
Initial osmolarity (mOsm/L approximately)	1400	1150
Volume of water added (mL)	240	300
Final volume after addition (mL)	480	600
Osmolarity after addition (mOsm/L approximately)	700	575

Addition of additives

Light exposure of solutions for intravenous parenteral nutrition, especially after admixture with trace elements and/or vitamins, may have adverse effects on the clinical outcome in neonates, due to the generation of peroxides and other degradation products, When used in neonates and children below 2 years, Numeta G13%E Preterm should be protected from ambient light until administration is completed..

Compatible additives may be added via the injection site into the reconstituted mixture (after the non-permanent seals have been opened and after the contents of the two or three chambers have been mixed).

Vitamins may also be added into the glucose chamber before the mixture is reconstituted (before opening the non-permanent seals and before mixing the solutions and the emulsion).

Possible additions of commercially available trace element solutions (identified as TE1 and TE4), vitamins (identified as lyophilizate V1 and emulsion V2), and electrolytes in defined quantities are shown in Tables 1-4.

1. *Compatibility with TE4, V1 and V2*

Table 1: Compatibility of 3-in-1 (Activated 3CB) with and without dilution with water

Per 300 mL (3 in 1 admixture with lipids)						
	Admixture without dilution			Admixture with dilution		
Additives	Included level	Maximum further addition	Maximum total level	Included level	Maximum further addition	Maximum total level
Sodium (mmol)	6.6	5.0	11.6	6.6	5.0	11.6
Potassium (mmol)	6.2	4.2	10.4	6.2	4.2	10.4
Magnesium (mmol)	0.47	0.83	1.3	0.47	0.83	1.3
Calcium (mmol)	3.8	3.5	7.3	3.8	3.5	7.3
Phosphate* (mmol)	3.8	2.5	6.3	3.8	2.5	6.3
Trace elements & vitamins	-	15 mL TE4 + 1.5 vial V1 + 25 mL V2	15 mL TE4 + 1.5 vial V1 + 25 mL V2	-	15 mL TE4 + 1.5 vial V1 + 25 mL V2	15 mL TE4 + 1.5 vial V1 + 25 mL V2
Water for Injection	-	-	-	-	300 mL	300 mL

* Organic phosphate

Table 2: Compatibility of 2-in-1 (Activated 2CB) with and without dilution with water

Per 240 mL (2 in 1 admixture without lipids)						
	Admixture without dilution			Admixture with dilution		
Additives	Included level	Maximum further addition	Maximum total level	Included level	Maximum further addition	Maximum total level
Sodium (mmol)	6.4	17.6	24	6.4	0.0	6.4
Potassium (mmol)	6.2	17.8	24	6.2	0.0	6.2
Magnesium (mmol)	0.47	2.13	2.6	0.47	0.0	0.47
Calcium (mmol)	3.8	3.5	7.3	3.8	0.0	3.8
Phosphate* (mmol)	3.2	4.0	7.2	3.2	0.0	3.2
Trace elements & vitamins	-	2.5mL TE4 + ¼ vial V1	2.5mL TE4 + ¼ vial V1	-	2.5mL TE4 + ¼ vial V1	2.5mL TE4 + ¼ vial V1
Water for Injection	-	-	-	-	240 mL	240 mL

* Organic phosphate

2. *Compatibility with TE1, V1 and V2*

Table 3: Compatibility of 3-in-1 (Activated 3CB) with and without dilution with water

Per 300 mL (3 in 1 admixture with lipids)						
	Admixture without dilution			Admixture with dilution		
Additives	Included level	Maximum further addition	Maximum total level	Included level	Maximum further addition	Maximum total level
Sodium (mmol)	6.6	5.0	11.6	6.6	0.0	6.6
Potassium (mmol)	6.2	4.2	10.4	6.2	0.0	6.2
Magnesium (mmol)	0.47	0.83	1.3	0.47	0.0	0.47
Calcium (mmol)	3.8	1.9	5.7	3.8	0.0	3.8
Phosphate* (mmol)	3.8	2.5	6.3	3.8	0.0	3.8
Trace elements & vitamins	-	2.5 mL TE1 + ¼ vial V1 + 2.5 mL V2	2.5 mL TE1 + ¼ vial V1 + 2.5 mL V2	-	2.5 mL TE1 + ¼ vial V1 + 2.5 mL V2	2.5 mL TE1 + ¼ vial V1 + 2.5 mL V2
Water for Injection	-	-	-	-	300 mL	300 mL

* Organic phosphate

Table 4: Compatibility of 2-in-1 (Activated 2CB) with and without dilution with water

Per 240 mL (2 in 1 admixture without lipids)						
	Admixture without dilution			Admixture with dilution		
Additives	Included level	Maximum further addition	Maximum total level	Included level	Maximum further addition	Maximum total level
Sodium (mmol)	6.4	17.6	24	6.4	0.0	6.4
Potassium (mmol)	6.2	17.8	24	6.2	0.0	6.2
Magnesium (mmol)	0.47	2.13	2.6	0.47	0.0	0.47
Calcium (mmol)	3.8	3.5	7.3	3.8	0.0	3.8
Phosphate* (mmol)	3.2	4.0	7.2	3.2	0.0	3.2
Trace elements & vitamins	-	2.5 mL TE1 + ¼ vial V1	2.5 mLTE1 + ¼ vial V1	-	2.5 mL TE1 + ¼ vial V1	2.5 mL TE1 + ¼ vial V1
Water for Injection	-	-	-	-	240 mL	240 mL

* Organic phosphate

The composition of vitamins and trace elements preparations are illustrated in Tables 5 and 6.

Table 5:Composition of the commercial trace elements preparation used:

Composition per vial	**TE1 (10 ml)**	**TE4 (10 ml)**
Zinc	38.2µmol or 2.5mg	15.3µmol or 1mg
Selenium	0.253µmol or 0.02mg	0.253µmol or 0.02mg
Copper	3.15µmol or 0.2mg	3.15µmol or 0.2mg
Iodine	0.0788µmol or 0.01mg	0.079µmol or 0.01mg
Fluorine	30µmol or 0.57mg	-

Composition per vial	TE1 (10 ml)	TE4 (10 ml)
Manganese	0.182µmol or 0.01mg	0.091µmol or 0.005mg

Table 6: Composition of the commercial vitamin preparations used:

Composition per vial	V1	V2
Vitamin B1	2.5 mg	-
Vitamin B2	3.6 mg	-
Nicotinamide	40 mg	-
Vitamin B6	4.0 mg	-
Pantothenic acid	15.0 mg	-
Biotin	60 µg	-
Folic acid	400 µg	-
Vitamin B12	5.0 µg	-
Vitamin C	100 mg	-
Vitamin A	-	2300 IU
Vitamin D	-	400 IU
Vitamin E	-	7 IU
Vitamin K	-	200 µg

To perform an addition:

- Aseptic conditions must be observed
- Prepare the injection site of the bag
- Puncture the injection site and inject the additives using an injection needle or a reconstitution device
- Mix content of the bag and the additives

Preparation of the infusion:

- Aseptic conditions must be observed
- Suspend the bag
- Remove the plastic protector from the administration outlet
- Firmly insert the infusion set spike into the administration outlet

Administration of the infusion:

- For single use only

- Only administer the product after the non-permanent seals between the two or three chambers have been opened and the contents of the two or three chambers have been mixed
- Ensure that the final activated 3CB emulsion for infusion does not show any evidence of phase separation or the final 2CB solution for infusion does not show any evidence of particles

  Immediate use once non-permanent seals are broken is recommended. Numeta G13%E Preterm should not be stored for subsequent infusion.
- Do not connect any partially used bag
- Do not connect in series in order to avoid the possibility of air embolism due to possible residual gas contained in the primary bag.
- When used in neonates and children below 2 years protect from light exposure until administration is completed. Exposure of Numeta G13%E Preterm to ambient light, expecially after admixtures with trace elements and/or vitamins, generates peroxides and other degradation products that can be reduced by protection from light exposure.
- Any unused product or waste material and all necessary disposable devices must be properly discarded.

Shelf life after the Solutions are Mixed

Use the product immediately after the non-permanent seals between the two or three chambers have been opened. Stability studies of the mixtures have been performed for 7 days between 2°C and 8°C followed by 48 hours at 30°C.

Shelf life after Supplementation (electrolytes, trace elements, vitamins, water)

For specific admixtures physical stability of the Numeta formulation has been demonstrated for 7 days between 2°C and 8°C followed by 48 hours at 30°C.

Information on these additions is specified in section 6.6 of the SmPC (summary of product characterisitics).

From a microbiological point of view, the product 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 to 8°C, unless reconstitution /dilution /supplementation has taken place in controlled and validated aseptic conditions

Do not use Numeta G13%E Preterm if the bag is damaged. A damaged bag looks like this:

- The non-permanent seals are broken
- Any one of the chambers contains a mixture of any of the solutions
- The amino acid solution and the glucose solution are not clear, colorless, or slightly yellow, and/or contain visible particles

- The lipid emulsion is not a uniform liquid with a milky white appearance.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

What Numeta G13%E Preterm contains

The active substances are:

Active Substance	Activated 2CB (240 mL)	Activated 3CB (300 mL)
Amino Acid Chamber		
Alanine	0.75 g	0.75 g
Arginine	0.78 g	0.78 g
Aspartic acid	0.56 g	0.56 g
Cysteine	0.18 g	0.18 g
Glutamic acid	0.93 g	0.93 g
Glycine	0.37 g	0.37 g
Histidine	0.35 g	0.35 g
Isoleucine	0.62 g	0.62 g
Leucine	0.93 g	0.93 g
Lysine monohydrate (equivalent to Lysine)	1.15 g (1.03 g)	1.15 g (1.03 g)
Methionine	0.22 g	0.22 g
Ornithine hydrochloride (equivalent to Ornithine)	0.30 g (0.23 g)	0.30 g (0.23 g)
Phenylalanine	0.39 g	0.39 g
Proline	0.28 g	0.28 g
Serine	0.37 g	0.37 g
Taurine	0.06 g	0.06 g
Threonine	0.35 g	0.35 g
Tryptophan	0.19 g	0.19 g
Tyrosine	0.07 g	0.07 g
Valine	0.71 g	0.71 g
Potassium acetate	0.61 g	0.61 g
Calcium chloride dihydrate	0.55 g	0.55 g
Magnesium acetate tetrahydrate	0.10 g	0.10 g
Sodium glycerophosphate hydrated	0.98 g	0.98 g
Glucose Chamber		
Glucose monohydrate (equivalent to glucose anhydrous)	44.00 g (40.00 g)	44.00 g (40.00 g)
Lipid Chamber		
Refined olive oil (approximately 80%) + Refined soya-bean oil (approximately 20%)	-	7.5 g

2CB= two chamber bag, 3CB = three chamber bag

The reconstituted solution/emulsion provides the following:

Composition				
	Activated 2CB		**Activated 3CB**	
Per volume unit (mL)	**240**	**100**	**300**	**100**
Nitrogen (g)	1.4	0.59	1.4	0.47
Amino acids (g)	9.4	3.9	9.4	3.1
Glucose (g)	40.0	16.7	40.0	13.3
Lipids (g)	0	0	7.5	2.5
Energy				
Total calories (kcal)	198	82	273	91
Non-protein calories (kcal)	160	67	235	78
Glucose calories (kcal)	160	67	160	53
Lipid calories [a] (kcal)	0	0	75	25
Non-prot calories / nitrogen (kcal/g N)	113	113	165	165
Lipid calories (% non-protein calories)	N/A	N/A	32	32
Lipid calories (% total calories)	N/A	N/A	28	28
Electrolytes				
Sodium (mmol)	6.4	2.7	6.6	2.2
Potassium (mmol)	6.2	2.6	6.2	2.1
Magnesium (mmol)	0.47	0.20	0.47	0.16
Calcium (mmol)	3.8	1.6	3.8	1.3
Phosphate [b] (mmol)	3.2	1.3	3.8	1.3
Acetate (mmol)	7.2	3.0	7.2	2.4
Malate (mmol)	3.2	1.3	3.2	1.1
Chloride (mmol)	9.3	3.9	9.3	3.1
pH (approx.)	5.5	5.5	5.5	5.5
Osmolarity approx. (mOsm/L)	1400	1400	1150	1150

[a] Includes calories from egg phospholipids for injection
[b] Includes phosphate from egg phospholipids for injection component of the lipid emulsion

The other ingredients are:
L-Malic acid [a]
Hydrochloric acid [a]
Egg phospholipids for injection
Glycerol
Sodium oleate
Sodium hydroxide [a]
Water for injections

[a] for pH adjustment