Northwell Health
Staten Island University Hospital

Consent for Participation in a Compassionate Use Protocol

Parental Informed Consent Form

Title: Compassionate Use of Omegaven® IV Fat Emulsion

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This consent form is written from the point of view of a research participant. If the parent or legal guardian of a minor or a legally authorized representative will be providing consent, the words "you" and "your" should be read as ("your child").

Introduction
You are being asked to allow your infant/child to receive Omegaven® intravenous fat emulsion in place of currently used intravenous fat emulsion. This is an experimental therapy not approved for use in the United States (US), but is approved for short-term use in adults in Europe. This means the drug has not yet been approved by the Food and Drug Administration (FDA) and is considered investigational.

However, given your infant/child's condition, we have received permission through the Food and Drug Administration (FDA) to provide this product to infants and children on a "compassionate use" basis. This means that it is being used outside the conduct of a clinical trial (a type of research study) in a small number of extremely ill patients for whom standard therapy is unlikely to be effective. Information from the use of this therapy will help determine whether the FDA should approve it in the future.

This consent form will explain:
- the purpose of the study
- what you will be asked to do
- the potential risks and benefits

It will also explain that you do not have to be in this study to receive medical care. You should ask questions before you decide if you want to participate. You can also ask questions at any time during the study.

Why is this being done?
Infants and children who have had intestinal diseases and/or surgery may require intravenous nutrition for a long period. Although this intravenous nutrition is necessary and life sustaining, it can result in severe liver disease. Your child has developed the severe liver disease that is getting worse.

Experimental data has shown that the current intravenous fat mixture (called Intralip may contribute to this liver disease. We have an alternative form of intravenous fat mixture, called Omegaven® that could be used in place of Intralipid® for your child. Omegaven® contains 10% fish oil, which is different from Intralipid®, which contains soybean oils. It has been shown in a small number of studies that use of this fish oil improves the function of the liver disease.

Omegaven® is given IV through a central or peripheral catheter together with solutions containing dextrose (sugar) and amino acids (protein). Because we believe other fat mixtures are contributing to your infant/child's liver disease, we would administer Omegaven® alone or in combination with the dextrose and amino acid solution (PN).

How long will your child's treatment last?
We plan to use this therapy during your child's hospitalization, until the liver function starts to get better. It may be necessary to continue to use Omegaven once your child goes home if he/she is still requiring IV nutrition with Omegaven at the time of discharge. We monitor the jaundice level and other liver functions by blood tests every 1 to 4 weeks depending on the length of time, your baby/child has been receiving Omegaven® and his/her tolerance to the therapy. These tests are usually being done as part of standard care.

What will happen?
If you chose to allow your infant or child to participate, the following applies:

- Your child or infant will receive Omegaven until IV nutrition is no longer required. It may be necessary for your child or infant to continue to use Omegaven at home after discharge from the hospital.
- A blood test will be drawn prior to receiving Omegaven and every 1-4 weeks thereafter to check for the following:
    - Blood chemistry, blood cell count, blood clotting, cholesterol and triglycerides (levels of fatty substances), and liver function (levels of substances that help us determine the degree of liver injury referred to as liver enzymes).
- Growth measurements of weight, body length (height), and head circumference will be recorded every 1-2 weeks.
- Omegaven is given by the vein: alone or with a solution containing sugars, protein, vitamins and minerals. Your child may receive Omegaven alone (if the child is feeding) or with a solution previously described.
- If your infant or child is transferred from another Neonatal Intensive Care Unit for Staten Island University Hospital's neonatal services such as this alternative for infants with liver disease, she/he will be admitted to the NICU for continuation of medical treatment and initiation of Omegaven.
- If your infant or child has never been admitted to Staten Island University Hospital, and is referred to the site for home therapy of Omegaven treatment, he/she will be admitted for 72 hours to initiate the administration of Omegaven, to be observed for any reactions, and to educate you as to how to care for your child at home.
- If your child or infant has already received Omegaven either at Staten Island University Hospital or at another hospital and treatment was stopped but IV nutrition including Omega becomes medically necessary, he or she will not be required to be admitted for this 72- hour inpatient admission prior to starting Omegaven at home.
- Appropriate outpatient follow-up care will continue through appropriate providers designated by

Staten Island University Hospital.

- There is no minimum or maximum length of time to receive the Omegaven. Omegaven will be given for as long as the child requires IV nutrition, and this protocol will remain open to follow the child or infant enrolled in this study for as long as the child/infant has liver disease and therefore requires follow-up.
- This protocol will end if the product is approved for use in the United States or if an FDA clinical trial proves Omegaven® treatment to be ineffective.

What are the benefits?

We hope the immediate benefit of using this experimental therapy is for your infant or child to gain essential fatty acids that are important for the body to survive and help in the healing of the liver disease. In addition, we hope that the treatment may allow your infant/child to receive essential fatty acids not normally provided intravenously. It is possible, however, that your infant or child will not benefit from this experimental treatment.

What are the risks? What could go wrong?

The infusion of Omegaven can lead to a prolonged bleeding time and an inhibited platelet aggregation (clotting). Undesirable effects observed in adults include:

- Slight rise in body temperature,
- Heat sensation and/or cold sensations, chills,
- Flushing or a bluish discoloration of the skin,
- Lack of appetite, nausea vomiting,
- Difficult or labored breathing,
- Headache, pain in the back chest or loins, bone-pain,
- Priapism (persistent erection of the penis) in very rare cases,
- Increase or decrease in blood pressure, anaphylactic reactions.

Thus far, the data on this therapy indicate no special risks of its use. The manufacturer has indicated that there may be a risk of an allergic reaction to this product in patients with egg or shellfish allergies. Its use is not recommended for patients with abnormal fat metabolism, severe hemorrhagic (bleeding) disorders, or unstable diabetes mellitus.

Due to lack of experience in certain life threatening situations, the manufacturer does not recommend the use of this product in patients with severe liver or renal insufficiency (liver or kidney problems). However, published studies in infants with liver disease have not shown any unusual risks and have reported improvements in the liver disease. Even though Omegaven® is an essential fatty acid, it is conceivable that it will be given in too small a dose, so there is a small risk of developing essential fatty acid deficiency. To minimize the potential for deficiency in essential fatty acids, essential fatty acid levels will be monitored. There is a potential risk of a prolonged bleeding time, but this also will be monitored in the lab tests.

This therapy provides less total calories and so potentially, growth may be slowed. However, if this occurs the intravenous nutrition may be adjusted to increase the calories.

If you do not want to take part, what are your other choices?
If you do not join this study, you have other choices for treatment. Talk to your doctor about your choices. Your other choices may include:

- Another research treatment
- Standard treatment
- No treatment
- Comfort care
- Treatment provided on this study

Your doctor can also tell you the important risks and benefits associated with the alternative treatment. Since Omegaven® will only be offered if no other usual therapy is likely to be safe and effective, the risks of not being treated are those allowing for the liver disease to continue and to progress. Participation in this experimental treatment is entirely voluntary. If you choose to not have your infant or child participate, the alternative is to continue the current medical management your infant is receiving. You are under no obligation to agree to the use of this therapy. If you decide to have your infant or child use of the experimental therapy, you may choose to stop at any time. Refusal to participate in this treatment will in no way interfere with current or future care at this hospital.

Are there any costs or compensation for participation?
The FDA has recently granted approval for charging for the cost of Omegaven®. Your child's insurance will be billed for the cost of the Omegaven®. In the event the claim is denied, the hospital will cover the cost of Omegaven®, while an inpatient. Your child will not be compensated in any way for participation in this experimental treatment. There is no compensation or reimbursement for travel expenses provided to you for your child's or infant's participation in this treatment protocol.

What happens if you are injured while participating in this study?
If injury occurs as a result of this Omegaven® therapy, your infant will receive medical care and treatment as needed from theNorthwell Health. However, you will be responsible for the costs of such medical treatment, directly or through your child's medical insurance and/or other forms of medical coverage. No money will be given to you/ your child.

What are your rights as a research participant?
Your child's participation in this project is voluntary. The quality of your child's medical care will be the same, whether you join, refuse to join, or decide to leave the study.

If you do not join the study you will not be penalized or lose benefits to which you are entitled. If you join the study, you may withdraw at any time without prejudice to your future care at the Northwell Health. Follow-up examinations may be needed to assure your well-being.

Could you be taken off the study before it is over?
It is also possible that your participation in this study may end without your consent. This decision may be made by a researcher, study sponsor or the Institutional Review Board (IRB- the committee that oversees research at this institution).

Reasons for withdrawal may include:
- It is not in your best interest to continue on this study, or
- The study is stopped.

If we detect a significant change in any lab tests or the way in which your infant or child can handle lipids, we may choose to terminate this treatment. We will discuss these decisions with you.

What happens if new information is learned?
You will be told of any new findings that may change your decision to continue to participate. Your consent to continue to take part may be obtained again.

What information will be collected and used for this study?
If you agree to allow this therapy, we will collect health information that identifies your infant. We may collect the results of tests or information from the medical record. We will only collect information that is needed for monitoring this therapy. This information has been described in this consent form. If you sign this consent form, you are giving us permission to collect, and use your infant's health information. This permission is called authorization.

Who else will see your information?
Study records that identify you will be kept private. You will not be identified in study records or publications disclosed outside the Northwell Health, except as detailed below.

Investigators will share the results of your tests and procedures with clinical staff not involved in the compassionate use protocol who may be involved in his/her therapy.

The following reviewers may access your study and medical records to make sure that this study is being done properly:
- Representatives from federal and state government oversight agencies such as the FDA
- Representatives from the Northwell Health System Institutional Review Board (IRB - the committee that reviews research at this institution)

We will do our best to protect the privacy of your records but it is possible that once information is shared with people listed on this form, it will be released to others.

In the future, we may publish results of this study in scientific journals and may present it at scientific meetings. If we do we will not identify you.

If we learn about potential serious harm to you or someone else or other public health concerns, it will be shared with the appropriate authorities.

Will you be able to access your records?
If your research records are used for decisions related to your clinical care, then you have the right to review this information and request changes. This is limited to information about your treatment, and does not include information related to procedures or tests that are for research purposes only. You may access this information only after the study analysis is complete. You have the right to know who has and who will see your records. To request this information, or for any questions related to your health information, you may contact the Research Privacy Officer at 516-562-2018.

How long will your health information be kept?
There is no limit on the length of time we will keep your information for this research because it may be analyzed for many years. We will keep it as long as it is useful, unless you decide you no longer want to take part or we close the study. You are allowing access to this information indefinitely.

Can you change your mind?
If you change your mind about allowing this therapy, you may withdraw your infant at any time. If you want us to stop collecting your child's health information, you need to send a letter to the physician at the following address:
Dr. Jonathan Blau Department of Pediatrics 475 Seaview Avenue Staten Island, NY 10305

Your letter needs to say that you have changed your mind and do not want us to collect and share your infant's health information. We may still use the information we have already collected. We may still use the information we have already collected. We need to know what happens to everyone who starts investigational therapies, not just those people who stay in it

Will information about this study be available to the public?
If this research study is a clinical trial of a drug or medical device, then add: A description of this clinical trial will be available on http://www.Clinical Trials.gov , as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this website at any time.

Who can answer your questions about this study?
If you have any questions about the protocol, or about side effects or injury caused by the therapy you should call Dr. Jonathan Blau at (718)-226-9767. If your child needs emergency care you may dial 911 or go to the nearest Emergency Department. For questions on your child's rights as a recipient of this therapy you may call the Office of the Institutional Review Board (the committee that oversees research at this Institution) at (516) 562-3101.

A signed copy of this consent form will be given to you.

[Signature Page Follows]

Summation/Signature

You have read the above description of this experimental therapy. You have been told of the risks and benefits involved and all your questions have been answered to your satisfaction. A member of the team will answer any future questions you may have. You voluntarily agree to allow your infant/child to receive this therapy and know that you can withdraw your child from participating from this therapy at any time without penalty. By signing this form, you have not given up any of your/your child's legal rights.

_____
Infant/Child's printed name

_____ _____
Parent/Legal Guardian's signature Date Parent/Legal Guardian's printed name

_____
Witness's signature Date

_____ _____
Witness's printed name

Investigator's Statement
In addition to advising the above subject of other forms of treatment and therapy which are appropriate, I have offered an opportunity for further explanation of the risks and discomforts which are, or may be associated with this therapy and to answer any further questions relating to it.

_____ _____
Investigator's signature Date

_____
Investigator's printed name