Omegaven

Single Patient IND Packet

Table of Contents

1. Omegaven Background

Omegaven 10% Emulsion is a fish oil emulsion administered intravenously in patients who require parenteral nutrition supplementation with long chain omega-3 fatty acids, especially eicosapentaenoic and docosahexaenoic acid, when oral or enteral nutrition is impossible, insufficient or contraindicated. Omegaven is often used to provide parenteral nutritional support to patients with Parenteral Nutrition Associated Cholestasis (PNAC). Omegaven is not approved for marketing in the United States but is approved in Germany. Fresenius Kabi, the manufacturer, has been supplying it for Investigational New Drug (IND) Applications in the United States.

2. Application Process for Single Patient INDs

Submitting an IND

Physicians can obtain Omegaven for a single patient by submitting a Single Patient IND application to the FDA (see 21 CFR 312.310[1]). Single Patient INDs are made available under the FDA Expanded Access Program, and are processed according to the following steps which should occur in less than 30 days but often can be done in less than 1 week. Every effort will be made to meet a physician's request for expedited review. **It is imperative that you are available during our review of your application in the event that we have questions. Unresolved issues may lead to a clinical hold.**

[1]To search Code of Federal Regulations (CFR) Title 21, visit:
http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm

Application Checklist for Omegaven Single Patient IND

1. Cover letter (see Appendix A for template)
2. FDA Form 3926 (see Appendix B for instructions)[2]. All fields should be complete, including additional requests in red.
3. Curriculum Vitae (CV) or resume
4. Copy of Informed Consent Document planned for use (see Informed Consent Document section)

Please ensure each item is enclosed, otherwise the application will be considered incomplete. Only complete applications will be reviewed.

Financial Responsibility

U.S. regulations prohibit charging a patient for an investigational drug unless FDA gives authorization to do so. The FDA has determined that the investigational use of Omegaven may qualify for drug cost recovery. A request to charge must be made if the sponsor or pharmacy plans to charge the patient or health insurance provider for the cost of the drug. In this case, cost recovery would extend only to the cost of the drug and associated shipping costs. Commercialization of an investigational drug is prohibited.

IND Sponsor-Investigators who wish to recover the cost of an investigational drug by charging the patient or patient's insurer must submit a request to do so in the IND application. Sponsors may request to charge for Omegaven under 21 CFR 312.8 by checking the box next to the charging request paragraph in the cover letter provided in this packet. Justification for the cost to be recovered should also be submitted, e.g., in the form of a bill or receipt. The FDA will respond in writing with the authorization to charge (likely, as part of the Acknowledgement letter for the IND). Note that under 21 CFR 312.8, the price charged may not be larger than necessary to recover direct costs; and that under 21 CFR 312.8, authorization to charge for an investigational drug may be withdrawn by FDA if we find that the conditions underlying the authorization are no longer satisfied.

Securing Omegaven Shipment

You may begin arranging a supply of Omegaven prior to requesting an IND from the FDA. Once you are granted an IND number, you would provide it to your supplier and they will ship Omegaven to you or an infusion pharmacy if you have this type of arrangement. Pharmacy International in Hamburg, Germany currently supplies Omegaven (email: wholesale@pharmacy-international.de).

Human Protection

Contacting your IRB

An Institutional Review Board (IRB) means any board, committee, or other group formally designated by an institution to review, approve the initiation of, and conduct periodic review of

[2] Note that FDA Forms 1571 and 1572 are still acceptable. See the following website for forms and instructions: http://www.fda.gov/AboutFDA/ReportsManualsForms/Forms/default.htm

biomedical research involving human subjects. The primary purpose of IRB review is to assure that the rights and welfare of human subjects are protected, including by determining that informed consent is obtained in accordance with and to the extent required by Federal requirements. Many institutions have their own IRB to oversee human subjects research conducted within the institution or by the staff of the institution. If the physician does not have access to a local IRB, an independent IRB may be used. The Department of Health & Human Services' Office for Human Research Protections maintains a database of registered IRBs. Go to http://ohrp.cit.nih.gov/search/irbsearch.aspx?styp=bsc and click on "Advanced Search." Enter your state to find registered IRBs in your area.

For questions about locating an IRB, you may email FDA's Office of Scientific Investigations at CDER-OSI-GCPReferrals@fda.hhs.gov, or contact Quynh-Van Tran at 301-796-0185.

Informed Consent Documents

Your IRB may have an Informed Consent Document that they prefer you use. When creating an Informed Consent, please consult the elements of informed consent: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=50.25

The informed consent document (ICD) should adequately address the potential risks associated with Omegaven and should specifically include the risk of bleeding, hypertriglyceridemia, allergic reactions and additional unknown risks from the use of Omegaven.

Secure Email

Secure email between FDA and sponsors is useful for informal communications when confidential information may be included in the message (e.g., confidential patient information). Parties who would like to establish secure email with FDA should email a request to SecureEmail@fda.hhs.gov.

Follow-up Submissions

Form FDA 3926 may be used for original individual patient expanded access INDs and follow up submissions (e.g., withdrawal request, safety report, annual reports). Remember to check to appropriate box in item 3 to indicate the intent.

Appendix A – Cover Letter Template

[Date]

Dragos Roman, M.D.
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Gastroenterology and Inborn Errors Products
Central Document Room
5901-B Ammendale Rd.
Beltsville, Md. 20705-1266

Subject: New Single Patient IND Application for Omegaven

Dear Dr. Roman,

I am hereby submitting an Investigational New Drug (IND) application under section 505(i) of the Federal Food, Drug, and Cosmetic Act and in accord with 21 CFR 312 for Omegaven.

This application contains the following (*please check all that apply*):

☐ Form 3926 (all fields complete including clinical history)
or completed Forms 1571 and 1572
☐ Copy of Informed Consent
☐ CV or resume

You must check the following box if you are requesting to charge for Omegaven:

☐ Permission is requested, under 21 CFR 312.8, to charge for the investigational drug used in this IND. I have included justification for the cost to be recovered (or will submit documentation after purchase) which is consistent with 21 CFR 312.8 and agree not to profit.

I claim a categorical exclusion from environmental assessment requirements (under 21 CFR 25.31[e]) for this IND. To my knowledge, no extraordinary circumstances exist.

Sincerely,

Appendix B – FDA Form 3926 and Instructions

Download and complete the form online before printing and signing:
http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM504572.pdf

The form below is for instructional purposes only. You may type directly into the online form. You can expand any field to fit pertinent information or may attach a separate sheet. Please do not hand-write on the example form below.

Some instructions are overlaid in red below, and additional instructions can be found at:
http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM504574.pdf

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Individual Patient Expanded Access Investigational New Drug Application (IND)

(Title 21, Code of Federal Regulations (CFR) Part 312)

Form Approved: OMB No. 0910-0814
Expiration Date: April 30, 2019
See PRA Statement on last page.

1. Patient's Initials

2. Date of Submission *(mm/dd/yyyy)*

3.a. Initial Submission

☐ Select this box if this form is an initial submission for an individual patient expanded access IND, and complete only fields 4 through 8, and fields 10 and 11.

3.b. Follow-Up Submission

☐ Select this box if this form accompanies a follow-up submission to an existing individual patient expanded access IND, and complete the items to the right in this section, and fields 8 through 11.

Investigational Drug Name

Physician's IND Number

4. Clinical Information

Indication

to provide parenteral nutritional support to patients with Parenteral Nutrition Associated Cholestasis (PNAC)

Brief Clinical History *(Patient's age, gender, weight, allergies, diagnosis, prior therapy, response to prior therapy, reason for request, including an explanation of why the patient lacks other therapeutic options)*

The following information is crucial to making a determination for treatment.

You can expand this field or attach a separate sheet if you cannot fit all of the pertinent information.

The Clinical History should describe the patient's clinical course including past medical and surgical history. In addition, include any relevant clinical work-up to evaluate the underlying cause(s) of cholestasis. Also include the most recent lab values, including total and direct bilirubin, aminotransferases (ALT, AST), GGT, ALP, CBC and dates obtained (preferably 3 consecutive values). List therapies that have been attempted and have failed to reduce the bilirubin (e.g., cycling the TPN, reduction/removal of trace elements, reduction of the lipid dose, ursodiol, advancement of feeds, etc) including dose and duration if applicable. Please include the patient's DOB, gender, race.

(form continued on next page)

5. Treatment Information

Investigational Drug Name

Omegaven

Name of the entity that will supply the drug *(generally the manufacturer)*

e.g., Pharmacy International

FDA Review Division *(if known)*

Division of Gastroenterology and Inborn Errors Products (DGIEP)

Treatment Plan *(Including the dose, route and schedule of administration, planned duration, and monitoring procedures. Also include modifications to the treatment plan in the event of toxicity.)*

You can expand this field or attach additional information

6. Letter of Authorization (LOA), if applicable *(generally obtained from the manufacturer of the drug)*

☐ I have attached the LOA. *(Attach the LOA; if electronic, use normal PDF functions for file attachments.)*

Note: If there is no LOA, consult the Form Instructions. N/A if using a Fresenius Kabi product from Pharmacy International

7. Physician's Qualification Statement *(Including medical school attended, year of graduation, medical specialty, state medical license number, current employment, and job title. Alternatively, attach the first few pages of physician's curriculum vitae (CV), provided they contain this information. If attaching the CV electronically, use normal PDF functions for file attachments.)*

Include listed information or attach the first few pages of your CV

8. Physician Name, Address, and Contact Information

Physician Name *(Sponsor)*	Email Address of Physician Email is essential to communication about your IND and is our primary method of contact.
Address 1 *(Street address, No P.O. boxes)*	
Address 2 *(Apartment, suite, unit, building, floor, etc.)*	Telephone Number of Physician
City / State	Facsimile (FAX) Number of Physician
ZIP Code	Physician's IND number, if known

9. Contents of Submission

This submission contains the following materials, which are attached to this form (select all that apply). If none of the following apply to the follow-up communications, use Form FDA 1571 for your submission.

- ☐ Initial Written IND Safety Report
- ☐ Follow-up to a Written IND Safety Report
- ☐ Annual Report
- ☐ Summary of Expanded Access Use (treatment completed)
- ☐ Change in Treatment Plan
- ☐ General Correspondence
- ☐ Response to FDA Request for Information
- ☐ Response to Clinical Hold

10.a. Request for Authorization to Use Form FDA 3926

☐ I request authorization to submit this Form FDA 3926 to comply with FDA's requirements for an individual patient expanded access IND.

10.b. Request for Authorization to Use Alternative IRB Review Procedures

☐ I request authorization to obtain concurrence by the Institutional Review Board (IRB) chairperson or by a designated IRB member, before the treatment use begins, in order to comply with FDA's requirements for IRB review and approval. This concurrence would be in lieu of review and approval at a convened IRB meeting at which a majority of the members are present.

11. Certification Statement: I will not begin treatment until 30 days after FDA's receipt of a completed application and all required materials unless I receive earlier notification from FDA that treatment may begin. I also agree not to begin or continue clinical investigations covered by the IND if those studies are placed on clinical hold. I also certify that I will obtain informed consent, and that an Institutional Review Board (IRB) will be responsible for initial and continuing review and approval of this treatment use, consistent with applicable FDA requirements. I understand that in the case of an emergency request, treatment may begin without prior IRB approval, provided the IRB is notified of the emergency treatment within 5 working days of treatment. I agree to conduct the investigation in accordance with all other applicable regulatory requirements.

WARNING: A willfully false statement is a criminal offense (U.S.C. Title 18, Sec. 1001).

Signature of Physician	**Date**
To enable the signature field, please fill out all prior required fields. For a list of required fields which have not yet been filled out, please click here.	

For FDA Use Only

Date of FDA Receipt	Is this an emergency individual patient IND?	Is this indication for a rare disease (prevalence < 200,000 in the U.S.)?
IND Number	☐ Yes ☐ No	☐ Yes ☐ No

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 45 minutes per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Operations
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."