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APPROVAL PACKAGE FOR:

APPLICATION NUMBER
20-430/S-003

Approval Letter

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F HEALTH & HUMAN SERVICES

Pt *N20430*

Food and Drug Administration
Rockville MD 20857

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7/31/01
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NDA 20-430/S-003

6/26/01

Organon Inc.
Attention: Ashok K. Didolkar, Ph.D.
375 Mt. Pleasant Avenue
West Orange, New Jersey 07052

Dear Dr. Didolkar:

Please refer to your supplemental new drug application dated August 25, 2000, received August 28, 200, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Orgaran® (danaparoid sodium) Injection, 0.6 mL (750 anti-Xa units) ampules and prefilled syringes.

This supplemental new drug application provides for the following changes: (1) in the CLINICAL PHARMACOLOGY section, the addition of a subsection titled "Special Populations", with three sub-subsections titled "Geriatrics", "Pediatrics", and "Hepatic Insufficiency"; (2) in the PRECAUTIONS section, additional information in the "Geriatric Use" subsection; and (3) in the DOSAGE AND ADMINISTRATION section, the addition of a subsection titled "Use in Geriatrics".

We have completed the review of this supplemental application and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text and with the minor editorial revisions listed below. Accordingly, the supplemental application is approved effective on the date of this letter.

1. In the CONTRAINDICATIONS section, the first sentence, the italics should be re-instated in the phrase "in vitro" and the "I" in the word "Injection" should be capitalized to read:

   ORGARAN® (danaparoid sodium) Injection is contraindicated in the following conditions: severe hemorrhagic diathesis, e.g., hemophilia and idiopathic thrombocytopenic purpura; active major bleeding state, including hemorrhagic stroke in the acute phase; hypersensitivity to ORGARAN®; Type II thrombocytopenia associated with a positive *in vitro* test for antiplatelet antibody in the presence of ORGARAN® Injection.

2. Throughout the text, references to other sections should be bolded, i.e, "(see **DOSAGE AND ADMINISTRATION**)".

3. In the ADVERSE REACTIONS section, the first table, the title of the table was changed from capital and small letters, to all capital letters. For consistency throughout the text, the title of the table should be changed to read as follows:

   Blood Loss and Transfusions
   DVT and PE Prophylaxis for Orthopedic Hip Surgery
   All Patients Treated

4. In the DOSAGE AND ADMINISTRATION section, the "Use in Geriatrics" subsection should be revised to read as follows:

   Use in Geriatrics

   No overall differences in safety and effectiveness of ORGARAN® (danaparoid sodium) Injection were observed in patients ≥65 years when compared with patients <65 years undergoing elective hip replacement surgery. No dosage adjustments are recommended in elderly patients.

5. After the HOW SUPPLIED section, delete the phrase " **only**" and replace with the phrase "℞ **only**".

The final printed labeling (FPL) must be identical, and include the minor editorial revisions indicated, to the submitted draft labeling (package insert submitted August 25, 2000). These revisions are terms of the approval of this application.

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 20-430/S-003." Approval of this submission by FDA is not required before the labeling is used.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). We note that you have not fulfilled the requirements of 21 CFR 314.55 (or 601.27). We are deferring submission of your pediatric studies until January 5, 2003. However, in the interim, please submit your pediatric drug development plans within 120 days from the date of this letter unless you believe a waiver is appropriate. Within approximately 120 days of receipt of your pediatric drug development plan, we will review your plan and notify you of its adequacy.

If you believe that this drug qualifies for a waiver of the pediatric study requirement, you should submit a request for a waiver with supporting information and documentation in accordance with the provisions of 21 CFR 314.55 within 60 days from the date of this letter. We will notify you within 120 days of receipt of your response whether a waiver is granted. If a waiver is not granted, we will ask you to submit your pediatric drug development plans within 120 days from the date of denial of the waiver.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the *Guidance for Industry on Qualifying for Pediatric Exclusivity* (available on our web site at www.fda.gov/cder/pediatric) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request" (PPSR) in addition to your plans for pediatric drug development described above. We recommend that you submit a Proposed Pediatric Study Request within 120 days from the date of this letter. If you are unable to meet this time frame but are interested in pediatric exclusivity, please notify the division in writing. FDA generally will not accept studies submitted to an NDA before issuance of a Written Request as responsive to a Written Request. Sponsors should obtain a Written Request before submitting pediatric studies to an NDA. If you do not submit a PPSR or indicate that you are interested in pediatric exclusivity, we will review your pediatric drug development plan and notify you of its adequacy. Please note that satisfaction of the requirements in 21 CFR 314.55 alone may not qualify you for pediatric exclusivity. FDA does not necessarily ask a sponsor to complete the same scope of studies to qualify for pediatric exclusivity as it does to fulfill the requirements of the pediatric rule.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Karen Oliver, Regulatory Project Manager, at (301) 827-7457.

Sincerely,

{See appended electronic signature page}

Lilia Talarico, M.D.
Director
Division of Gastrointestinal and Coagulation Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research