

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

**APPLICATION NUMBER: 21-345**

**ADMINISTRATIVE DOCUMENTS**

**Division of Gastrointestinal & Coagulation Drug Products**

**CONSUMER SAFETY OFFICER REVIEW**

**Application Number:** NDA 21-345

**Name of Drug:** ARIXTRA™ (fondaparinux sodium) Injection

**Sponsor:** Fonda BV

**Material Reviewed**

**Submission Date(s):** August 31, 2001

**Receipt Date(s):** August 31, 2001

**Background and Summary Description:**

On February 15, 2001, Fonda BV (a joint venture between NV Organon and Sanofi-Synthelabo SA) submitted an NDA for fondaparinux sodium injection for the following indication: "prevention of venous thromboembolic events in patients undergoing major orthopedic surgery of the lower limbs such as hip fracture, major knee or hip replacement surgeries". Fondaparinux sodium is provided in a prefilled, disposable syringe affixed with an automatic needle protection system as secondary packaging. Each prefilled syringe contained 2.5 mg fondaparinux sodium in 0.5 mL of an isotonic solution of sodium chloride and water for injection. Fondaparinux sodium, a single molecular entity, is a new anti-thrombotic agent obtained by chemical synthesis.

On August 15, 2001, an approvable letter was issued. On October 9, 2001, the sponsor submitted a full response to the action letter. An August 31, 2001 submission contained revised text for the package insert and color mock-ups for the immediate container label, cartons, and container tray labels. The revised package insert has been extensively revised by the review team during a series of labeling meetings and the revised package insert labeling will be included in the action letter. This review pertains to the immediate container label, cartons, and tray labels only.

**Review**

**Immediate Container Label**

The computer generated black and white mock-ups for the immediate container label, identified as "65957" (professional sample) and "65968", were compared to the labeling requirements set forth in 21 CFR 201.1, 201.2, 201.5, 201.10, 201.15, 201.17, 201.18, 201.50, and 201.55 and to the revisions requested in the August 15, 2001 action letter.

**The immediate container labels are ACCEPTABLE.**

**Cartons**

The computer generated color mock-ups for two cartons [10 x 0.5 mL and 5 x 0.5 mL (professional sample)] were compared to the labeling requirements set forth in 21 CFR 201.1, 201.2, 201.5, 201.10, 201.15, 201.17, 201.18, 201.50, and 201.55 and to the revisions requested in the August 15, 2001 actoin letter. The following changes should be implemented.

1. The "X" in the word "Arixtra" is larger than the "r", "i", "t", and "a". This is consistent with an agreement made between the sponsor and DDMAC. The "X" can be no larger than any other letter in the word "Arixtra".
2. The following information was added:

Distributed by: Organon Sanofi-Synthelabo LLC  
West Orange, NJ 07052  
Made in: France  
For inquiries call 1-800-446-6267

**This additional information is ACCEPTABLE.**

3. The words "Organon" and oval logo and the words "sanofi-synthelabo", were added to the front panel.

**This addition is ACCEPTABLE.**

4. The NDC numbers have been added to the 10 x 0.5 mL carton [NDC 66203-2300-1].

**This addition is ACCEPTABLE.**

5. The following code letters have been added to the left corner of the front and back panels, "A-001" and "AS-05" (professional sample).

**This addition is ACCEPTABLE.**

**Container Tray Labels**

The computer generated color mock-ups for the container tray labels (10 x 0.5 mL and 5 x 0.5 mL professional sample) were compared to the labeling requirements set forth in 21 CFR 201.1, 201.2, 201.5, 201.10, 201.15, 201.17, 201.18, 201.50, and 201.55 and to the revisions requested in the August 15, 2001 action letter. The following changes should be implemented.

6. The "X" in the word "Arixtra" is larger than the "r", "i", "t", and "a". This is consistent with an agreement made between the sponsor and DDMAC. The "X" can be no larger than any other letter in the word "Arixtra".

7. The following information was added:

Distributed by: Organon Sanofi-Synthelabo LLC  
West Orange, NJ 07052  
Made in: France  
For inquiries call 1-800-446-6267

**This additional information is ACCEPTABLE.**

8. The words "Organon" and oval logo and the words "sanofi-synthelabo", were added to the front panel.

**This addition is ACCEPTABLE.**

9. The NDC numbers have been added to the 10 x 0.5 mL carton [NDC 66203-2300-1].

**This addition is ACCEPTABLE.**

10. The following code letters have been added to the left corner of the front and back panels, "A-001" and "AS-05" (professional sample).

**This addition is ACCEPTABLE.**

11. On the upper right corner, the following words have been added, "PEEL TO OPEN".

**This addition is ACCEPTABLE.**

**Conclusion**

The draft, color mock-up immediate container, tray, and carton labels are ACCEPTABLE.

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Karen Oliver, RN, MSN  
Project Manager

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Victor F. C. Raczkowski, M.D., M.Sc.  
Acting Division Director

R/D init: V.Raczkowski 12/07/01  
draft: Novmeber 8, 2001  
final: KO/12/07/01/

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CSO REVIEW

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/s/

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Karen Oliver  
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CSO

Victor Raczkowski  
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MEDICAL OFFICER

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**Division of Gastrointestinal & Coagulation Drug Products**

**CONSUMER SAFETY OFFICER REVIEW**

**Application Number:** NDA 21-345

**Name of Drug:** Arixtra™ (fondaparinux sodium) Injection

**Sponsor:** Fonda BV

**Material Reviewed**

**Submission Date(s):** February 15, 2001

**Receipt Date(s):** February 15, 2001

**Background and Summary Description:**

On February 15, 2001, Fonda BV (a joint venture between NV Organon and Sanofi-Synthelabo SA) submitted an NDA for fondaparinux sodium injection for the following indication: "prevention of venous thromboembolic events in patients undergoing major orthopedic surgery of the lower limbs such as hip fracture, major knee or hip replacement surgeries". Fondaparinux sodium is provided in a prefilled, disposable syringe affixed with an automatic needle protection system as secondary packaging. Each prefilled syringe contained 2.5 mg fondaparinux sodium in 0.5 mL of an isotonic solution of sodium chloride and water for injection. Fondaparinux sodium, a single molecular entity, is a new anti-thrombotic agent obtained by chemical synthesis. Submitted labeling included a package insert, immediate container label, cartons, and container tray labels. The submitted package insert has been extensively revised by the review team during a series of labeling meetings and the revised package insert labeling will be included in the action letter. This review pertains to the immediate container label, cartons, and tray labels only.

**Review**

**Immediate Container Label**

The computer generated black and white mock-ups for the immediate container label and the immediate container label professional sample were compared to the labeling requirements set forth in 21 CFR 201.1, 201.2, 201.5, 201.10, 201.15, 201.17, 201.18, 201.50, and 201.55. The following changes should be implemented.

1. Provide an acceptable tradename, with all letters of the name in the same type face and font size.

2. Below the tradename, prominently display the following:

2.5 mg/0.5 mL

3. Provide manufacturing information (as space permits):

Manufactured by:	Provide name and address
Manufactured for:	Provide name and address
Distributed by:	Provide name and address
Made in:	Provide country

### **Cartons**

The computer generated color mock-ups for two cartons [10 x 0.5 mL and 5 x 0.5 mL (professional sample)] were compared to the labeling requirements set forth in 21 CFR 201.1, 201.2, 201.5, 201.10, 201.15, 201.17, 201.18, 201.50, and 201.55. The following changes should be implemented.

4. Provide an acceptable tradename, with all letters of the name in the same type face and font size.
5. Delete the following information from the upper right corner of the front and back panels:

[ ]

6. Revise the phrase in the upper right corner of the front and back panels to read as follows:

10 x 0.5 mL Single Dose, Prefilled Syringes  
5 x 0.5 mL Single Dose, Prefilled Syringes

7. After the title section, prominently display the following information:

2.5 mg/0.5 mL Single Dose, Prefilled Syringes Affixed with an Automatic Needle  
Protection System  
For Subcutaneous Injection



8. On the front panel, delete the information in the blue box \_\_\_\_\_
9. Provide appropriate information regarding the following:
- |                   |                          |
|-------------------|--------------------------|
| Manufactured by:  | Provide name and address |
| Manufactured for: | Provide name and address |
| Distributed by:   | Provide name and address |
| Made in:          | Provide country          |
10. On the back panel, in the "Contents" section, revise the first sentence to read as follows:
- Each single dose, prefilled syringe contains 2.5 mg of fondaparinux sodium in 0.5 mL of an isotonic solution of sodium chloride and water for injection.
11. On the flaps, revise the phrase \_\_\_\_\_ to read:
- 10 x 0.5 mL Single Dose, Prefilled Syringes  
5 x 0.5 mL Single Dose, Prefilled Syringes

**Container Tray Labels**

The computer generated color mock-ups for two cartons (10 x 0.5 mL and 5 x 0.5 mL professional sample) were compared to the labeling requirements set forth in 21 CFR 201.1, 201.2, 201.5, 201.10, 201.15, 201.17, 201.18, 201.50, and 201.55. The following changes should be implemented.

12. Provide an acceptable tradename, with all letters of the name in the same type face and font size.
13. Delete the following information from the upper right corner:

[ ]

14. Revise the phrase in the upper right corner of the front and back panels to read as follows:

10 x 0.5 mL Single Dose, Prefilled Syringes  
5 x 0.5 mL single Dose, Prefilled Syringes

15. After the title section, prominently display the following information:

2.5 mg/0.5 mL Single Dose, Prefilled Syringes Affixed with an Automatic Needle  
Protection System  
For Subcutaneous Injection

16. Provide appropriate information regarding the following:

Manufactured by: Provide name and address  
Manufactured for: Provide name and address  
Distributed by: Provide name and address  
Made in: Provide country

17. In the "Contents" section, revise the first sentence to read as follows:

Each single dose, prefilled syringe contains 2.5 mg of fondaparinux sodium in  
0.5 mL of an isotonic solution of sodium chloride and water for injection.

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Karen Oliver, RN, MSN  
Project Manager

**APPEARS THIS WAY  
ON ORIGINAL**

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Lilia Talarico, M.D.  
Division Director

cc:

Original NDA 21-345  
HFD-180/Div. Files  
HFD-180/K.Oliver  
HFD-180/L.Talarico  
HFD-180/K.Robie-Suh  
HFD-180/A.Al-Hakim  
HFD-180/L.Zhou

R/D init: A.Al-Hakim 07/23/01

R/D init: K.Robie-Suh 07/18/01

R/D init: L.Talarico 07/20/01

draft: July 17, 2001

final: KO/07/17/01/

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CSO REVIEW

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/s/

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Karen Oliver  
7/23/01 01:28:12 PM  
CSO

Lilia Talarico  
7/23/01 02:27:40 PM  
MEDICAL OFFICER

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Draft

Labeling

**3. FOREIGN MARKETING HISTORY (NOT APPLICABLE)**

Org31540/SR90107A currently is not and has not ever been marketeing anywhere.

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**Office of Post-Marketing  
Drug Risk Assessment**

# Memo

**To:** Lilia Talarico, M.D.  
Director, Division of Gastrointestinal and Coagulation Drug Products  
HFD-180

**From:** Nora Roselle, Pharm.D.  
Safety Evaluator, Office of Post-Marketing Drug Risk Assessment  
HFD-400

**Through:** Jerry Phillips, R.Ph.  
Associate Director, Office of Post-Marketing Drug Risk Assessment  
HFD-400

**CC:** Karen Oliver  
Project Manager, Division of Gastrointestinal and Coagulation Drug Products  
HFD-180

**Date:** October 29, 2001

**Re:** OPDRA Consult 01-0143-1; Arixtra (Fondaparinux Sodium Injection), 2.5 mg/0.5 mL; NDA 21-345

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This memorandum is in response to an October 15, 2001, request from your Division for a second re-review of the proprietary name, Arixtra. The proposed proprietary name, Arixtra, was found acceptable by OPDRA in the initial name review on February 9, 2001 (OPDRA Consult# 00-0239) and in the re-review on July 19, 2001 (OPDRA Consult# 01-0143). The goal date for this application is December 9, 2001.

OPDRA has not identified any additional proprietary or established names that have the potential for confusion with Arixtra since we conducted our initial re-review on July 19, 2001 (OPDRA Consult# 01-0143), that would render the name objectionable. Therefore, we have no objections to the use of this proprietary name.

We consider this a final review. However, if the approval of the NDA is delayed beyond 90 days from the date of this review, the name must be re-evaluated. A re-review of the name before NDA approval will rule out any objections based upon approvals of other proprietary/established names from this date forward.

If you have any questions or need clarification, please contact the medication errors project manager, Sammie Beam at 301-827-3242.

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/s/

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Nora L. Roselle  
11/1/01 01:37:21 PM  
CSO

Jerry Phillips  
11/5/01 10:20:17 AM  
DIRECTOR

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DEPARTMENT OF HEALTH AND HUMAN SERVICE

Public Health Service  
Food and Drug Administration

Memorandum

**Date:** July 17, 2001

**To:** Lilia Talarico, M.D.  
Director, Division of Gastrointestinal and Coagulation Drug Products  
HFD-180

**From:** Jennifer Fan, Pharm.D.  
Safety Evaluator, Office of Post-Marketing Drug Risk Assessment  
HFD-400

**Through:** Jerry Phillips, R.Ph.  
Associate Director, Office of Post-Marketing Drug Risk Assessment  
HFD-400

**CC:** Karen Oliver  
Project Manager, Division of Gastrointestinal and Coagulation Drug Products  
HFD-180

**Subject:** NDA 21-345 Arixtra (Fondaparinux Sodium Injection), 2.5 mg/0.5 mL; OPDRA Consult 01-0143

This memorandum is in response to a June 18, 2001 request from your Division for a re-review of the proprietary name, "Arixtra". "Arixtra" was found acceptable by OPDRA on February 9, 2001 in the OPDRA consult 00-0239. The goal date for this application is August 15, 2001.

OPDRA has not identified any safety concerns that would render the proposed name objectionable. Therefore, we have no objections to the use of this proprietary name.

We consider this a final review. However, if the approval of the NDA is delayed beyond 90 days from the date of this review, the name must be re-evaluated. A re-review of the name before NDA approval will rule out any objections based upon approvals of other proprietary/established names from this date forward.

If you have any questions or need clarification, please contact the Medication Errors Project Manager, Sammie Beam, at 301-827-3231.

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/s/

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Jennifer Fan  
7/19/01 09:28:26 AM  
PHARMACIST

Jerry Phillips  
7/19/01 09:32:38 AM  
DIRECTOR

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**CONSULTATION RESPONSE**  
**Office of Post-Marketing Drug Risk Assessment**  
**(OPDRA; HFD-400)**

**DATE RECEIVED:** February 26, 2001

**DUE DATE:**  
May 1, 2001

**OPDRA CONSULT #:** 00-0239

**TO:** Lilia Talarico, MD  
Director, Division of Gastrointestinal and Coagulation Drug Products  
HFD-180

**THROUGH:** Karen Oliver, Project Manager  
HFD-180

**PRODUCT NAME:**

Xantidar (primary) or Arixtra (alternate)  
(Fondaparinux Sodium Injection)  
2.5 mg/0.5 mL

**DISTRIBUTOR:** Organon Sanofi-Synthelabo LLC

**NDA #:** 21-345

**SAFETY EVALUATOR:** Alina R. Mahmud, RPh.

**SUMMARY:** In response to a consult from the Division of Gastrointestinal and Coagulation Drug Products (HFD-180), OPDRA conducted a review of the proposed proprietary names "Xantidar" or "Arixtra" to determine the potential for confusion with approved proprietary and generic names as well as pending names.

**OPDRA RECOMMENDATION:** OPDRA does not recommend the use of the proprietary name "Xantidar". However, OPDRA has no objections to the use of the name "Arixtra". See the checked box below.

**FOR NDA/ANDA WITH ACTION DATE BEYOND 90 DAYS OF THIS REVIEW**

This name must be re-evaluated approximately 90 days prior to the expected approval of the NDA. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary names/NDA's from the signature date of this document. A re-review request of the name should be submitted via e-mail to "OPDRAREQUEST" with the NDA number, the proprietary name, and the goal date. OPDRA will respond back via e-mail with the final recommendation.

**FOR NDA/ANDA WITH ACTION DATE WITHIN 90 DAYS OF THIS REVIEW**

OPDRA considers this a final review. However, if the approval of the NDA is delayed beyond 90 days from the date of this review, the name must be re-evaluated. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary names/NDA's from this date forward.

**FOR PRIORITY 6 MONTH REVIEWS**

OPDRA will monitor this name until approximately 30 days before the approval of the NDA. The reviewing division need not submit a second consult for name review. OPDRA will notify the reviewing division of any changes in our recommendation of the name based upon the approvals of other proprietary names/NDA's from this date forward.

Jerry Phillips, R.Ph.  
Associate Director for Medication Error Prevention  
Office of Post-Marketing Drug Risk Assessment  
Phone: (301) 827-3242  
Fax: (301) 480-8173

Martin Himmel, M.D.  
Deputy Director  
Office of Post-Marketing Drug Risk Assessment  
Center for Drug Evaluation and Research  
Food and Drug Administration

**Office of Post-Marketing Drug Risk Assessment  
HFD-400; Rm. 15B03  
Center for Drug Evaluation and Research**

**PROPRIETARY NAME REVIEW**

**DATE OF REVIEW:** February 9, 2001

**NDA NUMBER:** 21-345

**NAME OF DRUG:** Xantidar (primary) or Arixtra (alternate)  
(Fondaparinux Sodium injection)  
2.5 mg/0.5 mL

**NDA HOLDER:** Organon Sanofi-Synthelabo LLC

**I. INTRODUCTION**

This consult was written in response to a request from the Division of Gastrointestinal and Coagulation Drug Products (HFD-180), for assessment of the tradename "Xantidar" and "Arixtra", regarding potential name confusion with other proprietary/generic drug names.

**PRODUCT INFORMATION**

Xantidar/Arixtra is the proposed proprietary name for Fondaparinux Sodium. Xantidar/Arixtra is indicated for the prevention of venous thromboembolic events in patients undergoing major orthopedic surgery of the lower limbs such as hip fracture, major knee or hip replacement surgeries. The usual dose of Xantidar/Arixtra is 2.5 mg subcutaneously once daily. Xantidar/Arixtra Injection will be available in packages of 10 pre-filled — single use syringes. Each pre-filled syringe contains 2.5 mg fondaparinux sodium in 0.5 ml of an isotonic solution of sodium chloride and water for injection, and is affixed with a 27 gauge x ½ inch needle.

**II. RISK ASSESSMENT**

The medication error staff of OPDRA conducted a search of several standard published drug product reference texts<sup>i,ii,iii</sup> as well as several FDA databases<sup>iv</sup> for existing drug names which sound-alike or look-alike to "Xantidar" and "Arixtra" to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the

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<sup>i</sup> MICROMEDEX Healthcare Intranet Series, 2000, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes the following published texts: DrugDex, Poisindex, Martindale (Parfitt K (Ed), Martindale: The Complete Drug Reference. London: Pharmaceutical Press. Electronic version.), Index Nominum, and PDR/Physician's Desk Reference (Medical Economics Co. Inc, 2000).

<sup>ii</sup> American Drug index, 42<sup>nd</sup> Edition, 1999, Facts and Comparisons, St. Louis, MO.

<sup>iii</sup> Facts and Comparisons, 2000, Facts and Comparisons, St. Louis, MO.

<sup>iv</sup> COMIS, The Established Evaluation System [EES], the Labeling and Nomenclature Committee [LNC] database of Proprietary name consultation requests, New Drug Approvals 98-00, and online version of the FDA Orange Book.

electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted<sup>v</sup>. An Expert Panel discussion was conducted to review all findings from the searches. In addition, OPDRA conducted three prescription analysis studies, to simulate the prescription ordering process.

**A. EXPERT PANEL DISCUSSION**

An Expert Panel discussion was held by OPDRA to gather professional opinions on the safety of the proprietary name "Xantidar" and "Arixtra". Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of OPDRA Medication Errors Prevention Staff and representation from the Division of Drug Marketing and Advertising Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

Six product names were identified in the Expert Panel Discussion that were thought to have potential for confusion with Xantidar and three products were thought to have potential for confusion with Arixtra. These products are listed in Table 1 and 2 (respectively), along with the dosage forms available and usual FDA-approved dosage.

DDMAC did not have any concerns with the name in regard to promotional claims.

**TABLE 1**

Fansidar	500 mg sulfadoxine and 25 mg pyrimethamine tablets (Rx)	<i>Acute attack of malaria. Adult dose: 2 to 3 tablets as a single dose</i> <i>Malaria prophylaxis: 1 tablet once weekly</i>	S/A, L/A per OPDRA
Zaditor	Ketotifen Fumurate 0.025% ophthalmic solution (Rx)	Instill 1 drop every 8-12 hours to affected eye(s)	S/A, L/A per OPDRA
Zanosar	Streptozocin 1gm Powder for injection (Rx)	500 mg/m <sup>2</sup> for 5 consecutive days every 6 weeks	S/A, L/A per OPDRA
Temodor	Temazolomide 5 mg, 20 mg, 100 mg, 250 mg tablets (Rx)	150 mg/m <sup>2</sup> every day for 5 consecutive days of 28 day treatment cycle	S/A, L/A per OPDRA
Xalatin	Latanoprost 0.05% ophthalmic solution (Rx)	Instill 1 drop to affected eye once daily	S/A, L/A per OPDRA

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<sup>v</sup> WWW location <http://www.uspto.gov/tmdb/index.html>.

Comptosar	Irinotecan HCl 20 mg/mL injection (Rx)	<p><b>Regimen 1:</b> (6 wk course with <i>bolus</i> 5-FU/LV) 90min infusion on days 1, 8, 15, and 22. Starting dose: 125 mg/m<sup>2</sup> Dose level 1: 100 mg/m<sup>2</sup> Dose level 2: 75 mg/m<sup>2</sup></p> <p><b>Regimen 2:</b> (6 wk course with <i>infusional</i> 5-FU/LV) 90 min infusion on days 1, 15 and 29. Starting dose: 100 mg/m<sup>2</sup> Dose level 1: 150 mg/m<sup>2</sup> Dose level 2: 120 mg/m<sup>2</sup></p>	S/A, L/A per OPDRA
		*Frequently used, not all-inclusive	**L/A (look-alike), S/A (sound-alike)

TABLE 2

Imitrex	Sumatriptan <i>tablets</i> : 25 mg and 50 mg; <i>injection</i> : 12 mg/mL; <i>nasal spray</i> 5 mg and 20 mg	<p><i>Oral</i>: adult dose is 100 mg as early as possible after the onset of a migraine attack. If headache returns, additional doses may be taken at intervals of 2 hours up to a daily maximum of 200 mg.</p> <p><i>Injection</i>: The maximum single adult dose is 6 mg injected SC</p> <p><i>Intranasal</i>: A single dose of 5, 10, or 20 mg administered in one nostril</p>	S/A, L/A per OPDRA
Evista	Raloxifene 60 mg tablets	1 tablet once daily	S/A, L/A per OPDRA
Atarax	Hydroxyzine <i>tablets</i> : 10 mg, 25 mg, 50 mg, 100 mg; <i>Syrup</i> 10 mg/5 mL;	<p><i>Anxiety-</i> - <i>Adults</i>: 50 to 100 mg 4 times a day.</p> <p><i>Pruritus-</i> - <i>Adults</i>: 25 mg 3 or 4 times a day.</p> <p><i>Sedative (as premedication and following general anesthesia)-</i> - <i>Adults</i>: 50 to 100 mg.</p> <p><i>Antiemetic/Analgesia, adjunctive therapy (parenteral only)-</i> - <i>Adults</i>: 25 to 100 mg IM</p>	S/A, L/A per OPDRA

## B. STUDY CONDUCTED BY OPDRA

### 1. Methodology

A separate study was conducted within FDA for the proposed proprietary name to determine the degree of confusion of Xantidar and Arixtra with other U.S. drug names due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name.

These studies employed a total of 87 health care professionals (nurses, pharmacists, and physicians). This exercise was conducted in an attempt to simulate the prescription ordering process. OPDRA staff members wrote an inpatient and an outpatient prescription, each consisting of a combination of marketed and unapproved drug products and prescriptions for Xantidar and Arixtra (see below). These written prescriptions were optically scanned and one prescription was delivered via email to each study participant. In addition, one OPDRA staff member recorded a verbal outpatient prescription that was then delivered to a group of study participants via telephone voicemail. Each reviewer was then requested to provide an interpretation of the prescription via email.

HANDWRITTEN PRESCRIPTIONS	VERBAL PRESCRIPTION
<b>Outpatient:</b>  Xantidar Sig: 2.5 mg SQ QD Disp #10	Xantidar  2.5 mg subcutaneously once daily Dispense #10
<b>Inpatient:</b>  Xantidar 2.5 mg SQ QD	

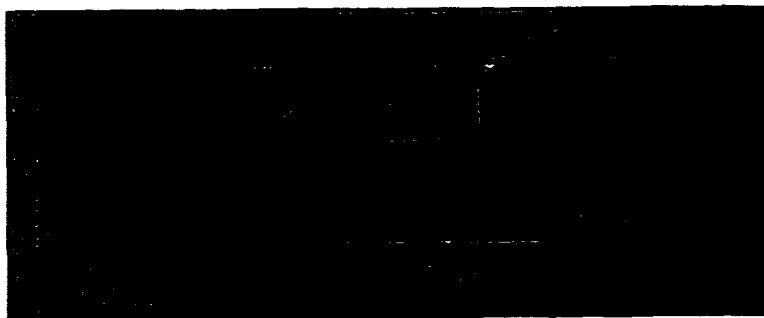
HANDWRITTEN PRESCRIPTIONS	VERBAL PRESCRIPTION
<b>Outpatient:</b>  Arixtra Sig: 2.5 mg SQ QD Disp #10	Arixtra  2.5 mg subcutaneously once daily Dispense #10
<b>Inpatient:</b>  Arixtra 2.5 mg SQ QD	

## 2. Results

Results of these exercises are summarized below:

<b>Xantidar</b>				
Study	No. of participants	# of responses (%)	"Xantidar" response	Other response
Written: Outpatient	28	19 (68%)	9 (47%)	10 (53%)
Inpatient	29	19 (66%)	1 (5%)	18 (95%)
Verbal: Outpatient	30	9 (30%)	0 (0%)	9 (100%)
<b>Total:</b>	<b>87</b>	<b>47 (54%)</b>	<b>10 (21%)</b>	<b>37 (79%)</b>

Arixtra				
Study	No. of participants	# of responses (%)	"Arixtra" response	Other response
Written: Outpatient	28	19 (68%)	10 (53%)	9 (47%)
Inpatient	28	12 (43%)	11 (92%)	1 (8%)
Verbal: Outpatient	30	13 (43%)	0 (0%)	13 (100%)
Total:	86	44 (51%)	21 (48%)	23 (52%)



Correct  
 Incorrect

Among the participants in the two written prescription studies, 10 of 38 respondents (74%) interpreted the name incorrectly. The interpretations were misspelled/phonetic variations of "Xantidar", such as *Xantida*, *Xantider*, *Xartidar*, *Xantadan*, *Xanteden*, *Xantidan*, and *Xantiden*. Other interpretations included *Xantadine*, *Xantridan*, *Xantid*, *Xautida* and *Xantridan*.

Among the verbal prescription study participants, 100% of the participants interpreted the name incorrectly. Some of the incorrect name interpretations were phonetic variations of "Xantidar" such as *Zantida*, *Zantidar*, *Zontadol*, *Zantider*, *Xantidur* and *Xanthedra*.



Correct  
 Incorrect

Among the participants in the two written prescription studies, 10 of 31 respondents (32%) interpreted the name incorrectly. The interpretations were misspelled/phonetic variations of "Arixtra", such as *Arixtran* and *Anixtra*. Other interpretations included *Arirtru* and *Arifran*.

Among the verbal prescription study participants, 100% of the participants interpreted the name incorrectly. Twelve participants interpreted the name as *Atrixa* and one participant provided *Atrexa* as in interpretation.



## C. SAFETY EVALUATOR RISK ASSESSMENT

### 1. Xantidar

In reviewing the proprietary name "Xantidar", the primary concerns raised were related to a few sound-alike, look-alike names that already exist in the U.S. marketplace. Three products, Zanosar, Zaditor, and Fansidar were believed to be the most problematic in terms of potential medication errors.

We conducted prescription studies to simulate the prescription ordering process. In this case, there was no confirmation that Xantidar could be confused with Zanosar, Zaditor or Fansidar. However *negative* findings in these studies are not predictive as to what may occur once the drug is widely prescribed, as these studies have limitations primarily due to small sample size. The majority of the verbal and two written prescriptions were phonetic variations of the drug name Xantidar. Many verbal study participants interpreted the first letter "X" as "Z".

Zanosar is an antineoplastic alkylating agent containing 1 gram of streptozocin. Zanosar is indicated in the treatment of metastatic islet cell carcinoma of the pancreas. It is primarily administered intravenously. Although Zanosar has been administered intra-arterially, this route of administration is not recommended because adverse renal effects are evoked more rapidly. A daily or a weekly dosing schedule can be employed with the use of Zanosar. In regard to similarities and differences in comparison to Xantidar, a greater number of differences have been identified. The dose of Zanosar is based on the weight of the patient (500 mg/m<sup>2</sup>) whereas the dose of Xantidar is 2.5 mg once daily and is independent of the patient's weight. Xantidar will be available in a prefilled disposable syringe for subcutaneous administration whereas Zanosar is available as a sterile powder for reconstitution and is administered intravenously. Furthermore, Zanosar is administered under the supervision of a physician experienced in the use of cancer chemotherapeutic agents. Additional caution is also exercised when Zanosar is administered because of its ability to cause dose-related renal toxicity. Given the above differences in dosing, administration and availability (prefilled syringe vs. vial for reconstitution), there is insufficient evidence at this time to conclude that the proposed drug name would be confused with Zanosar.

Zaditor is a sterile ophthalmic solution containing ketotifen for topical administration to the eyes. Although the numerical strengths are similar with Zaditor (0.025%) and Xantidar (2.5 mg), the drug products share many differences such as route of administration, dosing schedule, dosage form and indication for use. However, post-marketing experience has demonstrated errors occurring between two drug products that share no other commonalities except for look-alike and/or sound-alike potential.

Fansidar tablets contain 500 mg of sulfadoxine and 25 mg of pyrimethamine. Fansidar is indicated in the prevention and treatment of malaria where chloroquine resistance is suspected. Dosage varies according to the treatment (prophylaxis or actual malaria) and the age of the patient. Xantidar and Fansidar not only share sound-alike potential but also look-alike potential (see prescription on page 8), each containing eight characters in length. Xantidar and Fansidar are each available in one strength, therefore, a prescription for either one may not contain the strength which may be necessary for distinguishing between the two drug names. Although the drug products differ in dosing schedule and route of administration, post-marketing experience has demonstrated errors

Xantidar Fansidar  
#10 #10  
Sig: UD Sig: UD

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occurring between drug products that share no other commonalities except for look-alike and/or sound-alike potential. The inadvertent confusion of these two drug products could prove fatal as Fansidar has caused Steven-Johnsons syndrome and toxic epidermal necrolysis. A potential for spinal/epidural hematomas has been associated with the use of Xantidar.

## 2. Arixtra

In reviewing the proprietary name "Arixtra", the primary concerns raised were related to a sound-alike, look-alike name that already exists in the U.S. marketplace. One product, Atarax was believed to be the most problematic in terms of potential medication errors.

We conducted prescription studies to simulate the prescription ordering process. In this case, there was no confirmation that Arixtra could be confused with Atarax. However *negative* findings in these studies are not predictive as to what may occur once the drug is widely prescribed, as these studies have limitations primarily due to small sample size. The majority of the responses to the two written prescriptions were phonetic variations of the drug name Arixtra. Almost all of the participants from the verbal prescription studies provided Atrixa as an interpretation.

Atarax is the proprietary name for hydroxyzine which is an antihistamine. Atarax is indicated for symptomatic relief of anxiety and tension associated with psychoneurosis and as an adjunct in organic disease states in which anxiety is manifested. It is also useful in the management of pruritus due to allergic conditions such as chronic urticaria and atopic and contact dermatoses, and in histamine-mediated pruritus. Atarax is also used as a sedative when used as premedication and following general anesthesia because hydroxyzine potentiates the effects of meperidine and barbiturates. Although the drug product with the proprietary name "Atarax" is not available as an injection, the generic drug "hydroxyzine" is available in injection form. Hydroxyzine is available as a 25 mg/mL and 50 mg/mL injection as well as other dosage forms. Arixtra and Atarax share similar numerical strengths (2.5 mg vs. 25 mg, respectively) and dosage form. However, Arixtra and Atarax differ in dosing frequency and lack convincing look-alike and sound-alike potential. Therefore, there is insufficient evidence at this time to conclude that the proposed name would be confused with Atarax.

### III. LABELING, PACKAGING AND SAFETY RELATED ISSUES

In the review of the draft container label and draft package insert for Xantidar/Arixtra, OPDRA has attempted to focus on safety issues relating to possible medication errors. We have identified one area of possible improvement, in the interest of minimizing potential user error and refer you to section IV.

### IV. COMMENTS TO BE PROVIDED TO THE SPONSOR

1. OPDRA does not recommend the proposed proprietary name Xantidar.

In reviewing the proprietary name "Xantidar", the primary concerns raised were related to a few sound-alike, look-alike names that already exists in the U.S. marketplace. Three products, Zanosar, Zaditor, and Fansidar were believed to be the most problematic in terms of potential medication errors.

We conducted prescription studies to simulate the prescription ordering process. In this case, there was no confirmation that Xantidar could be confused with Zanosar, Zaditor or Fansidar. However *negative* findings in these studies are not predictive as to what may occur once the drug is widely prescribed, as these studies have limitations primarily due to small sample size. The majority of the verbal and two written prescriptions were phonetic variations of the drug name Xantidar. Many verbal study participants interpreted the first letter "X" as "Z".

In regard to similarities and differences in comparison to Xantidar, a greater number of differences have been identified. The dose of Zanosar is based on the weight of the patient ( $500 \text{ mg/m}^2$ ) whereas the dose of Xantidar is 2.5 mg once daily and is independent of the patient's weight. Xantidar will be available in a prefilled disposable syringe for subcutaneous administration whereas Zanosar is available as a sterile powder for reconstitution and is administered intravenously. Furthermore, Zanosar is administered under the supervision of a physician experienced in the use of cancer chemotherapeutic agents. Additional caution is also exercised when Zanosar is administered because of its ability to cause dose-related renal toxicity. Given the above differences in dosing, administration and availability (prefilled syringe vs. vial for reconstitution), there is insufficient evidence at this time to conclude that the proposed drug name would be confused with Zanosar.

Although the numerical strengths are similar with Zaditor (0.025%) and Xantidar (2.5 mg), the drug products share many differences such as route of administration, dosing schedule, dosage form and indication for use. However, post-marketing experience has demonstrated errors occurring between two drug products that share no other commonalties except for look-alike and/or sound-alike potential.

Xantidar and Fansidar not only share sound-alike potential but also look-alike potential (see prescription on page 10), each containing eight characters in length. Xantidar and Fansidar are each available in one strength therefore a prescription for either one may not contain the strength which may necessary for distinguishing between the two drug names. Although the drug products differ in dosing schedule and route of administration, post-marketing experience has demonstrated errors occurring between drug products that share no other commonalties except for look-alike and/or sound-alike potential. The inadvertent confusion of these two drug products could prove fatal as Fansidar has caused Steven-Johnsons syndrome and toxic epidermal necrolysis. A potential for spinal/epidural hematomas has been associated with the use of Xantidar.

Xantidar Farnedar  
#10 #10  
Seq: UD Seq: UD

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2. OPDRA has no objections to the use of the proposed proprietary name Arixtra.

## LABELING, PACKAGING AND SAFETY RELATED ISSUES

### CARTON LABELING

We recommend relocating the strength (2.5 mg/ 0.5 mL) to appear prominently and immediately beneath the established name on both the primary and side panels.

## V. RECOMMENDATIONS

A. OPDRA does not recommend the use of the proprietary name "Xantidar". However OPDRA has no objections to the use of the proprietary name "Arixtra".

B. OPDRA has recommended some labeling interventions that might minimize user error.

OPDRA would appreciate feedback of the final outcome of this consult (e.g., copy of revised labels/labeling). We are willing to meet with the Division for further discussion as well. If you have any questions concerning this review, please contact Sammie Beam, R.Ph. at 301-827-3231.

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Alina R. Mahmud, R.Ph.  
Safety Evaluator  
Office of Postmarketing Drug Risk Assessment (OPDRA)

Concur:

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Jerry Phillips, R.Ph.  
Associate Director for Medication Error Prevention  
Office of Postmarketing Drug Risk Assessment (OPDRA)

**This is a representation of an electronic record that was signed electronically and  
this page is the manifestation of the electronic signature.**

/s/  
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Alina Mahmud  
4/20/01 11:05:35 AM  
PHARMACIST

Jerry Phillips  
4/20/01 11:10:54 AM  
DIRECTOR

Martin Himmel  
4/20/01 12:38:42 PM  
MEDICAL OFFICER

APPEARS THIS WAY  
ON ORIGINAL

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		<b>REQUEST FOR CONSULTATION</b>		
Division/Office: Microbiology, HFD-160 ATTENTION: Dr. Peter Cooney, Team Leader		FROM: HFD-180 (Division of Gastrointestinal and Coagulation Drug Products) Phone # 827-7457		
DATE: 02/27/01	IND NO.:	NDA NO.: NDA 21-345	TYPE OF DOCUMENT :	DATE OF DOCUMENT 02-15-01
NAME OF DRUG: Xantidar (fondaparinux sodium) Injection	PRIORITY CONSIDERATION: Standard	CLASSIFICATION OF DRUG:	DESIRED COMPLETION DATE: User fee Due Date: 10 mo: Dec. 15, 2001 12mo: Feb. 15, 2002	
NAME OF FIRM: Fonda BV				
<b>REASON FOR REQUEST</b>				
<b>I. GENERAL</b>				
<input type="checkbox"/> NEW PROTOCOL	<input type="checkbox"/> PRE-NDA MEETING	<input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER		
<input type="checkbox"/> PROGRESS REPORT	<input type="checkbox"/> END OF PHASE II MEETING	<input type="checkbox"/> FINAL PRINTED LABELING		
<input type="checkbox"/> NEW CORRESPONDENCE	<input type="checkbox"/> RESUBMISSION	<input type="checkbox"/> LABELING REVISION		
<input type="checkbox"/> DRUG ADVERTISING	<input type="checkbox"/> SAFETY/EFFICACY	<input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE		
<input type="checkbox"/> ADVERSE REACTION REPORT	<input type="checkbox"/> PAPER NDA	<input type="checkbox"/> FORMULATIVE REVIEW		
<input type="checkbox"/> MANUFACTURING CHANGE/ADDITION	<input type="checkbox"/> CONTROL SUPPLEMENT	<input type="checkbox"/> OTHER (SPECIFY BELOW):		
<input type="checkbox"/> MEETING PLANNED BY				
<b>II. BIOMETRICS</b>				
STATISTICAL EVALUATION BRANCH		STATISTICAL APPLICATION BRANCH		
<input type="checkbox"/> TYPE A OR B NDA REVIEW		<input type="checkbox"/> CHEMISTRY REVIEW		
<input type="checkbox"/> END OF PHASE II MEETING		<input type="checkbox"/> PHARMACOLOGY		
<input type="checkbox"/> CONTROLLED STUDIES		<input type="checkbox"/> BIOPHARMACEUTICS		
<input type="checkbox"/> PROTOCOL REVIEW		<input type="checkbox"/> OTHER:		
<input type="checkbox"/> OTHER:				
<b>III. BIOPHARMACEUTICS</b>				
<input type="checkbox"/> DISSOLUTION		<input type="checkbox"/> DEFICIENCY LETTER RESPONSE		
<input type="checkbox"/> BIOAVAILABILITY STUDIES		<input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS		
<input type="checkbox"/> PHASE IV STUDIES		<input type="checkbox"/> IN-VIVO WAIVER REQUEST		
<b>IV. DRUG EXPERIENCE</b>				
<input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL		<input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY		
<input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES		<input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE		
<input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below)		<input type="checkbox"/> POISON RICK ANALYSIS		
<input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP				
<b>V. SCIENTIFIC INVESTIGATIONS</b>				
<input type="checkbox"/> CLINICAL		<input type="checkbox"/> PRECLINICAL		
<b>COMMENTS/SPECIAL INSTRUCTIONS:</b> New NDA-ELECTRONIC SUBMISSION. The network path location is: _____ I am consulting (1) volume that contains table of contents and summary information. Although the sponsor states that microbiology is "NA", please review appropriate data in the "chemistry" portion of the submission. This is a sterile product. If you have difficulty locating the submission in the EDR, please call me. The chemistry reviewer is Dr. Ali Al-Hakim. Thanks, Karen Oliver, Project Manager				
NATURE OF REQUESTER:		METHOD OF DELIVERY (Check one): <input type="checkbox"/> MAIL <input checked="" type="checkbox"/> HAND		
SIGNATURE OF RECEIVER:		SIGNATURE OF DELIVERER:		

/s/

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Karen Oliver

2/27/01 03:40:49 PM

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ON ORIGINAL

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		<b>REQUEST FOR CONSULTATION</b>		
(Division/Office): <b>Associate Director, Medication Error Prevention Office of Post Marketing Drug Risk Assessment, HFD-400 (Rm. 15B-03, PKLN Bldg.)</b>		FROM: GI and Coagulation Drug Products, HFD-180		
DATE February 26, 2001	IND NO. IND _____	NDA NO. NDA 21-345	TYPE OF DOCUMENT IND _____ and NDA 21-345	DATE OF DOCUMENT February 15, 2001
NAME OF DRUG Xantidar (fondaparinux sodium) Alternate choice name "Arixtra"	PRIORITY CONSIDERATION Unknown until after the filing meeting	CLASSIFICATION OF DRUG Heparinoid; anticoagulant	DESIRED COMPLETION DATE May 1, 2001	
NAME OF FIRM: Sanofi-Synthelabo Research				
<b>REASON FOR REQUEST</b>				
<b>I. GENERAL</b>				
<input type="checkbox"/> NEW PROTOCOL <input type="checkbox"/> PROGRESS REPORT <input type="checkbox"/> NEW CORRESPONDENCE <input type="checkbox"/> DRUG ADVERTISING <input type="checkbox"/> ADVERSE REACTION REPORT <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION <input type="checkbox"/> MEETING PLANNED BY <input type="checkbox"/> PRE-NDA MEETING <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> SAFETY/EFFICACY <input type="checkbox"/> PAPER NDA <input type="checkbox"/> CONTROL SUPPLEMENT <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER <input type="checkbox"/> FINAL PRINTED LABELING <input type="checkbox"/> LABELING REVISION <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE <input type="checkbox"/> FORMULATIVE REVIEW <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): Trade name review				
<b>II. BIOMETRICS</b>				
STATISTICAL EVALUATION BRANCH		STATISTICAL APPLICATION BRANCH		
<input type="checkbox"/> TYPE A OR B NDA REVIEW <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> CONTROLLED STUDIES <input type="checkbox"/> PROTOCOL REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW):		<input type="checkbox"/> CHEMISTRY REVIEW <input type="checkbox"/> PHARMACOLOGY <input type="checkbox"/> BIOPHARMACEUTICS <input type="checkbox"/> OTHER (SPECIFY BELOW):		
<b>III. BIOPHARMACEUTICS</b>				
<input type="checkbox"/> DISSOLUTION <input type="checkbox"/> BIOAVAILABILITY STUDIES <input type="checkbox"/> PHASE IV STUDIES		<input type="checkbox"/> DEFICIENCY LETTER RESPONSE <input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS <input type="checkbox"/> IN-VIVO WAIVER REQUEST		
<b>IV. DRUG EXPERIENCE</b>				
<input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL <input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP		<input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE <input type="checkbox"/> POISON RICK ANALYSIS		
<b>V. SCIENTIFIC INVESTIGATIONS</b>				
<input type="checkbox"/> CLINICAL		<input type="checkbox"/> PRECLINICAL		
<b>COMMENTS, CONCERNS, and/or SPECIAL INSTRUCTIONS:</b> Please review the proposed tradename "XANTIDAR". The drug is an anticoagulant, a "synthetic" pentasaccharide. A previous consult was sent on August 20, 2000, for the Xanitidar" tradename review under IND _____ In a separate submission (February 15, 2001) to the IND _____ the sponsor submitted a second choice tradename, "Arixtra". I am consulting (1) NDA volume and (1) IND volume for your review. If questions, please call me. Thanks, Karen Oliver 7-7457				
cc: archival IND _____ HFD-180/Division File; HFD-180/K.Oliver; HFD-180/L.Talarico; HFD-180/K.Robie-Suh				
NATURE OF REQUESTER		METHOD OF DELIVERY (Check one) MAIL XHAND		
SIGNATURE OF RECEIVER		SIGNATURE OF DELIVERER		



/s/

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Karen Oliver

2/26/01 03:18:47 PM

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DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		<b>REQUEST FOR CONSULTATION</b>		
TO (Division/Office): <b>Associate Director, Medication Error Prevention Division of Post Marketing Drug Risk Assessment, HFD-400 (Rm. 15B-03, PKLN Bldg.)</b>		FROM: GI and Coagulation Drug Products, HFD-180		
DATE August 30, 2000	IND NO. IND _____	NDA NO. 1	TYPE OF DOCUMENT Medical Amendment (IM)	DATE OF DOCUMENT August 28, 2000
NAME OF DRUG Pentasaccharide Injection (Org31540/SR90107A)	PRIORITY CONSIDERATION Standard	CLASSIFICATION OF DRUG Heparinoid; anticoagulant	DESIRED COMPLETION DATE October 1, 2000	
NAME OF FIRM: _____				
<b>REASON FOR REQUEST</b>				
<b>I. GENERAL</b>				
<input type="checkbox"/> NEW PROTOCOL <input type="checkbox"/> PROGRESS REPORT <input type="checkbox"/> NEW CORRESPONDENCE <input type="checkbox"/> DRUG ADVERTISING <input type="checkbox"/> ADVERSE REACTION REPORT <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION <input type="checkbox"/> MEETING PLANNED BY				
<input type="checkbox"/> PRE-NDA MEETING <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> SAFETY/EFFICACY <input type="checkbox"/> PAPER NDA <input type="checkbox"/> CONTROL SUPPLEMENT				
<input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER <input type="checkbox"/> FINAL PRINTED LABELING <input type="checkbox"/> LABELING REVISION <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE <input type="checkbox"/> FORMULATIVE REVIEW <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): Trade name review				
<b>II. BIOMETRICS</b>				
STATISTICAL EVALUATION BRANCH		STATISTICAL APPLICATION BRANCH		
<input type="checkbox"/> TYPE A OR B NDA REVIEW - <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> CONTROLLED STUDIES <input type="checkbox"/> PROTOCOL REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW):		<input type="checkbox"/> CHEMISTRY REVIEW <input type="checkbox"/> PHARMACOLOGY <input type="checkbox"/> BIOPHARMACEUTICS <input type="checkbox"/> OTHER (SPECIFY BELOW):		
<b>III. BIOPHARMACEUTICS</b>				
<input type="checkbox"/> DISSOLUTION <input type="checkbox"/> BIOAVAILABILITY STUDIES <input type="checkbox"/> PHASE IV STUDIES		<input type="checkbox"/> DEFICIENCY LETTER RESPONSE <input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS <input type="checkbox"/> IN-VIVO WAIVER REQUEST		
<b>IV. DRUG EXPERIENCE</b>				
<input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL <input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP		<input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE <input type="checkbox"/> POISON RISK ANALYSIS		
<b>V. SCIENTIFIC INVESTIGATIONS</b>				
<input type="checkbox"/> CLINICAL		<input type="checkbox"/> PRECLINICAL		
<b>COMMENTS, CONCERNS, and/or SPECIAL INSTRUCTIONS:</b> Sponsor requests proprietary name review for their future application. The proposed name is "XANTIDAR". The drug is an anticoagulant, a "synthetic" pentasaccharide. One volume consulted. Please review. If questions, please call me.				
Thanks, Karen Oliver 7-7457				
CC: Archival IND _____ HFD-180/Division File; HFD-180/K.Oliver; HFD-180/L.Talarico; HFD-180/K.Robie-Suh				
SIGNATURE OF REQUESTER <i>IS/</i>		METHOD OF DELIVERY (Check one) MAIL <input type="checkbox"/> HAND <input checked="" type="checkbox"/>		
SIGNATURE OF RECEIVER <i>IS/</i>		SIGNATURE OF DELIVERER <i>IS/</i>		

73242

IS/

EXCLUSIVITY SUMMARY for NDA # 21-345 SUPPL #

Trade Name Arixtra™ Generic Name fondaparinux sodium injection

Applicant Name Fonda BV HFD- 180

Approval Date December 7, 2001

**PART I: IS AN EXCLUSIVITY DETERMINATION NEEDED?**

1. An exclusivity determination will be made for all original applications, but only for certain supplements. Complete Parts II and III of this Exclusivity Summary only if you answer "YES" to one or more of the following questions about the submission.

a) Is it an original NDA? YES/ X / NO / \_\_\_ /

b) Is it an effectiveness supplement? YES / \_\_\_ / NO / X /

If yes, what type (SE1, SE2, etc.)? N/A

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "NO.")

YES / X / NO / \_\_\_ /

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

d) Did the applicant request exclusivity?

YES /X/ NO /\_\_\_/

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

5 years

e) Has pediatric exclusivity been granted for this Active Moiety?

YES /\_\_\_/ NO /X/

**IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.**

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule previously been approved by FDA for the same use? (Rx to OTC Switches should be answered No - Please indicate as such).

YES /\_\_\_/ NO /X/

If yes, NDA # \_\_\_\_\_ Drug Name

**IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.**

3. Is this drug product or indication a DESI upgrade?

YES /\_\_\_/ NO /X/

**IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9 (even if a study was required for the upgrade).**

**PART II: FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES**

(Answer either #1 or #2, as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES /\_\_\_/ NO /\_X\_/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA #

NDA #

NDA #

2. Combination product.

If the product contains more than one active moiety (as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES /\_\_\_/ NO /\_\_\_/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA #

NDA #

NDA #

**IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9. IF "YES," GO TO PART III.**

**PART III: THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS**

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2, was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES /\_\_\_/ NO /\_\_\_/

**IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.**

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis

for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

For the purposes of this section, studies comparing two products with the same ingredient(s) are considered to be bioavailability studies.

- (a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES /\_\_\_/ NO /\_\_\_/

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval **AND GO DIRECTLY TO SIGNATURE BLOCK ON Page 9:**

- (b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES /\_\_\_/ NO /\_\_\_/

- (1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES /\_\_\_/ NO /\_\_\_/

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES /\_\_\_/ NO /\_\_\_/

If yes, explain:

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Investigation #1, Study #

Investigation #2, Study #

Investigation #3, Study #

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

(a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES /\_\_\_/ NO /\_\_\_/

Investigation #2 YES /\_\_\_/ NO /\_\_\_/

Investigation #3 YES /\_\_\_/ NO /\_\_\_/

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:



NDA # \_\_\_\_\_ Study #  
NDA # \_\_\_\_\_ Study #  
NDA # \_\_\_\_\_ Study #

- (b) For each investigation identified as "essential to the approval," does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1                      YES /\_\_\_/                      NO /\_\_\_/  
Investigation #2                      YES /\_\_\_/                      NO /\_\_\_/  
Investigation #3                      YES /\_\_\_/                      NO /\_\_\_/

If you have answered "yes" for one or more investigations, identify the NDA in which a similar investigation was relied on:

NDA # \_\_\_\_\_ Study #  
NDA # \_\_\_\_\_ Study #  
NDA # \_\_\_\_\_ Study #

- (c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Investigation #\_\_, Study #  
Investigation #\_\_, Study #  
Investigation #\_\_, Study #

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

(a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1 !  
IND # \_\_\_\_\_ YES /\_\_\_/ ! NO /\_\_\_/ Explain:  
!  
!  
!  
!

Investigation #2 !  
IND # \_\_\_\_\_ YES /\_\_\_/ ! NO /\_\_\_/ Explain:  
!  
!  
!  
!

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1 !  
YES /\_\_\_/ Explain \_\_\_\_\_ ! NO /\_\_\_/ Explain \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

Investigation #2 !  
YES /\_\_\_/ Explain \_\_\_\_\_ ! NO /\_\_\_/ Explain \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /\_\_\_/                      NO /\_\_\_/

If yes, explain: \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

Karen Oliver, RN, MSN  
Signature of Preparer  
Title: Regulatory Health Project Manager

Date: 11/07/01

Signature of Office or Division Director

Date

cc:  
Archival NDA  
HFD- /Division File  
HFD- /RPM  
HFD-093/Mary Ann Holovac  
HFD-104/PEDS/T.Crescenzi

Form OGD-011347  
Revised 8/7/95; edited 8/8/95; revised 8/25/98, edited 3/6/00

**This is a representation of an electronic record that was signed electronically and  
this page is the manifestation of the electronic signature.**

/s/

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Victor Raczkowski  
12/7/01 12:56:50 PM

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## Regulatory Compliance Statement

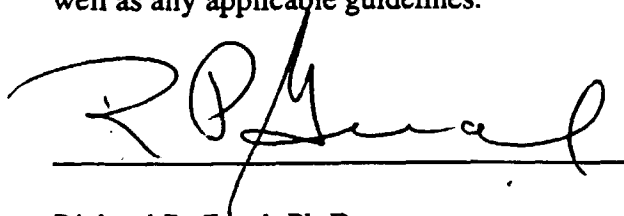
The following four studies (2 Phase II and 2 Phase III), included in this NDA, were conducted under the indicated IND:

IND — 095-001 — and 095-002 —

IND — DRI2643 — and EFC2442 —

Fonda BV certifies that these four clinical studies were initiated after Institutional Review Board approval was obtained, in compliance with the regulations set forth in 21 CFR, Part 56, and were conducted in compliance with the informed consent regulations under 21 CFR, Part 50.

All other studies included in this NDA were not conducted under an IND, and therefore, were not subject to the regulations under Parts 50 or 56. These other studies were conducted in accordance with the laws and regulations of the country in which the trial was performed, as well as any applicable guidelines.



Richard P. Gural, Ph.D.  
Vice President  
Regulatory Affairs  
Sanofi-Synthelabo, Inc.  
U.S. Agent for Fonda BV

APPEARS THIS WAY  
ON ORIGINAL

**ITEM 13. PATENT INFORMATION**

Pursuant to § 505 of the Federal Food, Drug and Cosmetics Act (FFDCA), as amended by the Drug Price Competition and Patent Term Restoration Act of 1984, applicants hereby submit information on each patent that claims the drug, drug product, or a method of using the drug and with respect to which a claim of infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use or sale of the drug product described in this application.

United States Patent Number	Expiration Date	Type of Patent	Patent Owner
4,818,816	August 19, 2003	Drug	Sanofi-Synthelabo

The following party is authorized to receive notice of patent certification under § 505(b)(3) and (j)(2)(B) of the FFDCA and §§ 314.52 and 314.95 of 21 C.F.R:

Sanofi-Synthelabo Inc.  
 Patent Counsel  
 9 Great Valley Parkway  
 P.O. Box 3026  
 Malvern, Pennsylvania  
 19355

**REQUEST FOR EXCLUSIVITY**

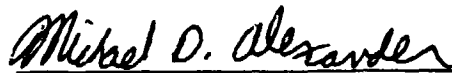
Pursuant to §§ 505(j)(4)(D)(ii) and 505(c)(3)(D)(ii) of the Federal Food, Drug and Cosmetics Act, applicants are requesting a five-year period of marketing exclusivity from the date of approval of this NDA for Org31540/SR90107A (fondaparinux sodium).

This request for exclusivity is based upon the following:

- (a) No active ingredient of the drug product for which approval is being sought has ever been approved in another drug product in the United States either as a single entity or as a part of a combination product; and
- (b) No active ingredient of the drug product has ever been previously marketed in a drug product in the United States.

**ITEM 14. PATENT DECLARATION**

No patent declaration is required as U.S. Patent No. 4,818,816 does not cover a formulation, composition, and/or method of use of Org31540/SR90107A (fondaparinux sodium).

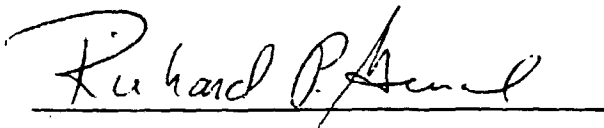


MICHAEL D. ALEXANDER  
Sr. Managing Attorney, Intellectual Property  
Sanofi-Synthelabo Inc.

APPEARS THIS WAY  
ON ORIGINAL

### Item 16. Debarment Certification

Fonda BV hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug and Cosmetic Act in connection with this application.



Richard P. Gural

Richard P. Gural, Ph.D.  
Vice President  
Regulatory Affairs  
Sanofi-Synthelabo, Inc.  
U.S. Agent for Fonda BV

APPEARS THIS WAY  
ON ORIGINAL



## CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

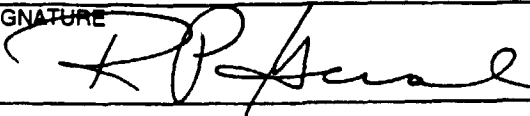
With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

- (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators		

- (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).
- (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME Richard P. Gural, Ph.D.	TITLE Vice President, Regulatory Affairs Sanofi-Synthelabo Inc.
FIRM/ORGANIZATION U.S. Authorized Agent for Fonda BV	
SIGNATURE 	DATE 24 January 2001

### Paperwork Reduction Act Statement

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 control number. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Department of Health and Human Services  
Food and Drug Administration  
5600 Fishers Lane, Room 14C-03  
Rockville, MD 20857

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
PUBLIC HEALTH SERVICE  
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0  
Expiration Date: 04-30-01

# USER FEE COVER SHEET

**See Instructions on Reverse Side Before Completing This Form**

1. APPLICANT'S NAME AND ADDRESS  Fonda BV c/o _____ Tripolos 300 Burgerweeshuispad 311 1076 HS Amsterdam, The Netherlands		3. PRODUCT NAME Xantidar™ (fondaparinux sodium)
2. TELEPHONE NUMBER (Include Area Code) ( 610 ) 889-6637		4. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL? IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM.  IF RESPONSE IS "YES", CHECK THE APPROPRIATE RESPONSE BELOW: <input checked="" type="checkbox"/> THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION <input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO _____ (APPLICATION NO. CONTAINING THE DATA).
5. USER FEE I.D. NUMBER	6. LICENSE NUMBER / NDA NUMBER NDA 21-345	
7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.  <input type="checkbox"/> A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 (Self Explanatory) <input type="checkbox"/> A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE (See item 7, reverse side before checking box.) <input type="checkbox"/> THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act (See item 7, reverse side before checking box.) <input type="checkbox"/> THE APPLICATION IS A PEDIATRIC SUPPLEMENT THAT QUALIFIES FOR THE EXCEPTION UNDER SECTION 736(a)(1)(F) of the Federal Food, Drug, and Cosmetic Act (See item 7, reverse side before checking box.) <input type="checkbox"/> THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALY (Self Explanatory)  <b>FOR BIOLOGICAL PRODUCTS ONLY</b> <input type="checkbox"/> WHOLE BLOOD OR BLOOD COMPONENT FOR TRANSFUSION <input type="checkbox"/> A CRUDE ALLERGENIC EXTRACT PRODUCT <input type="checkbox"/> AN APPLICATION FOR A BIOLOGICAL PRODUCT FOR FURTHER MANUFACTURING USE ONLY <input type="checkbox"/> AN "IN VITRO" DIAGNOSTIC BIOLOGICAL PRODUCT LICENSED UNDER SECTION 351 OF THE PHS ACT <input type="checkbox"/> BOVINE BLOOD PRODUCT FOR TOPICAL APPLICATION LICENSED BEFORE 9/1/92		
8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO (See reverse side if answered YES)		


**A completed form must be signed and accompany each new drug or biologic product application and each new supplement. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment.**

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

DHHS, Reports Clearance Officer  
Paperwork Reduction Project (0910-0297)  
Hubert H. Humphrey Building, Room 531-H  
200 Independence Avenue, S.W.  
Washington, DC 20201

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Please DO NOT RETURN this form to this address.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE 	TITLE Richard P. Gural, Ph.D. Vice-President, Regulatory Affairs Authorized U.S. Agent for Fonda BV	DATE 22 January 2001
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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville MD 20857

NDA 21-345

Fonda BV  
c/o U.S. Agent: Richard P. Gural, Ph.D.  
9 Great Valley Parkway  
P.O. 3026  
Malvern, PA 19355

Dear Dr. Gural:

We have received your pre-submission of nonclinical pharmacology and toxicology information for the following:

Name of Drug Product: Xantidar™ (fondaparinux sodium) Injection

Date of Application: December 19, 2000

Date of Receipt: December 20, 2000

Our Reference Number: NDA 21-345

We will review this early submission as resources permit. Presubmissions are not subject to a review clock or to a filing decision by FDA until the application is complete.

Please cite the NDA number listed above at the top of the first page of any communications concerning this application. Address all additional pre-submissions as follows:

Food and Drug Administration  
Center for Drug Evaluation and Research  
Attention: CENTRAL DOCUMENT ROOM  
12229 Wilkins Avenue  
Rockville, Maryland 20852-1833

If you have any questions, call me at (301) 827-7457.

Sincerely,

Karen Oliver  
Regulatory Project Manager  
Division of Gastrointestinal and Coagulation Drug Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

/s/

-----  
Karen Oliver

12/27/00 03:42:52 PM

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## Printable Pediatric Page

Welcome to the Pediatric Page Printed Page. To produce your pediatric page, simply print this page (this paragraph will not print). However, most versions of Internet Explorer will print a header on each page (i.e., the name of the web site, etc.) To eliminate these when printing the Pediatric Page, go to 'File', then 'Page Setup', and clear the 'Header' and 'Footer' Boxes. (Cut and paste to a document [or write down] the contents of these boxes first if you want to restore the headers and footers afterwards.)

### PEDIATRIC PAGE

**NDA Number:** 021345    **Trade Name:** XANTIDAR (FONDAPHARINX SODIUM)  
**Supplement Number:** 000    **Generic Name:** FONDAPHARINX SODIUM  
**Stamp date:** 2/15/01    **Action Date:** 8/15/01  
**Supplement Type:** N  
**COMIS Indication:** PROPHYLAXIS OF DEEP VENOUS THROMBOSIS

**Indication #1: Prophylaxis of deep vein thrombosis, which may lead to pulmonary embolism in patients undergoing hip fracture surgery. -**

Date Entered: 12/7/01

Status: A full waiver was granted for this Indication.

Reason for This Waiver: Disease or condition does not exist in children

**Indication #2: The prophylaxis of deep vein thrombosis, which may lead to pulmonary embolism in patient undergoing hip replacement surgery. -** Date Entered: 12/7/01

Status: A full waiver was granted for this Indication.

Reason for This Waiver: Disease or condition does not exist in children

**Indication #3: The prophylaxis of deep vein thrombosis, which may lead to pulmonary embolism, in patient undergoing knee replacement surgery. -** Date Entered: 12/7/01

Status: A full waiver was granted for this Indication.

Reason for This Waiver: Too few children with the disease to study

**This page was printed on 12/7/01**

/S/

Signature

12/07/01

Date

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