



iPLEDGE™
Committed to Pregnancy Prevention

Wholesaler Registration Letter

Dear wholesaler or chain drug executive,

The iPLEDGE Program requires annual registration of all wholesalers distributing isotretinoin. For the purposes of the iPLEDGE Program, the term wholesaler refers to a wholesaler and each of its individual distribution centers, a distributor and each of its individual distribution centers, and/or each warehousing chain pharmacy distribution center.

A Registration Form is enclosed with this letter.

Key Elements of the iPLEDGE Program, Which Relate to Your Business Practices:

- The program covers all isotretinoin products (brand and generic)
- To be registered, each wholesaler must agree to meet all iPLEDGE requirements for wholesale distribution of isotretinoin products by completing the enclosed agreement
- Wholesalers registered in the iPLEDGE Program will only ship isotretinoin to:
 - Wholesalers registered in the iPLEDGE Program with prior written consent from the manufacturer, or
 - Pharmacies registered with and activated in the iPLEDGE Program
- The registration of wholesalers that do not abide by the terms of the agreement will be revoked after an investigation process, and manufacturers of FDA-approved isotretinoin products will not continue to provide them with isotretinoin for distribution
- Registration in the iPLEDGE Program expires in 12 months and requires re-registration annually.

To Register in the iPLEDGE Program, Mail the Completed Agreement to:

iPLEDGE Program
P.O. Box 29094
Phoenix, AZ 85038

OR

Fax the completed form, using the following iPLEDGE fax number: 1-866-495-0660

We thank you for your support in complying with the iPLEDGE Program.

Sincerely,

Karin Greenberg, Pharm.D., BCPS
Sr. Director and Global Head of Pharmacovigilance
Dr. Reddy's Laboratories, Inc.

Eric H. Davis, M.D.
Director, Medical Services
Global Product Safety & Risk Management
Mylan Pharmaceuticals

Ashish Anvekar
Senior Director, Brand
Ranbaxy Laboratories, Inc.

Kishore Gopu
Director, REMS
Teva Pharmaceuticals USA

John Franolic, Ph.D.
Vice President of Regulatory Affairs
VersaPharm Incorporated



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Wholesaler Registration (continued)

SAFETY NOTICE

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected. Because of this toxicity, isotretinoin can only be marketed under a special restricted distribution program. This program is called iPLEDGE™. Under this program, prescribers must be registered and activated with the iPLEDGE Program and can prescribe isotretinoin only to registered patients who meet all the requirements of iPLEDGE. Isotretinoin can be dispensed only by a pharmacy registered and activated with iPLEDGE. Registered and activated pharmacies can only receive isotretinoin from wholesalers registered with iPLEDGE.

Patients on isotretinoin have been known to become depressed or to develop other serious mental health problems. Some people have had thoughts of hurting themselves or putting an end to their own lives. Some people tried to end their own lives and some have ended their own lives. There have been reports that people on isotretinoin were aggressive or violent. No one knows if isotretinoin caused these problems or behaviors, or if they would have happened even if the person did not take isotretinoin.

Isotretinoin use has been associated with pseudotumor cerebri, a condition caused by increased pressure on the brain. This condition may occur more often in patients also taking tetracycline. Patients should be aware of other serious side effects, including problems with the skin, pancreas, liver, stomach, bones, muscles, hearing, vision, lipids, allergic reactions, blood sugar, or red and white blood cells. The most common, less serious adverse events include dry skin, chapped lips, dry eyes, and dry nose that may lead to nosebleeds. Patients should be advised about these adverse events and routinely monitored by a doctor during treatment with isotretinoin.



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iPLEDGE Program
P.O. Box 29094
Phoenix, AZ 85038

Wholesaler Registration Form On Behalf of the Wholesaler Listed Below, I Acknowledge That:

For the purpose of the iPLEDGE Program, the term wholesaler refers to a wholesaler and each of its individual distribution centers, a distributor and each of its individual distribution centers, and/or each warehousing chain pharmacy distribution center. To distribute isotretinoin, wholesalers must be registered with the iPLEDGE Program and agree to meet all iPLEDGE Program requirements for wholesaler distribution of isotretinoin products. Wholesalers must register with the iPLEDGE Program by signing and returning this agreement that affirms they will comply with all iPLEDGE Program requirements for distribution of isotretinoin. The registration of wholesalers that do not abide by the terms of the agreement will be revoked after an investigation process, and manufacturers of FDA approved isotretinoin products will not continue to provide them with isotretinoin for distribution. Each distribution center operated by a wholesaler must register if they are to distribute isotretinoin. These requirements include:

- Registering prior to distributing isotretinoin and registering annually thereafter
- Distributing only FDA approved isotretinoin product obtained directly from the isotretinoin manufacturers (or delegate) or another registered wholesaler
- Beginning November 1, 2005 only ship isotretinoin to:
 - Wholesalers registered in the iPLEDGE Program with prior written consent from the manufacturer, or
 - Pharmacies licensed in the US and registered and activated in the iPLEDGE Program
- Notifying immediately the isotretinoin manufacturer (or delegate) of any nonregistered and/or nonactivated pharmacy or unregistered wholesaler that attempts to order isotretinoin
- Complying with inspection of wholesaler records by the isotretinoin manufacturer (or delegate) for verification of compliance with the iPLEDGE Program
- Returning to the manufacturer (or delegate) any undistributed product if registration is revoked by the iPLEDGE Program or if the wholesaler chooses to not reregister annually.

An agreement must be completed for each distributor center.

I am authorized to execute this agreement on behalf of the wholesaler (and its distribution centers, if applicable)

Wholesaler Name _____

(Type or Print)



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Distribution Center's DEA# _____

Distribution Center's Address _____

Distribution Center's City _____

Distribution Center's State _____ Distribution Center's ZIP _____

Distribution Center's Phone Number _____

Distribution Center's Fax Number _____

Authorized Representative _____

(Print First, MI, Last)

Title _____

E-mail Address for Key Contact _____

E-mail Address for Pharmacy Eligibility File Delivery* _____

Authorized Representative's Signature _____

Date ____/____/____
Month Day Year

*The list of registered and activated pharmacies will be e-mailed to this address daily.

This agreement expires 12 months from agreement date. Annual registration is required.

www.ipledeprogram.com | 1-866-495-0654



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Wholesaler Product Return Letter

Isotretinoin Return Customer Instruction Guide - Wholesaler

Wholesaler Name
Address 1
Address 2
City, State Postal Code

Dear Wholesaler:

You are no longer registered in the iPLEDGE Program for the following reason:

- Your facility is closing, and will no longer be a wholesaler in the iPLEDGE Program.

Therefore, you are required to return all isotretinoin inventories in stock **effective immediately**.

This action is pursuant to the FDA approval of the iPLEDGE Program through the special restricted distribution program. If you have questions about your status in the iPLEDGE Program, please call 1-866-495-0654 or visit www.ipledgeprogram.com for more information.

Action required by a wholesaler no longer registered in the iPLEDGE Program:

- Immediately remove all isotretinoin from your stock.
- If you have isotretinoin inventory, please call **1-866-495-0654** for further instructions on returning this product to the manufacturer.

Sincerely,

iPLEDGE Program

www.ipledgeprogram.com | 1-866-495-0654



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Wholesaler Product Return Letter (continued)

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iPLEDGE, an enhanced pregnancy risk management program designed to minimize fetal exposure to isotretinoin, has been approved by the FDA through a special restricted distribution program

www.ipledgeprogram.com | 1-866-495-0654