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# **An Introduction to the Improved FDA Prescription Drug Labeling**

# Introduction

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# Learning Objectives

- Describe prescription drug labeling and related FDA requirements.
- Describe the history of the drug labeling initiative.
- Describe the staged implementation schedule for the revised prescription drug labeling.
- Describe the major content and format changes to prescription drug labeling and the rationale for the changes.
- Describe other related FDA electronic labeling initiatives.

# What Is Prescription Drug Labeling?

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# What Is Prescription Drug Labeling?

- Definition of labeling - (21 U.S.C. 321(m))
- Prescription drug labeling information is also known as
  - Prescribing information
  - Package insert
  - Professional labeling
  - Direction circular
  - Package circular

# General Requirements for Prescription Drug Labeling (21 CFR 201.56)

- Summary for the safe and effective use of the drug
- Informative and accurate
- Not promotional, false, or misleading
- No implied claims or suggestions for use if evidence of safety or effective is lacking
- Based whenever possible on data derived from human experience



# Test Your Knowledge

**True or False:** The primary purpose of prescription drug labeling is to give patients information they need to take medications properly.

**Answer: False.** Although patients may obtain useful information from prescription drug labeling, its primary purpose is to give healthcare professionals the information they need to prescribe drugs appropriately.

# **History of the Prescription Drug Labeling Initiative**

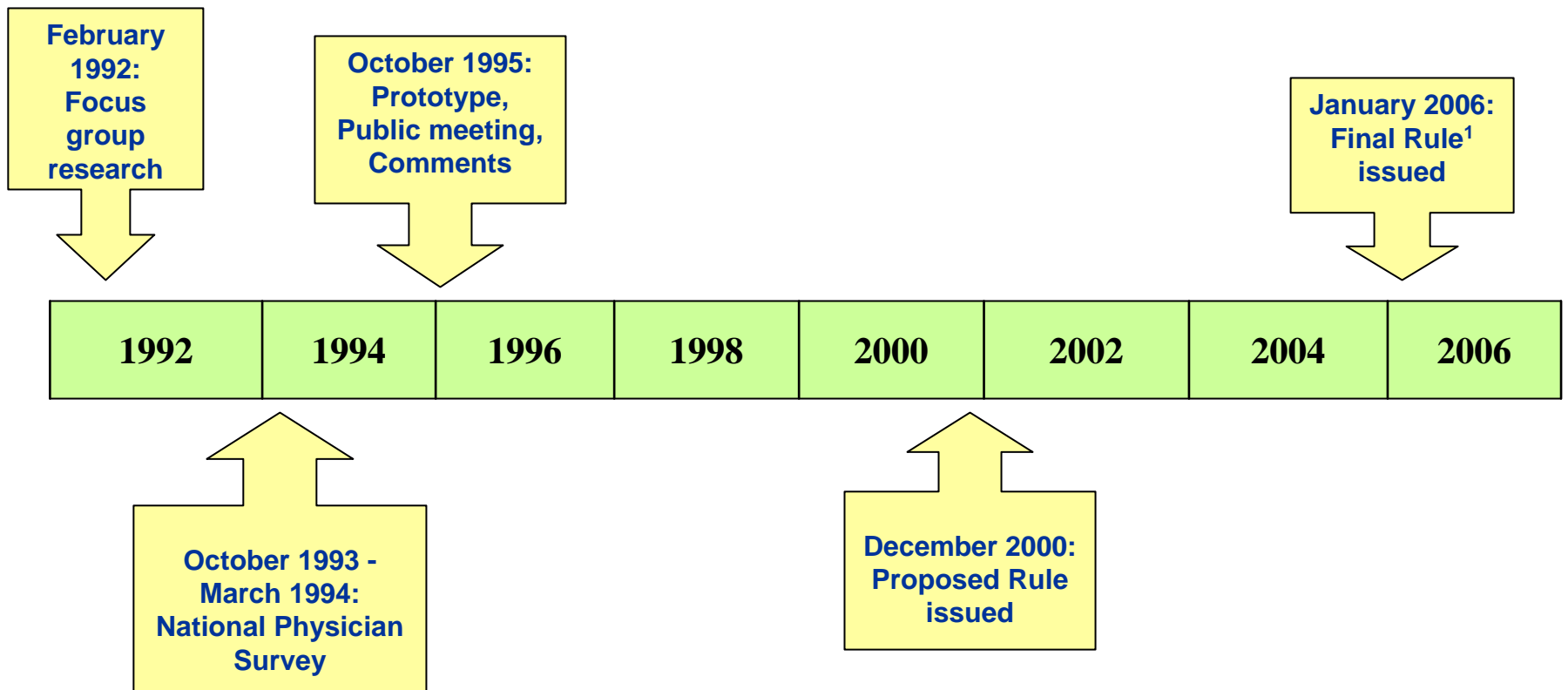
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# Drug Labeling Changed Over Time

- Increased in length, detail, and complexity
- Did not identify approval date or any recent change to the labeling
- Made specific information more difficult to locate
- Did not facilitate finding answers to specific questions

# Prescription Drug Labeling Initiative



<sup>1</sup> [Final Rule: Requirements on the Content and Format of Labeling for Human Prescription Drug and Biological Products](#)



Proposed Rule



Public comments



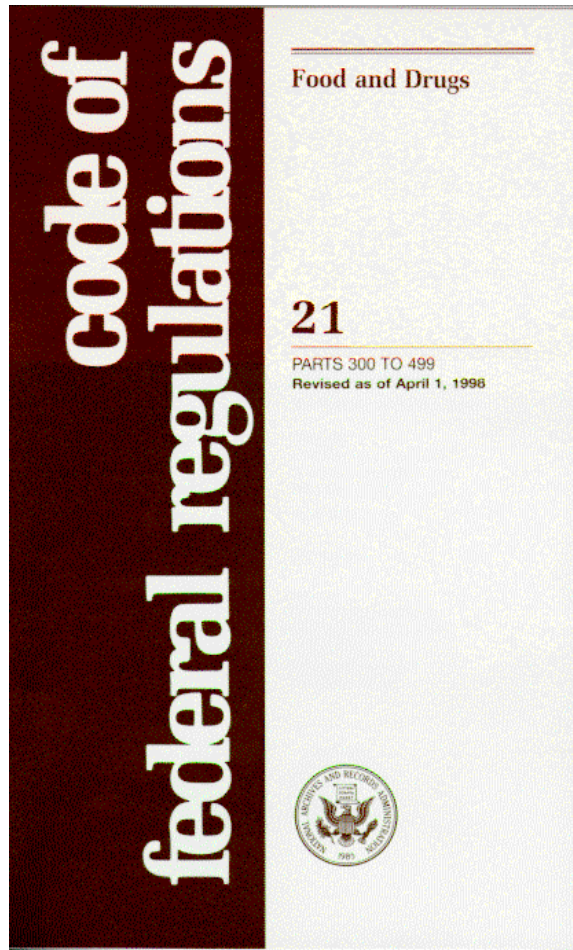
Comments are analyzed



Rule is modified to address comments



Final Rule is published in the *Federal Register*



The Final Rule is incorporated into next edition of the

*Code of Federal Regulations*

# Products Affected by the Rule

Prescription drugs and biologics:

- Submitted to FDA on or after June 30, 2006
- Approved by FDA 5 years prior to June 30, 2006
- With a major change in prescribing information approved 5 years prior to, on, or after June 30, 2006



# Test Your Knowledge

**True or False:** FDA conducted focus groups, surveys, and public meetings with prescribers to determine how the labeling should be changed.

**Answer: True**

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# Implementation Schedule

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# Implementation Schedule

<b>New Drug Application (NDA) or Biologics License Application (BLA):</b>	<b>Labeling must conform:</b>
Submitted 6/30/06 or after	At time of submission
Pending on 6/30/06 Approved 6/30/05-6/30/06	6/30/09 (3 years)
Approved 6/30/04-6/29/05	6/30/10 (4 years)
Approved 6/30/03-6/29/04	6/30/11 (5 years)
Approved 6/30/02-6/29/03	6/30/12 (6 years)
Approved 6/30/01-6/29/02	6/30/13 (7 years)
Approved Pre-6/30/01	Voluntary at any time (encouraged to conform)



# Test Your Knowledge

**True or False:** Labeling for all prescription drugs must conform to the new format by the year 2010.

**Answer: False.** FDA has provided for a flexible implementation schedule that phases in the new labeling requirements. The schedule for implementation depends on when the application was submitted to the agency. Companies whose products were approved many years ago have more time to update their labeling, while ensuring that new products will be updated first.

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# **Labeling Format and Content Changes**

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# Overview of New Labeling Format

- Adds Highlights section
- Adds Contents section
- Reorders and reorganizes sections
- Makes additional improvements

# Reformatting Drug Labeling

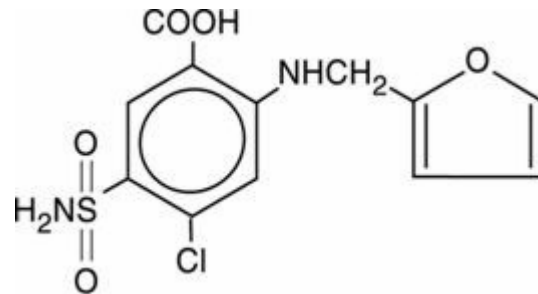
## Old format

BRAND NAME

(chemical name)

DESCRIPTION

The chemical structure is shown below:



Furosemide is a diuretic which is an anthranilic acid derivative. Chemically, it is 4-chloro-N-furfuryl-5-sulfamoylanthranilic acid. Furosemide is available as white tablets for oral administration in dosage strengths of 20, 40 and 80 mg. Furosemide is a white to off-white odorless crystalline powder. It is practically insoluble in water, sparingly soluble in alcohol, freely soluble in dilute alkali solutions and insoluble in dilute acids.

# Revised format

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Imdicon safely and effectively. See full prescribing information for Imdicon.

**IMDICON® (cholinaseol) CAPSULES**  
Initial U.S. Approval: 2000

### WARNING: LIFE-THREATENING HEMATOLOGICAL ADVERSE REACTIONS

See full prescribing information for complete boxed warning. Monitor for hematological adverse reactions every 2 weeks for first 3 months of treatment (5.2). Discontinue Imdicon immediately if any of the following occur:

- Neutropenia/agranulocytosis (5.1)
- Thrombotic thrombocytopenic purpura (5.1)
- Aplastic anemia (5.1)

### RECENT MAJOR CHANGES

Indications and Usage, Coronary Stenting (1.2) 2/200X  
Dosage and Administration, Coronary Stenting (2.2) 2/200X

### INDICATIONS AND USAGE

Imdicon is an adenosine diphosphate (ADP) antagonist platelet aggregation inhibitor indicated for:

- Reducing the risk of thrombotic stroke in patients who have experienced stroke precursors or who have had a completed thrombotic stroke (1.1)
- Reducing the incidence of subacute coronary stent thrombosis, when used with aspirin (1.2)

Important limitations:

- For stroke, Imdicon should be reserved for patients who are intolerant of or allergic to aspirin or who have failed aspirin therapy (1.1)

### DOSAGE AND ADMINISTRATION

- Stroke: 50 mg once daily with food. (2.1)
- Coronary Stenting: 50 mg once daily with food, with antiplatelet doses of aspirin, for up to 30 days following stent implantation (2.2)

Discontinue in renally impaired patients if hemorrhagic or hematopoietic problems are encountered (2.3, 8.6, 12.3)

## FULL PRESCRIBING INFORMATION: CONTENTS\*

### WARNING – LIFE-THREATENING HEMATOLOGICAL ADVERSE REACTIONS

#### 1 INDICATIONS AND USAGE

- 1.1 Thrombotic Stroke
- 1.2 Coronary Stenting

#### 2 DOSAGE AND ADMINISTRATION

- 2.1 Thrombotic Stroke
- 2.2 Coronary Stenting
- 2.3 Renally Impaired Patients

#### 3 DOSAGE FORMS AND STRENGTHS

#### 4 CONTRAINDICATIONS

#### 5 WARNINGS AND PRECAUTIONS

- 5.1 Hematological Adverse Reactions
- 5.2 Monitoring for Hematological Adverse Reactions
- 5.3 Anticoagulant Drugs
- 5.4 Bleeding Precautions
- 5.5 Monitoring: Liver Function Tests

#### 6 ADVERSE REACTIONS

- 6.1 Clinical Studies Experience
- 6.2 Postmarketing Experience

#### 7 DRUG INTERACTIONS

- 7.1 Anticoagulant Drugs
- 7.2 Phenytoin
- 7.3 Antipyrene and Other Drugs Metabolized Hepatically
- 7.4 Aspirin and Other Non-Steroidal Anti-Inflammatory Drugs
- 7.5 Cimetidine
- 7.6 Theophylline
- 7.7 Propranolol
- 7.8 Antacids
- 7.9 Digoxin
- 7.10 Phenobarbital
- 7.11 Other Concomitant Drug Therapy
- 7.12 Food Interaction

### DOSAGE FORMS AND STRENGTHS

Capsules: 50 mg (3)

### CONTRAINDICATIONS

- Hematopoietic disorders or a history of TTP or aplastic anemia (4)
- Hemostatic disorder or active bleeding (4)
- Severe hepatic impairment (4, 8.7)

### WARNINGS AND PRECAUTIONS

- Neutropenia (2.4 % incidence; may occur suddenly; typically resolves within 1-2 weeks of discontinuation), thrombotic thrombocytopenic purpura (TTP), aplastic anemia, agranulocytosis, pancytopenia, leukemia, and thrombocytopenia can occur (5.1)
- Monitor for hematological adverse reactions every 2 weeks through the third month of treatment (5.2)

### ADVERSE REACTIONS

Most common adverse reactions (incidence >2%) are diarrhea, nausea, dyspepsia, rash, gastrointestinal pain, neutropenia, and purpura (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact (manufacturer) at (phone # and Web address) or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

### DRUG INTERACTIONS

- Anticoagulants: Discontinue prior to switching to Imdicon (5.3, 7.1)
- Phenytoin: Elevated phenytoin levels have been reported. Monitor levels. (7.2)

### USE IN SPECIFIC POPULATIONS

- Hepatic impairment: Dose may need adjustment. Contraindicated in severe hepatic disease (4, 8.7, 12.3)
- Renal impairment: Dose may need adjustment (2.3, 8.6, 12.3)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling

Revised: 5/200X

#### 8 USE IN SPECIFIC POPULATIONS

- 8.1 Pregnancy
- 8.3 Nursing Mothers
- 8.4 Pediatric Use
- 8.5 Geriatric Use
- 8.6 Renal Impairment
- 8.7 Hepatic Impairment

#### 10 OVERDOSAGE

#### 11 DESCRIPTION

#### 12 CLINICAL PHARMACOLOGY

- 12.1 Mechanism of Action
- 12.2 Pharmacodynamics
- 12.3 Pharmacokinetics

#### 13 NONCLINICAL TOXICOLOGY

- 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

#### 14 CLINICAL STUDIES

- 14.1 Thrombotic Stroke
- 14.2 Coronary Stenting

#### 16 HOW SUPPLIED/STORAGE AND HANDLING

#### 17 PATIENT COUNSELING INFORMATION

- 17.1 Importance of Monitoring
- 17.2 Bleeding
- 17.3 Hematological Adverse Reactions
- 17.4 FDA-Approved Patient Labeling

\*Sections or subsections omitted from the full prescribing information are not listed.

# Highlights

## Concise, one-half page summary of information in the Full Prescribing Information

- Limitations Statement
- Product Names and Date of Initial U.S. Approval
- Boxed Warning
- Recent Major Changes
- Indications and Usage
- Dosage & Administration
- Dosage Forms & Strengths
- Contraindications
- Warnings & Precautions
- Adverse Reactions (listing of most common ARs)
- Drug Interactions
- Use in Specific Populations
- Patient Counseling Information Statement

# Example of Highlights for a Fictitious Drug

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Imdicon safely and effectively. See full prescribing information for Imdicon.

### IMDICON® (cholinazol) CAPSULES

Initial U.S. Approval: 2000

#### WARNING: LIFE-THREATENING HEMATOLOGICAL ADVERSE REACTIONS

*See full prescribing information for complete boxed warning.*

Monitor for hematological adverse reactions every 2 weeks for first 3 months of treatment (5.2). Discontinue Imdicon immediately if any of the following occur:

- Neutropenia/agranulocytosis (5.1)
- Thrombotic thrombocytopenic purpura (5.1)
- Aplastic anemia (5.1)

#### RECENT MAJOR CHANGES

Indications and Usage, Coronary Stenting (1.2) 2/200X  
Dosage and Administration, Coronary Stenting (2.2) 2/200X

#### INDICATIONS AND USAGE

Imdicon is an adenosine diphosphate (ADP) antagonist platelet aggregation inhibitor indicated for:

- Reducing the risk of thrombotic stroke in patients who have experienced stroke precursors or who have had a completed thrombotic stroke (1.1)
- Reducing the incidence of subacute coronary stent thrombosis, when used with aspirin (1.2)

Important limitations:

- For stroke, Imdicon should be reserved for patients who are intolerant of or allergic to aspirin or who have failed aspirin therapy (1.1)

#### DOSAGE AND ADMINISTRATION

- Stroke: 50 mg once daily with food. (2.1)
- Coronary Stenting: 50 mg once daily with food, with antiplatelet doses of aspirin, for up to 30 days following stent implantation (2.2)

Discontinue in renally impaired patients if hemorrhagic or hematopoietic problems are encountered (2.3, 8.6, 12.3)

#### DOSAGE FORMS AND STRENGTHS

Capsules: 50 mg (3)

#### CONTRAINDICATIONS

- Hematopoietic disorders or a history of TTP or aplastic anemia (4)
- Hemostatic disorder or active bleeding (4)
- Severe hepatic impairment (4, 8.7)

#### WARNINGS AND PRECAUTIONS

- Neutropenia (2.4 % incidence; may occur suddenly; typically resolves within 1-2 weeks of discontinuation), thrombotic thrombocytopenic purpura (TTP), aplastic anemia, agranulocytosis, pancytopenia, leukemia, and thrombocytopenia can occur (5.1)
- Monitor for hematological adverse reactions every 2 weeks through the third month of treatment (5.2)

#### ADVERSE REACTIONS

Most common adverse reactions (incidence >2%) are diarrhea, nausea, dyspepsia, rash, gastrointestinal pain, neutropenia, and purpura (6.1).

**To report SUSPECTED ADVERSE REACTIONS, contact (manufacturer) at (phone # and Web address) or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).**

#### DRUG INTERACTIONS

- Anticoagulants: Discontinue prior to switching to Imdicon (5.3, 7.1)
- Phenytoin: Elevated phenytoin levels have been reported. Monitor levels. (7.2)

#### USE IN SPECIFIC POPULATIONS

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- Renal impairment: Dose may need adjustment (2.3, 8.6, 12.3)

**See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling**

Revised: 5/200X23

# Example of Highlights for a Fictitious Drug

## HIGHLIGHTS OF PRESCRIBING INFORMATION

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IMDICON® (cholinazol) CAPSULES

Initial U.S. Approval: 2000

### WARNINGS

See

Monitor for  
months of  
following o

- Neu
- Thro
- Aplas

## HIGHLIGHTS OF PRESCRIBING INFORMATION

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### DOSAGE FORMS AND STRENGTHS

Capsules: 50 mg (3)

### CONTRAINDICATIONS

- Hematopoietic disorders or a history of TTP or aplastic anemia (4)
- Hemostatic disorder or active bleeding (4)

### ADVERSE REACTIONS

Identify; typically resolves  
otic thrombocytopenic  
sis, pancytopenia,  
(5.1)  
every 2 weeks through the

### ADVERSE REACTIONS

Most common adverse reactions (incidence >2%) are diarrhea, nausea, dyspepsia, rash, gastrointestinal pain, neutropenia, and purpura (6.1).

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See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling

Revised: 5/200X 24



# Example of Highlights for a Fictitious Drug

## HIGHLIGHTS OF PRESCRIBING INFORMATION

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### IMDICON® (cholinazol) CAPSULES

Initial U.S. Approval: 2000

#### WARNING: LIFE-THREATENING HEMATOLOGICAL ADVERSE REACTIONS

See full prescribing information for complete boxed warning.

Monitor for hematologic adverse reactions during the first 6 months of treatment. Discontinue Imdicon if the following occur:

- Neutropenia
- Thrombotic thrombocytopenic syndrome
- Aplastic anemia

**IMDICON® (cholinazol) CAPSULES**  
Initial U.S. Approval: 2000

#### RECENT MAJOR CHANGES

Indications and Usage, Coronary Stenting (1.2) 2/200X  
Dosage and Administration, Coronary Stenting (2.2) 2/200X

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Imdicon is an adenosine diphosphate (ADP) antagonist platelet aggregation inhibitor indicated for:

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Important limitations:

- For stroke, Imdicon should be reserved for patients who are intolerant of or allergic to aspirin or who have failed aspirin therapy (1.1)

#### DOSAGE AND ADMINISTRATION

- Stroke: 50 mg once daily with food. (2.1)
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Discontinue in renally impaired patients if hemorrhagic or hematopoietic problems are encountered (2.3, 8.6, 12.3)

#### DOSAGE FORMS AND STRENGTHS

Capsules: 50 mg (3)

#### CONTRAINDICATIONS

- Hematopoietic disorders or a history of TTP or aplastic anemia (4)
- Hemostatic disorder or active bleeding (4)
- Severe hepatic impairment (4, 8.7)

#### WARNINGS AND PRECAUTIONS

Neutropenia typically resolves within 2 weeks through the discontinuation of Imdicon. Thrombotic thrombocytopenic syndrome (TTP) may occur. Discontinue Imdicon if TTP is suspected. Hematopoietic recovery may take several weeks through the discontinuation of Imdicon.

#### ADVERSE REACTIONS

Most common adverse reactions (incidence >2%) are diarrhea, nausea, dyspepsia, rash, gastrointestinal pain, neutropenia, and purpura (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact (manufacturer) at (phone # and Web address) or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

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See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling

Revised: 5/200X

# Example of Highlights for a Fictitious Drug

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## IMDICON® (cholinase) CAPSULES

Initial U.S. Approval: 2000

### WARNING: LIFE-THREATENING HEMATOLOGICAL ADVERSE REACTIONS

See full prescribing information for Imdicon. Monitor for hematological adverse reactions every 2 weeks for first 3 months of treatment (5.2). Discontinue Imdicon immediately if any of the following occur:

- Neutropenia/agranulocytosis (5.1)
- Thrombotic thrombocytopenic purpura (5.1)
- Aplastic anemia (5.1)

RECENT INDICATIONS AND USAGE, CORONARY STENTING, DOSAGE AND ADMINISTRATION, CONTRAINDICATIONS, AND PRECAUTIONS

INDICATIONS AND USAGE  
Imdicon is an adenosine diphosphate (ADP) inhibitor indicated for:

- Reducing the risk of thrombotic stroke precursors or who have had a stroke (1.1)
- Reducing the incidence of thrombotic stroke when used with aspirin (1.2)

Important limitations:

- For stroke, Imdicon should not be used in patients who are allergic to aspirin or who have failed aspirin therapy (1.1)

### DOSAGE AND ADMINISTRATION

- Stroke: 50 mg once daily with food. (2.1)
- Coronary Stenting: 50 mg once daily with food, with antiplatelet doses of aspirin, for up to 30 days following stent implantation (2.2)

Discontinue in renally impaired patients if hemorrhagic or hematopoietic problems are encountered (2.3, 8.6, 12.3)

### DOSAGE FORMS AND STRENGTHS

Capsules: 50 mg (3)

### CONTRAINDICATIONS

- Hematopoietic disorders or a history of TTP or aplastic anemia (4)
- Hemostatic disorder or active bleeding (4)
- Severe hepatic impairment (4, 8.7)

### WARNING: LIFE-THREATENING HEMATOLOGICAL ADVERSE REACTIONS

See Full Prescribing Information for complete boxed warning.

Monitor for hematological adverse reactions every 2 weeks for first 3 months of treatment (5.2). Discontinue Imdicon immediately if any of the following occur:

- Neutropenia/agranulocytosis (5.1)
- Thrombotic thrombocytopenic purpura (5.1)
- Aplastic anemia (5.1)

- Hepatic impairment: Dose may need adjustment. Contraindicated in severe hepatic disease (4, 8.7, 12.3)
- Renal impairment: Dose may need adjustment (2.3, 8.6, 12.3)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling

Revised: 5/200X

# Example of Highlights for a Fictitious Drug

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Imdicon safely and effectively. See full prescribing information for Imdicon.

### IMDICON® (cholinazol) CAPSULES

Initial U.S.

WARNINGS	See
	Monitor for months of following of
•	Neutropenia/agranulocytosis (5.1)
•	Thrombotic thrombocytopenic purpura (5.1)
•	Aplastic anemia (5.1)

## RECENT MAJOR CHANGES

Indications and Usage, Coronary Stenting (1.2)	2/200X
Dosage and Administration, Coronary Stenting (2.2)	2/200X

## RECENT MAJOR CHANGES

Indications and Usage, Coronary Stenting (1.2)	2/200X
Dosage and Administration, Coronary Stenting (2.2)	2/200X

## INDICATIONS AND USAGE

Imdicon is an adenosine diphosphate (ADP) antagonist platelet aggregation inhibitor indicated for:

- Reducing the risk of thrombotic stroke in patients who have experienced stroke precursors or who have had a completed thrombotic stroke (1.1)
- Reducing the incidence of subacute coronary stent thrombosis, when used with aspirin (1.2)

Important limitations:

- For stroke, Imdicon should be reserved for patients who are intolerant of or allergic to aspirin or who have failed aspirin therapy (1.1)

## DOSAGE AND ADMINISTRATION

- Stroke: 50 mg once daily with food. (2.1)
- Coronary Stenting: 50 mg once daily with food, with antiplatelet doses of aspirin, for up to 30 days following stent implantation (2.2)

Discontinue in renally impaired patients if hemorrhagic or hematopoietic problems are encountered (2.3, 8.6, 12.3)

## DOSAGE FORMS AND STRENGTHS

Capsules: 50 mg (3)

## CONTRAINDICATIONS

leukemia, and thrombocytopenia can occur (5.1)
• Monitor for hematological adverse reactions every 2 weeks through the third month of treatment (5.2)

## ADVERSE REACTIONS

Most common adverse reactions (incidence >2%) are diarrhea, nausea, dyspepsia, rash, gastrointestinal pain, neutropenia, and purpura (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact (manufacturer) at (phone # and Web address) or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

## DRUG INTERACTIONS

- Anticoagulants: Discontinue prior to switching to Imdicon (5.3, 7.1)
- Phenytoin: Elevated phenytoin levels have been reported. Monitor levels. (7.2)

## USE IN SPECIFIC POPULATIONS

- Hepatic impairment: Dose may need adjustment. Contraindicated in severe hepatic disease (4, 8.7, 12.3)
- Renal impairment: Dose may need adjustment (2.3, 8.6, 12.3)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling

Revised: 5/200X

# Example of Highlights for a Fictitious Drug

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Imdicon safely and effectively. See full prescribing information for Imdicon.

## -----DOSAGE FORMS AND STRENGTHS-----

Capsules: 50 mg (3)

IMDICON®  
Initial U.S. Approval: 2014

## -----INDICATIONS AND USAGE-----

**Imdicon is an adenosine diphosphate (ADP) antagonist platelet aggregation inhibitor indicated for:**

**Reducing the risk of thrombotic stroke in patients who have experienced stroke precursors or who have had a completed thrombotic stroke (1.1)**

**Reducing the incidence of subacute coronary stent thrombosis, when used with aspirin (1.2)**

**Important limitations:**

**For stroke, Imdicon should be reserved for patients who are intolerant of or allergic to aspirin or who have failed aspirin therapy (1.1)**

## -----USE IN SPECIFIC POPULATIONS-----

- Hepatic impairment: Dose may need adjustment. Contraindicated in severe hepatic disease (4, 8.7, 12.3)
- Renal impairment: Dose may need adjustment (2.3, 8.6, 12.3)

**See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling**

Revised: 5/200X

## WARNING:

*See full prescribing information for complete details.*  
**Monitor for hemorrhage in patients who have been on Imdicon for several months of treatment following occurrence of:**

- Neutropenia
- Thrombocytopenia
- Aplastic anemia

Indications and Usage  
Dosage and Administration

Imdicon is an ADP antagonist platelet aggregation inhibitor indicated for:

- Reducing the risk of thrombotic stroke in patients who have experienced stroke precursors or who have had a completed thrombotic stroke (1.1)
- Reducing the incidence of subacute coronary stent thrombosis, when used with aspirin (1.2)

Important limitations:

- For stroke, Imdicon should be reserved for patients who are intolerant of or allergic to aspirin or who have failed aspirin therapy (1.1)

## -----DOSAGE AND ADMINISTRATION-----

- Stroke: 50 mg once daily with food. (2.1)
- Coronary Stenting: 50 mg once daily with food, with antiplatelet doses of aspirin, for up to 30 days following stent implantation (2.2)

Discontinue in renally impaired patients if hemorrhagic or hematopoietic problems are encountered (2.3, 8.6, 12.3)

# Example of Highlights for a Fictitious Drug

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Imdicon safely and effectively. See full prescribing information for Imdicon.

## IMDICON® (cholinasol) CAPSULES

Initial U.S. Approval: 2000

### WARNING: LIFE-THREATENING HEMATOLOGICAL ADVERSE REACTIONS

See full prescribing information for complete details. Monitor for hematology abnormalities during the first 6 months of treatment. The following occur:

- Neutropenia
- Thrombocytopenia
- Aplastic anemia

Indications and Usage  
Dosage and Administration

Imdicon is an acetylcholinesterase inhibitor indicated for:

- Reducing the risk of thrombotic stroke in patients who have experienced stroke precursors or who have had a completed thrombotic stroke (1.1)
- Reducing the incidence of subacute coronary stent thrombosis, when used with aspirin (1.2)

Important limitations:

- For stroke, Imdicon should be reserved for patients who are intolerant of or allergic to aspirin or who have failed aspirin therapy (1.1)

### -----DOSAGE AND ADMINISTRATION-----

**Stroke: 50 mg once daily with food. (2.1)**  
**Coronary Stenting: 50 mg once daily with food, with antiplatelet doses of aspirin, for up to 30 days following stent implantation (2.2)**  
**Discontinue in renally impaired patients if hemorrhagic or hematopoietic problems are encountered (2.3, 8.6, 12.3)**

### -----DOSAGE AND ADMINISTRATION-----

- Stroke: 50 mg once daily with food. (2.1)
- Coronary Stenting: 50 mg once daily with food, with antiplatelet doses of aspirin, for up to 30 days following stent implantation (2.2)

Discontinue in renally impaired patients if hemorrhagic or hematopoietic problems are encountered (2.3, 8.6, 12.3)

### -----DOSAGE FORMS AND STRENGTHS-----

Capsules: 50 mg (3)

### -----CONTRAINDICATIONS-----

- Hematopoietic disorders or a history of TTP or aplastic anemia (4)
- Hemostatic disorder or active bleeding (4)
- Severe hepatic impairment (4, 8.7)

### -----DRUG INTERACTIONS-----

- Anticoagulants: Discontinue prior to switching to Imdicon (5.3, 7.1)
- Phenytoin: Elevated phenytoin levels have been reported. Monitor levels. (7.2)

### -----USE IN SPECIFIC POPULATIONS-----

- Hepatic impairment: Dose may need adjustment. Contraindicated in severe hepatic disease (4, 8.7, 12.3)
- Renal impairment: Dose may need adjustment (2.3, 8.6, 12.3)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling

Revised: 5/200X

# Example of Highlights for a Fictitious Drug

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Imdicon safely and effectively. See full prescribing information for Imdicon.

### IMDICON® (cholinazol) CAPSULES

Initial U.S. Approval: 2000

#### WARNING: LIFE-THREATENING HEMATOLOGICAL ADVERSE REACTIONS

See full prescribing information for complete boxed warning.

Monitor for hematological adverse reactions every 2 weeks for first 3 months of treatment (5.2). Discontinue Imdicon immediately if any of the following occur:

- 
- 
- 

#### -----DOSAGE FORMS AND STRENGTHS----- Capsules: 50 mg (3)

Indications and Usage, Coronary Stenting (1.2) 2/200X  
Dosage and Administration, Coronary Stenting (2.2) 2/200X

#### -----INDICATIONS AND USAGE-----

Imdicon is an adenosine diphosphate (ADP) antagonist platelet aggregation inhibitor indicated for:

- Reducing the risk of thrombotic stroke in patients who have experienced stroke precursors or who have had a completed thrombotic stroke (1.1)
- Reducing the incidence of subacute coronary stent thrombosis, when used with aspirin (1.2)

Important limitations:

- For stroke, Imdicon should be reserved for patients who are intolerant of or allergic to aspirin or who have failed aspirin therapy (1.1)

#### -----DOSAGE AND ADMINISTRATION-----

- Stroke: 50 mg once daily with food. (2.1)
- Coronary Stenting: 50 mg once daily with food, with antiplatelet doses of aspirin, for up to 30 days following stent implantation (2.2)

Discontinue in renally impaired patients if hemorrhagic or hematopoietic problems are encountered (2.3, 8.6, 12.3)

#### -----DOSAGE FORMS AND STRENGTHS-----

Capsules: 50 mg (3)

#### -----CONTRAINDICATIONS-----

- Hematopoietic disorders or a history of TTP or aplastic anemia (4)
- Hemostatic disorder or active bleeding (4)
- Severe hepatic impairment (4, 8.7)

#### -----WARNINGS AND PRECAUTIONS-----

- Neutropenia (2.4 % incidence; may occur suddenly; typically resolves within 1-2 weeks of discontinuation), thrombotic thrombocytopenic purpura (TTP), aplastic anemia, agranulocytosis, pancytopenia

To report SUSPECTED ADVERSE REACTIONS, contact (manufacturer) at (phone # and Web address) or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

#### -----DRUG INTERACTIONS-----

- Anticoagulants: Discontinue prior to switching to Imdicon (5.3, 7.1)
- Phenytoin: Elevated phenytoin levels have been reported. Monitor levels. (7.2)

#### -----USE IN SPECIFIC POPULATIONS-----

- Hepatic impairment: Dose may need adjustment. Contraindicated in severe hepatic disease (4, 8.7, 12.3)
- Renal impairment: Dose may need adjustment (2.3, 8.6, 12.3)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling

Revised: 5/200X

# Example of Highlights for a Fictitious Drug

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Imdicon safely and effectively. See full prescribing information for Imdicon.

### IMDICON® (cholinasol) CAPSULES

Initial U.S. Approval: 2000

#### WARNING: LIFE-THREATENING HEMATOLOGICAL ADVERSE REACTIONS

See full prescribing information for complete boxed warning.

Monitor for hematological adverse reactions every 2 weeks for first 3 months of treatment (5.2). Discontinue Imdicon immediately if any of the following occur:

- Neutropenia/agranulocytosis (5.1)
- Thrombotic thrombocytopenic purpura (5.1)
- Aplastic anemia (5.1)

#### CONTRAINDICATIONS

Hematopoietic disorders or a history of TTP or aplastic anemia (4)  
Hemostatic disorder or active bleeding (4)  
Severe hepatic impairment (4, 8.7)

#### DOSAGE FORMS AND STRENGTHS

Capsules: 50 mg (3)

#### CONTRAINDICATIONS

- Hematopoietic disorders or a history of TTP or aplastic anemia (4)
- Hemostatic disorder or active bleeding (4)
- Severe hepatic impairment (4, 8.7)

#### WARNINGS AND PRECAUTIONS

- Neutropenia (2.4 % incidence; may occur suddenly; typically resolves within 1-2 weeks of discontinuation), thrombotic thrombocytopenic purpura (TTP), aplastic anemia, agranulocytosis, pancytopenia, leukemia, and thrombocytopenia can occur (5.1)
- Monitor for hematological adverse reactions every 2 weeks through the third month of treatment (5.2)

#### DRUG INTERACTIONS

- Anticoagulants: Discontinue prior to switching to Imdicon (5.3, 7.1)
- Phenytoin: Elevated phenytoin levels have been reported. Monitor levels. (7.2)

#### USE IN SPECIFIC POPULATIONS

- Hepatic impairment: Dose may need adjustment. Contraindicated in severe hepatic disease (4, 8.7, 12.3)
- Renal impairment: Dose may need adjustment (2.3, 8.6, 12.3)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling

Revised: 5/200X

Indication  
Dosage and

Imdicon is  
inhibitor i

- Reducing the incidence of stroke precursors or who have had a completed thrombotic stroke (1.1)
- Reducing the incidence of subacute coronary stent thrombosis, when used with aspirin (1.2)

Important limitations:

- For stroke, Imdicon should be reserved for patients who are intolerant of or allergic to aspirin or who have failed aspirin therapy (1.1)

#### DOSAGE AND ADMINISTRATION

- Stroke: 50 mg once daily with food. (2.1)
- Coronary Stenting: 50 mg once daily with food, with antiplatelet doses of aspirin, for up to 30 days following stent implantation (2.2)

Discontinue in renally impaired patients if hemorrhagic or hematopoietic problems are encountered (2.3, 8.6, 12.3)

1088

# Example of Highlights for a Fictitious Drug

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Imdicon safely and effectively. See full prescribing information for Imdicon.

### IMDICON® (cholinasol) CAPSULES

Initial U.S. Approval: 2000

#### WARNING: LIFE-THREATENING HEMATOLOGICAL ADVERSE REACTIONS

See full prescribing information for complete boxed warning.

Monitor for hematological adverse reactions every 2 weeks for first 3 months of treatment (5.2). Discontinue Imdicon immediately if any of the following occur:

- Neutropenia/agranulocytosis (5.1)
- Thrombotic thrombocytopenic purpura (5.1)
- Aplastic anemia (5.1)

-----**WARNINGS AND PRECAUTIONS**-----  
**Neutropenia (2.4 % incidence; may occur suddenly; typically resolves within 1-2 weeks of discontinuation), thrombotic thrombocytopenic purpura (TTP), aplastic anemia, agranulocytosis, pancytopenia, leukemia, and thrombocytopenia can occur (5.1)**  
**Monitor for hematological adverse reactions every 2 weeks through the third month of treatment (5.2)**

#### -----DOSAGE AND ADMINISTRATION-----

- Stroke: 50 mg once daily with food. (2.1)
- Coronary Stenting: 50 mg once daily with food, with antiplatelet doses of aspirin, for up to 30 days following stent implantation (2.2)

Discontinue in renally impaired patients if hemorrhagic or hematopoietic problems are encountered (2.3, 8.6, 12.3)

#### -----DOSAGE FORMS AND STRENGTHS-----

Capsules: 50 mg (3)

#### -----CONTRAINDICATIONS-----

- Hematopoietic disorders or a history of TTP or aplastic anemia (4)
- Hemostatic disorder or active bleeding (4)
- Severe hepatic impairment (4, 8.7)

#### -----WARNINGS AND PRECAUTIONS-----

- Neutropenia (2.4 % incidence; may occur suddenly; typically resolves within 1-2 weeks of discontinuation), thrombotic thrombocytopenic purpura (TTP), aplastic anemia, agranulocytosis, pancytopenia, leukemia, and thrombocytopenia can occur (5.1)
- Monitor for hematological adverse reactions every 2 weeks through the third month of treatment (5.2)

- Hepatic impairment: Dose may need adjustment. Contraindicated in severe hepatic disease (4, 8.7, 12.3)
- Renal impairment: Dose may need adjustment (2.3, 8.6, 12.3)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling

Revised: 5/200X



# Example of Highlights for a Fictitious Drug

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Imdicon safely and effectively. See full prescribing information for Imdicon.

### IMDICON® (cholinazol) CAPSULES

Initial U.S. Approval: 2000

#### WARNING: LIFE-THREATENING HEMATOLOGICAL ADVERSE REACTIONS

*See full prescribing information for complete boxed warning.*

Monitor for hematological adverse reactions every 2 weeks for first 3 months of treatment (5.2). Discontinue Imdicon immediately if any of the following occur:

- Neutropenia/agranulocytosis (5.1)
- Thrombotic thrombocytopenic purpura (5.1)
- Aplastic anemia (5.1)

#### RECENT MAJOR CHANGES

Indications and Usage, Coronary Stenting (1.2) 2/200X  
Dosage and Administration, Coronary Stenting (2.2) 2/200X

#### ADVERSE REACTIONS

Most common adverse reactions (incidence >2%) are diarrhea, nausea, dyspepsia, rash, gastrointestinal pain, neutropenia, and purpura (6.1). To report SUSPECTED ADVERSE REACTIONS, contact (manufacturer) at (phone # and Web address) or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

Discontinue in renally impaired patients if hemorrhagic or hematopoietic problems are encountered (2.3, 8.6, 12.3)

#### DOSAGE FORMS AND STRENGTHS

Capsules: 50 mg (3)

#### CONTRAINDICATIONS

- Hematopoietic disorders or a history of TTP or aplastic anemia (4)
- Hemostatic disorder or active bleeding (4)
- Severe hepatic impairment (4, 8.7)

#### WARNINGS AND PRECAUTIONS

- Neutropenia (2.4 % incidence; may occur suddenly; typically resolves within 1-2 weeks of discontinuation), thrombotic thrombocytopenic purpura (TTP), aplastic anemia, agranulocytosis, pancytopenia, leukemia, and thrombocytopenia can occur (5.1)
- Monitor for hematological adverse reactions every 2 weeks through the third month of treatment (5.2)

#### ADVERSE REACTIONS

Most common adverse reactions (incidence >2%) are diarrhea, nausea, dyspepsia, rash, gastrointestinal pain, neutropenia, and purpura (6.1).

#### SUSPECTED ADVERSE REACTIONS

approved patient labeling

Revised: 5/200X

# Example of Highlights for a Fictitious Drug

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Imdicon safely and effectively. See full prescribing information for Imdicon.

## IMDICON® (cholinasol) CAPSULES

Initial U.S. Approval: 2000

### WARNING: LIFE-THREATENING HEMATOLOGICAL ADVERSE

### -----DRUG INTERACTIONS-----

- **Anticoagulants: Discontinue prior to switching to Imdicon (5.3, 7.1)**
- **Phenytoin: Elevated phenytoin levels have been reported. Monitor levels. (7.2)**

### -----RECENT MAJOR CHANGES-----

Indications and Usage, Coronary Stenting (1.2)	2/200X
Dosage and Administration, Coronary Stenting (2.2)	2/200X

### -----INDICATIONS AND USAGE-----

Imdicon is an adenosine diphosphate (ADP) antagonist platelet aggregation inhibitor indicated for:

- Reducing the risk of thrombotic stroke in patients who have experienced stroke precursors or who have had a completed thrombotic stroke (1.1)
- Reducing the incidence of subacute coronary stent thrombosis, when used with aspirin (1.2)

Important limitations:

- For stroke, Imdicon should be reserved for patients who are intolerant of or allergic to aspirin or who have failed aspirin therapy (1.1)

### -----DOSAGE AND ADMINISTRATION-----

- Stroke: 50 mg once daily with food. (2.1)
- Coronary Stenting: 50 mg once daily with food, with antiplatelet doses of aspirin, for up to 30 days following stent implantation (2.2)

Discontinue in renally impaired patients if hemorrhagic or hematopoietic problems are encountered (2.3, 8.6, 12.3)

### -----DOSAGE FORMS AND STRENGTHS-----

Capsules: 50 mg (3)

### -----CONTRAINDICATIONS-----

- Hematopoietic disorders or a history of TTP or aplastic anemia (4)
- Hemostatic disorder or active bleeding (4)
- Severe hepatic impairment (4, 8, 7)

Most common adverse reactions (incidence >2%) are diarrhea, nausea, dyspepsia, rash, gastrointestinal pain, neutropenia, and purpura (6.1).

**To report SUSPECTED ADVERSE REACTIONS, contact (manufacturer) at (phone # and Web address) or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).**

### -----DRUG INTERACTIONS-----

- Anticoagulants: Discontinue prior to switching to Imdicon (5.3, 7.1)
- Phenytoin: Elevated phenytoin levels have been reported. Monitor levels. (7.2)

### -----USE IN SPECIFIC POPULATIONS-----

- Hepatic impairment: Dose may need adjustment. Contraindicated in severe hepatic disease (4, 8.7, 12.3)
- Renal impairment: Dose may need adjustment (2.3, 8.6, 12.3)

**See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling**

Revised: 5/200X

# Example of Highlights for a Fictitious Drug

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Imdicon safely and effectively. See full prescribing information for Imdicon.

## IMDICON® (cholinazol) CAPSULES

Initial U.S. Approval: 2000

## -----DOSAGE FORMS AND STRENGTHS-----

Capsules: 50 mg (3)

## -----CONTRAINDICATIONS-----

- Hematopoietic disorders or a history of TTP or aplastic anemia (4)

## -----USE IN SPECIFIC POPULATIONS-----

**Hepatic impairment: Dose may need adjustment. Contraindicated in severe hepatic disease (4, 8.7, 12.3)**

**Renal impairment: Dose may need adjustment (2.3, 8.6, 12.3)**

## -----RECENT MAJOR CHANGES-----

Indications and Usage, Coronary Stenting (1.2) 2/200X  
Dosage and Administration, Coronary Stenting (2.2) 2/200X

## -----INDICATIONS AND USAGE-----

Imdicon is an adenosine diphosphate (ADP) antagonist platelet aggregation inhibitor indicated for:

- Reducing the risk of thrombotic stroke in patients who have experienced stroke precursors or who have had a completed thrombotic stroke (1.1)
- Reducing the incidence of subacute coronary stent thrombosis, when used with aspirin (1.2)

Important limitations:

- For stroke, Imdicon should be reserved for patients who are intolerant of or allergic to aspirin or who have failed aspirin therapy (1.1)

## -----DOSAGE AND ADMINISTRATION-----

- Stroke: 50 mg once daily with food. (2.1)
- Coronary Stenting: 50 mg once daily with food, with antiplatelet doses of aspirin, for up to 30 days following stent implantation (2.2)

Discontinue in renally impaired patients if hemorrhagic or hematopoietic problems are encountered (2.3, 8.6, 12.3)

## -----ADVERSE REACTIONS-----

Most common adverse reactions (incidence >2%) are diarrhea, nausea, dyspepsia, rash, gastrointestinal pain, neutropenia, and purpura (6.1).

**To report SUSPECTED ADVERSE REACTIONS, contact (manufacturer) at (phone # and Web address) or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).**

## -----DRUG INTERACTIONS-----

- Anticoagulants: Discontinue prior to switching to Imdicon (5.3, 7.1)
- Phenytoin: Elevated phenytoin levels have been reported. Monitor levels. (7.2)

## -----USE IN SPECIFIC POPULATIONS-----

- Hepatic impairment: Dose may need adjustment. Contraindicated in severe hepatic disease (4, 8.7, 12.3)
- Renal impairment: Dose may need adjustment (2.3, 8.6, 12.3)

**See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling**

Revised: 5/200X

# Example of Highlights for a Fictitious Drug

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Imdicon safely and effectively. See full prescribing information for Imdicon.

## IMDICON® (cholinazol) CAPSULES

Initial U.S. Approval: 2000

### WARNING: LIFE-THREATENING HEMATOLOGICAL ADVERSE

**See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling**

Monitor monthly following

- Neutropenia/agranulocytosis (5.1)
- Thrombotic thrombocytopenic purpura (5.1)
- Aplastic anemia (5.1)

### RECENT MAJOR CHANGES

Indications and Usage, Coronary Stenting (1.2) 2/200X  
Dosage and Administration, Coronary Stenting (2.2) 2/200X

### INDICATIONS AND USAGE

Imdicon is an adenosine diphosphate (ADP) antagonist platelet aggregation inhibitor indicated for:

- Reducing the risk of thrombotic stroke in patients who have experienced stroke precursors or who have had a completed thrombotic stroke (1.1)
- Reducing the incidence of subacute coronary stent thrombosis, when used with aspirin (1.2)

Important limitations:

- For stroke, Imdicon should be reserved for patients who are intolerant of or allergic to aspirin or who have failed aspirin therapy (1.1)

### DOSAGE AND ADMINISTRATION

- Stroke: 50 mg once daily with food. (2.1)
- Coronary Stenting: 50 mg once daily with food, with antiplatelet doses of aspirin, for up to 30 days following stent implantation (2.2)

Discontinue in renally impaired patients if hemorrhagic or hematopoietic problems are encountered (2.3, 8.6, 12.3)

### DOSAGE FORMS AND STRENGTHS

Capsules: 50 mg (3)

### CONTRAINDICATIONS

- Hematopoietic disorders or a history of TTP or aplastic anemia (4)
- Hemostatic disorder or active bleeding (4)
- Severe hepatic impairment (4, 8.7)

- Monitor for hematological adverse reactions every 2 weeks through the third month of treatment (5.2)

### ADVERSE REACTIONS

Most common adverse reactions (incidence >2%) are diarrhea, nausea, dyspepsia, rash, gastrointestinal pain, neutropenia, and purpura (6.1).

**To report SUSPECTED ADVERSE REACTIONS, contact (manufacturer) at (phone # and Web address) or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).**

### DRUG INTERACTIONS

- Anticoagulants: Discontinue prior to switching to Imdicon (5.3, 7.1)
- Phenytoin: Elevated phenytoin levels have been reported. Monitor levels. (7.2)

### USE IN SPECIFIC POPULATIONS

- Hepatic impairment: Dose may need adjustment. Contraindicated in severe hepatic disease (4, 8.7, 12.3)
- Renal impairment: Dose may need adjustment (2.3, 8.6, 12.3)

**See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling**

Revised: 5/200X

# Test Your Knowledge

**True or False:** The *Adverse Reactions* section within the Highlights contains contact information for reporting suspected adverse reactions.

**Answer: True.** The *Adverse Reactions* section lists the telephone number and Web address for both the manufacturer and MedWatch, FDA's Adverse Event Reporting System.

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# **Contents and Full Prescribing Information**

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# FULL PRESCRIBING INFORMATION: CONTENTS

## **1 Navigational Tool**

1.1 to detailed safety information

1.2 to safety sections and subsections in the Full Prescribing Information

## **2 Ease of Reference**

2.1 electronic hyperlinks to sections in the Full Prescribing Information

# Example of Contents for a Fictitious Drug

## FULL PRESCRIBING INFORMATION: CONTENTS\*

### WARNING – LIFE-THREATENING HEMATOLOGICAL ADVERSE REACTIONS

#### 1 INDICATIONS AND USAGE

- 1.1 Thrombotic Stroke
- 1.2 Coronary Stenting

#### 2 DOSAGE AND ADMINISTRATION

- 2.1 Thrombotic Stroke
- 2.2 Coronary Stenting
- 2.3 Renally Impaired Patients

#### 3 DOSAGE FORMS AND STRENGTHS

#### 4 CONTRAINDICATIONS

#### 5 WARNINGS AND PRECAUTIONS

- 5.1 Hematological Adverse Reactions
- 5.2 Monitoring for Hematological Adverse Reactions
- 5.3 Anticoagulant Drugs
- 5.4 Bleeding Precautions
- 5.5 Monitoring: Liver Function Tests

#### 6 ADVERSE REACTIONS

- 6.1 Clinical Studies Experience
- 6.2 Postmarketing Experience

#### 7 DRUG INTERACTIONS

- 7.1 Anticoagulant Drugs
- 7.2 Phenytoin
- 7.3 Antipyrine and Other Drugs Metabolized Hepatically
- 7.4 Aspirin and Other Non-Steroidal Anti-Inflammatory Drugs
- 7.5 Cimetidine
- 7.6 Theophylline
- 7.7 Propranolol
- 7.8 Antacids
- 7.9 Digoxin
- 7.10 Phenobarbital
- 7.11 Other Concomitant Drug Therapy
- 7.12 Food Interaction

#### 8 USE IN SPECIFIC POPULATIONS

- 8.1 Pregnancy
- 8.3 Nursing Mothers
- 8.4 Pediatric Use
- 8.5 Geriatric Use
- 8.6 Renal Impairment
- 8.7 Hepatic Impairment

#### 10 OVERDOSAGE

#### 11 DESCRIPTION

#### 12 CLINICAL PHARMACOLOGY

- 12.1 Mechanism of Action
- 12.2 Pharmacodynamics
- 12.3 Pharmacokinetics

#### 13 NONCLINICAL TOXICOLOGY

- 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

#### 14 CLINICAL STUDIES

- 14.1 Thrombotic Stroke
- 14.2 Coronary Stenting

#### 16 HOW SUPPLIED/STORAGE AND HANDLING

#### 17 PATIENT COUNSELING INFORMATION

- 17.1 Importance of Monitoring
- 17.2 Bleeding
- 17.3 Hematological Adverse Reactions
- 17.4 FDA-Approved Patient Labeling

\*Sections or subsections omitted from the full prescribing information are not listed.



# Reorder and Reorganize

- “Indications and Usage” and “Dosage and Administration” sections moved
- “Dosage Forms and Strengths” created and “How Supplied” sections moved
- “Warnings and Precautions” sections consolidated
- “Drug Interactions,” “Use in Specific Populations,” and “Patient Counseling Information” sections added
- “Adverse Reactions” section consolidates risk information
- “Clinical Studies,” “Nonclinical Toxicology” sections now required

# Example

<b>Section in Previous Format</b>		<b>Section in Revised Format</b>
Warnings	→	Warnings and Precautions
Precautions		
General	→	Warnings and Precautions
Information for Patients	→	Patient Counseling Information
Monitoring: Laboratory Tests	→	Warnings and Precautions
Drug Interactions	→	Drug Interactions
Drug/Laboratory Test Interactions	→	Warnings and Precautions
Carcinogenesis, Mutagenesis, Impairment of Fertility	→	Nonclinical Toxicology (Carcinogenesis, Mutagenesis, Impairment of Fertility

# Test Your Knowledge

**Multiple Choice:** The most significant format and section reordering changes include:

- A) Moving the information practitioners refer to most frequently and consider most important to the bottom of the prescribing information
- B) Consolidating risk information
- C) Deleting the *Storage and Handling* section
- D) A and B
- E) All of the above

# New Section: *Drug Interactions*

- Drug interaction information typically appears in
  - section 7: *Drug Interactions* and
  - section 12: *Clinical Pharmacology*

# New Section: *Patient Counseling Information*

**Question:** Why does FDA require FDA-approved patient information to be reprinted in or accompany prescribing information when it also requires the *Patient Counseling Information* section?

**Answer:** The *Patient Counseling Information* section is written for healthcare professionals to remind them about what information is important to convey to the patient.

FDA-approved patient information (includes package inserts and medication guides), is written for a lay audience.



# New Section: *Patient Counseling Information*

**Question:** Will the *Patient Counseling Information* section be required for medications that are only administered in the hospital setting?

**Answer:** Yes, unless it is clearly inapplicable. There is almost always information about a drug that is important for the prescriber to convey to the patient, such as potential adverse drug reactions.

# Revisions and Improvements

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# Revisions

- Revises Safety Requirements
  - Contraindications
  - Warnings and Precautions
  - Adverse Reactions



# Revises Safety Requirements

- *Contraindications* section
  - Contraindication exists only when the risk clearly outweighs any possible therapeutic benefit
  - Includes only known hazards
    - No longer see “allergic to any component of the drug”
  - Order in which contraindications are listed is based on the likelihood of occurrence and the size of the population affected

# Revises Safety Requirements

- *Warnings and Precautions* section
  - Consolidates the *Warnings* section and the *Precautions* section
  - Includes *clinically significant adverse reactions*  
*Examples include:*
    - *Adverse reactions that require discontinuation, dose adjustment, or addition of another drug*
    - *Adverse reactions that could be prevented or managed with appropriate patient selection or avoidance of concomitant therapy*
    - *Adverse reactions that significantly affect patient compliance*

# Revises Safety Requirements

- *Adverse Reactions* section
  - *Requires separate listing of adverse reactions from clinical trial and postmarketing experience.*
  - *No longer contains the laundry lists of adverse reactions*

# Improvements

- Format Requires
  - Minimum 8-point font
  - Tables and bullets
  - Standardized bolding and white space
- Encourages Adverse Event Reporting, includes contact information

# Test Your Knowledge

**Multiple Choice:** What changes did FDA make to the prescription drug labeling to better communicate to healthcare professionals?

- A) Added the Highlights section which effectively organizes and chunks information into logical groups to enhance accessibility and retention
- B) Used graphic emphasis, such as standardized bolding and white space, to improve visual and cognitive access to information
- C) Limited the amount of text in the Dosage section
- D) A and B
- E) All of the above

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# Other Labeling Questions

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# Where Do I Find Microbiology Data?

	n	%	n	%
All patients with adverse events	240	86	234	85
Toothache <sup>1</sup>	143	51	113	41
Upper resp tract infection	81	29	72	26
Sinusitis	39	14	36	13
Bronchitis	17	6	8	3
Abscess	17	6	14	5
Gum hyperplasia	11	4	6	2
Pharyngitis	11	4	6	2
Arthrosis	8	3	6	2
Stomatitis ulcerative	8	3	3	1
Cellulitis	6	2	3	1

<sup>1</sup> Includes dental, gingival or mouth pain, tenderness, aching, throbbing, soreness, discomfort or sensitivity.

## 7 DRUG INTERACTIONS

There are no known drug interactions with FriendChip.

## 8 USE IN SPECIFIC POPULATIONS

### 8.1 Pregnancy

Pregnancy Category C. Animal reproduction studies have not been conducted in relation to FriendChip because animal models that would permit use of a clinically relevant route of administration are not available. Smilealot did not induce harm to the fetus when administered to rats by gavage at dosages up to 68 mg/kg/day. However, smilealot is known to be very poorly absorbed from the GI tract, therefore it is unclear whether these data are relevant to clinical use of FriendChip. Data from clinical studies suggest that substantial systemic exposure to smilealot does not occur [See *Clinical Pharmacology* (12.3)]. However, there are no adequate and well-controlled studies in pregnant women. It is not known whether FriendChip can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. FriendChip should be given to a pregnant woman only if clearly

chip insertion (mean:  $1445 \pm 764 \mu\text{g/mL}$ ), followed by a second peak at 72 hours (mean:  $1903 \pm 1074 \mu\text{g/mL}$ ). In a second study involving the insertion of 1 FriendChip under clinical conditions, the mean GCF level of smilealot peaked at  $1089 \pm 679 \mu\text{g/mL}$  at 4 hours. The mean GCF levels then declined in a highly erratic fashion to levels of  $483 \pm 448 \mu\text{g/mL}$  at 72 hours without producing a true second peak. The results of these studies confirm a high degree of intersubject variability in smilealot release from the FriendChip matrix *in vivo* that was not seen *in vitro*. Due to the nature and clinical use of the FriendChip dosage form, dose proportionality was not and would not be expected to be demonstrated between the two studies.

### 12.4 Microbiology

Studies with FriendChip showed reductions in the numbers of the putative periodontopathic organisms *Porphyromonas (Bacteriodes) gingivalis*, *Prevotella (Bacteriodes) intermedia*, *Bacteriodes forsythus*, and *Campylobacter rectus (Wolinella recta)* after placement of the chip. No overgrowth of opportunistic organisms or other adverse changes in the oral microbial ecosystem were noted. The relationship of the microbial findings to clinical outcome has not been established.

## 13 NONCLINICAL TOXICOLOGY

### 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Smilealot has not been evaluated for carcinogenic potential in connection with the FriendChip. No evidence that smilealot has potential to cause genetic toxicity was obtained in mutagenicity studies, including (*in vitro*) an Ames assay, a chromosome aberration assay in CHO cells, and (*in vivo*) a micronucleus assay conducted in mice.

## 14 CLINICAL STUDIES

In two double-blind, randomized, controlled clinical trials, 555 adult patients with periodontitis were entered who had at least 4 pockets with probing depth of 5-8 mm that bled on probing. Diabetics and patients with acutely abscessed periodontal pockets were excluded from the studies. The effects of scaling and root planing (SRP) alone, and SRP followed by FriendChip treatment, were compared. All patients received full mouth SRP

# Why Is Some Information in More Than One Section of the New Labeling?

- Important and appropriate to repeat some information in more than one section
- One section contains the detail; other sections contain a brief description with a cross-reference



# Drug Interaction Information

- Details in section 7: *Drug Interactions*
- Other sections briefly discuss interactions and cross-reference details
- Dose adjustments in section 2: *Dosage and Administration*
- Study details in section 12: *Clinical Pharmacology*

# Where Do I Find Dose Adjustment Information?

- Section 2 (DOSAGE AND ADMINISTRATION)  
Recommended dose regimen and dose adjustments for the drug.
- Section 7 (DRUG INTERACTIONS)  
May include instructions for dose adjustments for concomitant medications.

# Example – Fictitious Drug HIVAVIR

<b>Interaction Results</b>	<b>Section to find dose adjustment information for HIVAVIR in package insert</b>
HIVAVIR increases sinubact concentrations by 50%	Section 7: Drug interactions “A sinubact dose reduction up to 75% is recommended”
HIVAVIR concentrations are decreased by 60% when given with waramine	Section 2: DOSAGE AND ADMINISTRATION When coadministered with waramine the recommended dose of HIVAVIR is 500 mg once daily

# Case Study--HIVAVIR

LV is a 68 year old black male making a routine visit to his physician. LV's medical history includes depression and AIDS since April 23, 1999. Current medication profile includes:

- Hivavir 1000mg po qd
- Aidsudine 30mg po bid
- Deprexetine 20mg po q hs

LV reports no recent drug or alcohol use and has very good self-reported adherence with antiretroviral therapy. However, lab results showed LV's Hivavir concentration was suboptimal.

# Case Study - HIVAVIR

## Question:

To rule out a drug-food interaction and/or a drug-drug interaction involving Hivavir, LV's physician references which section(s) of the labeling?

## Answer:

section 7: Drug Interactions

(7.1 Deprexetine & 7.5 Food Interactions)

section 5: Warnings and Precautions

section 2: Dosage and Administration

section 12: Clinical Pharmacology

# Case Study - HIVAVIR

After Hivavir was marketed, FDA began receiving reports of life-threatening hematological reactions. As a result the labeling was revised.

**Question:** Which section(s) of the Highlights should LV's physician read to learn more?

**Answer:** Boxed Warning  
Recent Major Changes  
Warnings and Precautions

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# **FDA Electronic Labeling Initiatives**

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# Electronic Labeling Initiatives

## Structured Product Labeling

➔ standardized electronic file format

## Daily Med

➔ downloadable labeling resource



# Facts@FDA

Health information suppliers can download available content of labeling in structured product labeling format here.

[Link to download zip file](#)



For information on structured product labeling please see the [Structured Product Labeling Resources](#) web page.

<http://www.fda.gov/cder/news/FactsatFDA.htm>



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<http://dailymed.nlm.nih.gov>

# Resources on FDA's Web Page

<http://www.fda.gov/cder/regulatory/physLabel/default.htm>

- Final Rule
- Labeling Guidances
- Fictitious Examples of Revised Prescribing Information
- Information for Healthcare Professionals

# How Can I Contact FDA with Questions?

- (888) INFO-FDA
- [druginfo@fda.hhs.gov](mailto:druginfo@fda.hhs.gov)