FDA MedWatch and Patient Safety

Norman S Marks, MD, MHA
Medical Director, MedWatch
Office of the Commissioner
U S Food and Drug Administration
FDA MedWatch and Patient Safety
Some Context for this Presentation

- **Patient Safety** is on the agenda of many in recent years
  - Congress
  - Professional organizations
  - Academia [NEJM, JAMA]

- FDA is ‘in the news’ daily over its performance in post-marketing safety surveillance for drugs/devices
  - Vioxx [myocardial infarction]
  - Drug-eluting stents; ICD’s [defibrillators]
FDA MedWatch and Patient Safety
Some Context for this Presentation

- **Patient safety** is important to all healthcare providers
  - .....even while keeping current on the safety of the drugs, devices and diagnostics is getting more difficult
- FDA often is the first to learn about new safety issues critical to patient safety and wants to share this safety information with clinicians and their patients at the point of care
- These unexpected safety issues are identified and evaluated by FDA only with help from point of care providers and patients
- **Postmarket events of interest to FDA:**
  - Adverse Events for drugs and devices
  - Product Quality Problems
  - Medication and device use errors
  - Therapeutic failures/inequivalence
FDA MedWatch and Patient Safety
How FDA Monitors the Safety of Drugs and Devices

• Pre-Market Review and Approval
  • FDA does not develop or routinely test products itself
  • FDA reviews the results of laboratory, animal, and human clinical testing done by companies

• Post-Market Monitoring for Safety
  • Careful review of adverse experiences with products once they are marketed is essential
Why Postmarketing Adverse Event Surveillance is Necessary?

• Despite extensive evaluation of safety during drug development...

there are significant limitations of phase 3 trials to identify safety signals before marketing
Limitations of phase 3 trials

The Five Too’s

- Too few - seldom more than 3000 pts
- Too simple – patients with complicated medical conditions excluded
- Too narrow – patients receiving concurrent meds are excluded
- Too median-aged – pediatric and elderly populations excluded
- Too brief – trials often no longer weeks to months; precluding identification of reactions due to long term use or latent effects
Reporting In to MedWatch
What, when, how and why to report

• What
  – All clinical medical products

• When
  – If serious

• How
  – Online, or mail/fax/phone

• Why
  – Every report can make a difference
Reporting In to MedWatch
What products to report on

• Drugs
  • Prescription
  • Over the Counter
• Medical Devices
• Biologics, except vaccines

• Special Nutritional Products
  • Dietary supplements
  • Infant formulas
  • Medical foods

• Cosmetics
Reporting In to MedWatch
What To Report

- **Serious Adverse Events**
  - Drugs, biologics, devices, cosmetics and special nutritional products

- **Product Quality Problems**
  - Suspect counterfeit
  - Contamination, instability
  - Poor packaging, labeling
  - Defective components
  - Therapeutic failures

- **Medication and Device Use Errors**

- **Therapeutic Failures**
Any event that …

- Is fatal
- Is life-threatening
- Is permanently/significantly disabling
- Requires or prolongs hospitalization
- Causes a congenital anomaly
- Requires intervention to prevent permanent impairment or damage
Reporting to MedWatch

How to Report?

Phone (800-332-1088)
Fax
Mail

Online application for direct submission
www.fda.gov/medwatch/report.htm

Fillable pdf versions of voluntary form
offered for desktop use and submission by mail/fax
www.fda.gov/medwatch/getforms.htm
### Reporting In to MedWatch

#### How to report

<table>
<thead>
<tr>
<th>Patient</th>
<th>Product</th>
<th>Description of Event or Problem</th>
<th>Reporter</th>
</tr>
</thead>
</table>

![MedWatch Form](image)

For VOLUNTARY reporting of adverse events, product problems and product use errors:

**OBSERVATION INFORMATION**

1. Patient's Name
2. Age
3. Sex
4. Race
5. Nationality
6. Date of Birth
7. Date of Last Use
8. Other Information

**ADVERSE EVENT PRODUCT PROBLEM OR COMPLAINT**

1. Description of Event or Problem
2. Reporter's Name
3. Date of Onset
4. Date of Resolution
5. Other Information

**PRODUCT INFORMATION**

1. Product Name
2. Lot or Batch Number
3. Date of Manufacture
4. Expiration Date
5. Other Information

**MATERIALS/PRODUCTS**

1. Characteristic of Material
2. Property of Material
3. Other Information

**RESPONSES TO USES**

1. Response to Use
2. Other Information

**OBSERVATION SUMMARY**

1. Summary
2. Other Information

**SUBMITTED BY**

1. Name
2. Title
3. Address
4. Phone Number
5. Email

*Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.*
Reporting In to MedWatch

Why Report?

Every report can make a difference

Walla Walla, WA – Oncologist
Sacramento, CA – Nurse
Houston, TX - Dentist
Tallahassee, FL – Pharmacist
Portland, ME – Physician Assistant

Even a few voluntary reports from individual reporters can become a ‘signal’ and lead to a label change or other FDA action.
What Happens to Your Report

• When you report an ADE for a drug or biologic
• When you report a product quality problem for a drug or device
• When you report a medication or device use error
What Happens to Your Report
When you report a serious adverse event

- Report captured in a database
- Database monitored by an FDA professional
- Review of a case series
- Consultation with medical review division and manufacturer
- Further epidemiological studies as needed
What Happens to Your Report
When you provide information on a serious ADE

Labeling or Educational Options

- Boxed Warning
  - Drug-drug, drug-food interaction warnings
  - Monitoring recommendations
  - Dosage adjustments for sub-populations
- Contraindications, Warnings, Precautions or Adverse Reactions
- Medication Guide
What Happens to Your Report
When you report a serious ADE

- Special programs - REMS
  - Prescribing or dispensing limitations
  - Laboratory testing documentation
  - Registries
- Product withdrawal
What Happens to Your Report
When you report a product quality problem

- **For problems due to:**
  - Product design
  - Manufacturing quality or distribution/storage
  - Counterfeit product

- **FDA can:**
  - Work with manufacturer to issue a recall of product
  - Request a modification in product design
  - Request a modification in manufacturing process
  - Improve instructions or warnings for use
What Happens to Your Report
When you report a medication or device use error

- **Errors and ‘near misses’**
  - All reports are monitored and evaluated

- **For errors due to:**
  - Name confusion of drugs
  - Packaging or labeling of drugs
  - Device use

- **FDA can:**
  - Request name change or modification
  - Request packaging/labeling changes
  - Modify instructions for device use
Each Report Can Make a Difference
Every Report Can Make a Difference
Novantrone - mitoxantrone

- Single voluntary MedWatch report received by FDA
- Safety Evaluator review of AERS database
- Further evaluation of ongoing data in phase 4 study
- Revision of boxed warning to include new monitoring recommendations
- DHCP letter and MedWatch alert issued
Single voluntary MedWatch report received by FDA

• Direct Report made 9/18/2004
• A 34 year-old woman with multiple sclerosis developed cardiogenic shock with an ejection fraction of 5% after being treated with mitoxantrone for 2 and ½ years. The patient needed a heart transplant.
Safety Evaluator review of AERS database

- There appear to be cases of mitoxantrone-induced cardiac toxicity at cumulative doses less than the current monitoring threshold of 100 mg/m²
Further evaluation of ongoing data in phase 4 study
RENEW Interim Analysis

- 15 patients had a decline in LVEF to < 50%
  - Cumulative doses 47.6 – 126 mg/m²
- 9 patients had LVEF measurements that decreased at least 10% but remained above 50% and mitoxantrone was discontinued
  - Cumulative doses 55.3 – 105.3 mg/m²
- These LVEF screenings were done at the discretion of the investigator
Revision of boxed warning to include new monitoring recommendations

- LVEF should be reevaluated by echocardiogram or MUGA prior to each dose administered to patients with MS.
- Baseline evaluation of LVEF by echocardiogram or MUGA should be performed.
- MS patients with a baseline LVEF < 50% should not be treated with Novantrone.
- Additional doses should not be administered to MS patients with a drop in LVEF to below 50% or a clinically significant reduction in LVEF.
Dear Healthcare Professional:

This letter is sent to you to supplement previously provided information concerning the risks of cardiotoxicity associated with NOVANTRONE (mitoxantrone for injection concentrate) treatment for multiple sclerosis (MS) ….. Reports received through postmarketing surveillance, have shown that diminished cardiac function may occur early on in the treatment with NOVANTRONE. ….. cardiac monitoring of MS patients should be performed at baseline and prior to administration of every dose of NOVANTRONE.
How MedWatch Sends Safety Information To You
MedWatch

**E-list notification and RSS feeds**

Listserve growth from 5K to 153,000 subscribers since 2002

RSS feed – over 1 million pageviews in December 2008

E-list notification example:

“Novartis and FDA notified healthcare professionals that cases of Pure Red Cell Aplasia (PRCA) have been reported in patients treated with mycophenolate mofetil (MMF) in combination with other immunosuppressive agents. MMF is metabolized to mycophenolic acid (MPA), the active ingredient in Myfortic and the active form of the drug. The WARNINGS and ADVERSE REACTIONS sections of the Myfortic Prescribing Information have been revised.”
MedWatch website
Safety Alert example
Drug Safety - FDA’s Risk Management focus
Opportunities for improved risk communication

“Beyond the Label” strategies

• Request that sponsor send DHCP letter
• Announce the information to the press
• Post the information on the FDA website
• Notify targeted organizations and enlist their help in disseminating information to members
• Send a notification by email/text message to individual or RSS feed to work setting
• Incorporate notification into workflow at point at which provider is considering the product

Transparency and public health role
Reaching Point-of-Care Providers With Timely and Actionable Safety Information
The Oral Sodium Phosphate example

✔ Announce the information to the press

“As a result of new safety information received, FDA is requiring the manufacturer of Visicol and OsmoPrep, the two OSPs available by prescription only, to add a Boxed Warning to the labeling for these products. FDA is also requiring that the manufacturer develop and implement a risk evaluation……”
FDA MedWatch
Post the information on the FDA MedWatch website

Oral Sodium Phosphate (OSP) Products for Bowel Cleansing (marketed as Visicol and OsmoPrep, and oral sodium phosphate products available without a prescription)

Audience: All healthcare professionals, consumers

Posted 12/11/2008 FDA has become aware of reports of acute phosphate nephropathy, a type of acute kidney injury, associated with the use of oral sodium phosphate products (OSP) for bowel cleansing prior to colonoscopy or other procedures. These products include the prescription products, Visicol and OsmoPrep, and OSPs available over-the-counter without a prescription as laxatives (e.g., Fleet Phospho-soda). In some cases when used for bowel cleansing, these serious adverse events have occurred in patients without identifiable factors that would put them at risk for developing acute kidney injury.

FDA is requiring the manufacturer of Visicol and OsmoPrep, the two OSPs available by prescription only, to add a Boxed Warning to the labeling for these products. FDA is also requiring that the manufacturer develop and implement a risk evaluation and mitigation strategy (REMS), which will include a Medication Guide, to ensure that the benefits of these products outweigh the risk of acute phosphate nephropathy and to conduct a postmarketing clinical trial to further assess the risk of acute kidney injury with use of these products. FDA recommends, in light of the risk of acute phosphate nephropathy, over-the-counter laxative OSP products should not be used for bowel cleansing. Consumers should only use OSPs for bowel cleansing pursuant to a prescription from a healthcare professional.

[December 11, 2008 - Drug Information Page - FDA]

FDA MedWatch

Send notification by email/text message to individual or work setting

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1. **Alternative channel to individuals who want to avoid another email message**

2. **Automatic populating of intranet information for medical centers, hospital systems**
FDA MedWatch

Notify targeted organizations and enlist their help in disseminating information to their members

Professional society webpage
MedWatch Partners program
Am Gastroenterological Association

Information for HCPs [FDA]

MedWatch safety alert posting
FDA MedWatch

Incorporate new safety information into workflow at point when provider is considering the product

• **Mobile drug references**
  – 650,000 registered users
  – 250,000 confirmed M.D.’s
  – 40,000 medical students

• **Regular updates of references weekly/monthly**

• **DocAlerts** notify physicians when updates are made, such as new drug approvals, additional indications, recalls
  – received by 5607 GI docs
  – received by over 131,000 primary care docs
FDA MedWatch

Incorporate new safety information into workflow at point when provider is considering the product.
FDA MedWatch and Patient Safety

Visit us online at
www.fda.gov/medwatch
Safety Information Resources for HCPs

FDA MedWatch and Patient Safety

MedWatch: Safety Information and Adverse Event Reporting

http://www.fda.gov/Safety/MedWatch/ucm133050.htm
Your Guide to Reporting Problems to the FDA

http://www.fda.gov/downloads/ForConsumers/ConsumerUpdates/UCM143112.pdf