Post-marketing Drug Safety Surveillance: Pharmacovigilance in FDA/CDER

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Divisions of Pharmacovigilance (DPV) Overview

- Neurology
- Cardiovascular, Renal
- Psychiatry, Dermatology, Dental
- Gastroenterology, Pulmonary, Allergy, Rheumatology
- Metabolic, Endocrine

- Anti-infectives, Transplant, Ophthalmology
- Hematology, Over The Counter
- Oncology
- Addiction, Anesthesia, Analgesia, Medical Imaging
- Bone, Reproductive, Urologic

Advance public health by **detecting** safety signals from multiple data sources

**Evaluate** the safety of drug and therapeutic biologic products

**Recommend** appropriate regulatory actions,

**Communicate** relevant safety information
Sources of Possible Safety Signals

- Routine Pharmacovigilance
  - FDA Adverse Event Reporting System (FAERS) containing Individual Case Safety Reports (ICSRs)
    - Hands-on review of ICSRs
    - Data mining
- Manufacturers’ Periodic Safety Update Reports
- Study results
- Medical literature
- Media
- New Drug Application (NDA) safety database
- Outside inquiry
- Foreign Regulatory Agencies
- Others
Uninterpretable vs Interpretable ICSR

- Male
- Sotalol on 2/11
- QT prolongation, ?
- Reported by patient’s wife

- Male, 59, diabetes, hypertension, hyperlipidemia, normal echo and baseline QTc 420 ms. On simvastatin, insulin.
- Metoprolol → Sotalol 2/11 (HTN, new AF)
- “Blacked out” on 3/17
- ER evaluation:
  - BP 130/82, HR 52, “both lower than usual”
  - Dehydration
  - Creatinine 2.5
  - QT markedly prolonged 520 ms
  - ECG non-sustained polymorphic VT
- Treatment: hydration, discontinuation of Sotalol, resolved QT and non-sustained VT
What Information Does Good Quality ICSRs Contain for Adequate Assessment of Safety Signals?

- Description of adverse event
- Suspected and concomitant product therapy details (e.g., dose, dates of therapy)
- Patient characteristics (e.g., age, sex), baseline medical condition, co-morbid condition, family history, other risk factors
- Documentation of the diagnosis
- Clinical course and outcomes
- Relevant therapeutic measures and laboratory data
- Dechallenge and rechallenge information
- Reporter contact information
- Any other relevant information

*Guidance for Industry - Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment, March 2005*
# The FAERS Database

## More Useful For

- Detecting Adverse Events
  - That are serious and unlabeled
  - With low or rare background rate
- Identifying
  - Potential risk factors
  - Trends or clinically significant emerging safety concerns

## Less Useful For

- Detecting Adverse Events
  - Related to worsening of pre-existing disease
  - Related to disease manifestations for which drug is indicated for
  - Events with long latency
Sources of Drug Safety Information

- Spontaneous Adverse Event Reports
- Clinical Trials
- Observational Studies
- Registries
- Clinical Pharmacology Studies
- Pharmacogenomic Studies
- Animal Toxicology Studies
- Product Quality Reports
- Social media?
March 2001 Draft Guidance on Postmarketing Reporting:

“Adverse experience information that is submitted to an applicant via the Internet (e.g., e-mail) should be reported to the FDA if the applicant has knowledge of the four basic elements for an individual case safety report. Applicants should review any Internet sites sponsored by them for adverse experience information, but are not responsible for reviewing any Internet sites that are not sponsored by them. However, if an applicant becomes aware of an adverse experience on an Internet site that it does not sponsor, the applicant should review the adverse experience and determine if it should be reported to the FDA.”
How Does FDA Handle Adverse Event (AE) Reports From Social Media?

• For purposes of reporting by companies to FDA, AE reports from social media should be treated as spontaneous reports
  – Spontaneous reports are unsolicited communications from individuals (e.g., health care professional, consumer) to a company or regulatory authority that describes a suspected adverse experience

• They are reviewed like any other spontaneous report
  – FDA applies the same review process for all reports, regardless of source or product type
How to Report to FDA MedWatch

• How to Report:
  – Online
    (www.fda.gov/medwatch)
  – Download the form
    • Mail
    • Fax 1–800–332–0178

• For questions about the form:
  – 1–800–332–1088
FDA Guidances for Industry That Discusses Minimum Data Set

