Post-Market Drug Safety: Current Initiatives & Future Directions

Paul J. Seligman, MD, MPH

Director

Office of Pharmacoepidemiology & Statistical Science

Center for Drug Evaluation and Research

Presentation Overview

- Program Review
- Current Efforts to Strengthen Surveillance/Safety Assessment
- Future Directions

Post-Marketing Risk Assessment Program

- Primary roles:
  - Tracking adverse events of marketed drugs (note: includes medication errors)
  - Monitoring the utilization of marketed drugs
  - Soliciting/performing population-based epidemiologic studies

Post-Marketing Risk Assessment Program (cont'd)

- Expanding/evolving roles:
  - Pre-marketing safety assessment
    - reviewer's template
    - pre-approval safety conferences
  - Medication error prevention (names, packaging)
  - Pharmacovigilance planning
    - ICH E2E guidance

Post-Marketing Risk Assessment Program (cont'd)

- Expanding/evolving roles:
  - Risk minimization action plans (RiskMAPs)
    - greater focus of staff, interactions with review divisions
  - Risk communication
    - MedWatch
      - list serve and partners
    - patient information
      - consumer medication information
      - emerging issues

Current Initiatives

- Voluntary Reporting
- Improved Surveillance
- Access to Population-based Data
- Strengthening Internal Processes

Current Initiatives - Voluntary Reporting

- Adverse Event Reporting System
  - Improvements
    - what we get
    - how we get it
    - how we use it
    - how we make it accessible

Voluntary Reporting (cont'd)

- Improve quality of reporting
  - "Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment"
    - good reporting practice
    - characteristics of a good case report
- Make reporting easier
  - For HCP/consumer
    - web-fillable, interactive, "push a button to populate a MedWatch form and submit to the FDA"
  - For industry
    - electronic reporting, more timely receipt and efficient processing of data, rulemaking

Voluntary Reporting (cont'd)

- Get more out of data
  - 3 million reports in AERS, 420,000+/year
  - Analytic tools (e.g., data mining)
- Make it more accessible
  - Emerging issues
  - NTIS quarterly abstract available on website
    - http://www.fda.gov/cder/aers/extract.htm
  - AERS 2 - in development for '07-'08

Current Initiatives - Surveillance

- Purposeful ("active") surveillance
  - NEISS-CADES
  - DILIN
  - DAWN
  - Request for Information
  - Database linkage
    - administrative
    - pharmacy
    - clinical (i.e., electronic medical record)
    - examples - CMS, HMO

Current Initiatives
Population-based Data

- Access to broader range
  - Population-based studies
    - currently evaluating RFP submissions
    - indirect access to US claims databases
  - GPRD
  - Linked databases
    - support studies as well as surveillance, e.g. CMS
    - methods development

Current Initiatives
Internal Processes

- Accountability
  - Over 1,300 reviews a year
  - Tracking recommendations
- Communication
  - Pre-approval safety conferences
  - Risk management
  - Routine face-to-face on high priority issues
- Process Improvement Teams

Future Directions…

Future Directions - I

- Science of safety
  - Mechanistic understanding of drug injury processes
  - Population variability, who is at risk
  - Treatment “empirical” and assessment “circumstantial” until we have markers for drug-induced injury
  - Better pre- and post-market assessment

Future Directions - II

- Enhanced clinical assessment methods
  - Pre- and post-market
  - Improved trial design
    - enrichment, adaptive designs
    - better utilization of existing data
  - Robust post-marketing assessment program

Future Directions - III

- Strengthen the post-marketing toolkit
  - AE/ME reporting
  - Drug utilization databases
  - “Active” surveillance
  - US claims-based health encounter data (indirect access) - methods development

Future Directions - IV

- Strengthening CDER
  - Staffing for enlarging mandate
    - review and evaluation of risk minimization action plans
  - Improve internal processes
    - work processes, roles/responsibilities
      - communication
      - information flow
      - tracking and accountability
      - priority setting

Future Directions - V

- Strengthening Partnerships
  - Federal agencies
    - CMS, AHRQ, CDC, NIH, HRSA
  - Academia
    - CERTs
  - Healthcare institutions
    - payers, providers
  - Sponsors
    - pre- and post-marketing responsibilities

Future Directions -VI

- Effective communication
  - Improve therapeutics
    - realizing benefits
    - minimizing risks
  - Enhance patient safety
  - Reduce medication errors
  - Healthcare system issue

DSaRM AC Meeting May 18-19, 2005

- Explore issues related to FDA's risk assessment program for marketed drugs
  - Advantages, disadvantages of current system
  - Ways to improve current system
- Outcomes
  - Current passive system good for detecting rare, serious events with short latency periods
  - Develop external relationships/alliances
  - Need for adequate funding
  - Need for additional research

Conclusions

- Detecting, assessing, managing, communicating the risks and benefits of drugs is complex and demanding

- Number of initiatives, planned and ongoing, aimed at improving post-marketing risk assessment

Conclusions (cont'd)

- Post-marketing period should be considered an equally important phase of drug development
- Broaden lifecycle approach to development and monitoring