Topics in Drug Safety

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Presentation Overview

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

Drug Safety Initiative

- IOM Study
  - Study Goals
    - Examine the FDA's current role and the role of others (e.g., sponsors, health professionals, hospitals, patients, other public agencies) in ensuring drug safety as part of the U.S. health care delivery system;
    - Identify strengths, weaknesses and limitations of the current system;
    - Make recommendations in the areas of organization, legislation, regulation, and resources to improve risk assessment, surveillance and the safe use of drugs

Drug Safety Initiative: Drug Safety Oversight Board

- What is it?
  - A group of government scientists, both internal and external to FDA and CDER, whose role is to advise the Center Director on matters related to
    - Internal dispute resolution
    - Internal standard setting
    - Drugs that should be placed on the proposed Drug Watch page
  - Most logistical details still being worked out!
    - http://www.fda.gov/cder/drug/DrugSafety/DSOBmeetings/default.htm

Drug Safety Initiative: Proposed Drug Watch Page

- Draft Guidance issued May 2005
- http://www.fda.gov/cder/guidance/6657dft.htm
- What is it?
  - An Internet web page through which FDA is proposing to communicate “emerging” drug safety information to
    - Consumers
    - Health care professionals
  - Communication will occur via posted Patient or Healthcare Professional Information Sheets (current)
  - Comments to draft guidance are under review

Post-Marketing Risk Assessment Program

- Primary roles:
  - Tracking adverse events of marketed drugs (note: includes medication errors)
  - Monitoring the utilization of marketed drugs
  - Population-based pharmacoepidemiologic 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
    - Risk Management Guidances
      - http://www.fda.gov/cder/guidances
        - » /5766.dft.pdf RiskMAPs
        - » /5765dft.pdf Premarketing
        - » /5767dft.pdf Pharmacovigilence
      - ICH E2E Guidance

Post-Marketing Risk Assessment Program (cont'd)

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

Current Efforts to Strengthen Surveillance/Safety Assessment

- Voluntary Reporting (AERS program)
- Improved Surveillance
- Access to Population-based Data
- Strengthening Internal Processes

Current Initiatives - Voluntary Reporting

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

Current Initiatives: 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

Current Initiatives: Voluntary Reporting (cont'd)

- Get more out of data
  - 3 million reports in AERS, 420,000+/year
  - Analytic tools (e.g., data mining)
  - Inferences constrained by inherent limitations
- 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
  - National Electronic Injury Surveillance System (NEISS-CADES)
  - Drug Induced Liver Injury Network (DILIN)
  - Drug Abuse Warning Network (DAWN)
  - Request for Information (RFI) on existing US active surveillance systems
    - Reviewing responses and will determine next steps
  - Database linkage opportunities
    - administrative
    - pharmacy
    - clinical (i.e., electronic medical record)
    - examples - CMS, HMO

Current Initiatives: Surveillance Population-based Data

- Access to broader range
  - Population-based studies
    - Procurement of epidemiologic data is pending
    - Indirect access to US claims databases
    - Inferences more reliable; but may not fully reflect "real world" use
  - GPRD
    - Longitudinal electronic medical record data→ Contract to access GPRD awarded September 27, 2004
  - 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: Critical Path
  - Mechanistic understanding of drug injury processes
  - Population variability, who is at risk
  - Statistical assessment of genetic data
  - 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
    - understanding benefits
    - minimizing risks
  - Enhance patient safety
  - Reduce medication errors
  - Healthcare system issues
    - Cost
    - Access
    - Changing demographics

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