New Streams of Risk Management

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PMDA Third Mid-term Plan for Safety Measures

- Enhance Collection of ADRs
- Improve the System and Process of ADRs Evaluation
- Establish the System to Utilize Electronic Healthcare Data
- Enhance Feedback of Safety Information
- Enhance Dissemination of Information to the Patients
- Promote Appropriate Safety Measures based on the J-RMP
- Enhance Post-marketing Safety Measures in Cooperation with Review Teams
- Improve Follow-ups of Safety Measures Conducted
Today’s Topics

- Risk Management Plan and Risk Managers
- New Initiatives for Safety Evaluation
  - Utilization of Electronic Healthcare Data
  - MID-NET Project
- New Regulation
  - Notification of Package Insert
In order to ensure the safety of drugs, it is important to conduct an appropriate management of the risks of drugs throughout their lifecycle.

J-RMP is a document summarizing the risk management for a drug.

J-RMP is required for new drugs for which approval applications are submitted after April 1st, 2013, and for some of generic drugs after August 26, 2014.

J-RMP should be reviewed at every milestone;
- Submission of periodical reports
- Completion of any post-marketing surveillance
- Taking additional safety measures
**Risk Management Plan**

**Safety Specification**
- important identified risks
- important potential risks
- important unknown risks due to missing information

**Pharmacovigilance Plan**
- Plan for activities of collecting information of individual risks
  - Routine: Collecting information of ADRs
  - Additional: EPPV
    - Post-marketing observational studies
    - Post-marketing clinical trials
    - Pharmacoepidemiologic studies, etc

**Risk Minimization Action Plan**
- Plan for safety measures taken to minimize individual risks
  - Routine: Package insert
    - Patients Drug Guide
  - Additional: EPPV
    - Additional communications to HCP
    - Additional communications to patients
    - Special management of use
    - Special education of physicians, etc
Development of J-RMP

- At the time of approval application of new drugs and a part of generic drugs, a draft of J-RMP is required to submit to PMDA. Then, the applicant and PMDA review team and a risk manager discuss and agree on the J-RMP before the approval.

- When PMDA judges that additional activities are necessary, MAH is required to conducting appropriate post-marketing safety measures based on the agreed J-RMP as a condition of an approval.

- Sharing a J-RMP document among healthcare professionals is important to ensure post-marketing safety of drugs.

- J-RMP is made public via PMDA website at the earliest availability.
Risk Managers in PMDA

- Risk Managers are liaison officers between the review teams and the post-market safety teams to develop the suitable safety measures.
- PMDA has 14 risk managers for 12 review teams.
“MIHARI” means a guard or a watch in Japanese.

MIHARI Project is

- To utilize electronic healthcare data (health insurance claim data, medical records, etc) in order to evaluate possible safety issues more quickly and more securely.
- Launched in FY2009.
Since 2009, we have conducted pilot studies

- To ensure access to existing electronic healthcare data (EHD) such as medical records and health insurance claim data.

- To develop pharmacoepidemiological methodology and technique to use EHD for quantitative risk evaluation of drugs and for evaluation of impact of regulatory safety actions.

We are establishing a framework for a secondary utilization of EHD to evaluate safety issues for taking safety actions.
**MID-NET Project**

- **MID-NET** (Medical Information Database Network) is a national project initiated by MHLW to establish the DB network for MIHARI Project to utilize electronic healthcare data for drug safety.

- **7 hospitals**
  - Kyushu Univ.
  - Saga Univ.
  - Kagawa Univ.
  - Hamamatsu Univ.
  - Univ. of Tokyo
  - Chiba Univ.
  - Kitasato Univ.

- **3 hospital groups** (incl. 16 hospitals)
  - Tohoku Univ.
  - Tokushukai group
  - NTT hospital group
  - Univ. of Tokyo
  - Chiba Univ.
Electronic healthcare data at 10 hub medical institutions will be retrieved and standardized for analysis and evaluation of ADR.

A standardized database of EHD and an analysis system has been already established in each of 10 co-operating medical institutions.

Data quality check and system validations are now being conducted.

Full-scale utilization of the MID-NET data is expected to start in 2018.
A new regulation on notification and publication of product safety information has been introduced into the Pharmaceuticals and Medical Devices Law and came into effect in November, 2014.

MAHs are required to make prior notification of product safety information at the start of marketing and at the time of their revisions.

After the notification, MAHs shall immediately publish the package insert on the PMDA website.
Items to be notified

Among sections in package insert, sections listed below by red and underlined letters shall be notified.

1. Date of preparation or revision
2. Japan Standard Commodity Classification Number
3. Therapeutic category
4. Regulatory classification
5. Name
6. Warnings
7. Contraindications
8. Description
9. Indications
10. Dosage and administration
11. Precautions
   - Precautions related to the indications
   - Precautions related to the dosage and administration
   - Careful administration
   - Important precautions
   - Drug interactions
   - Adverse reactions

   • Geriatric use
   • Use during pregnancy, delivery or lactation
   • Pediatric use
   • Effects on laboratory tests
   • Overdosage
   • Precautions concerning use
   • Other precautions
12. Pharmacokinetics
13. Clinical studies
14. Pharmacology
15. Physicochemistry
16. Precautions for handling
17. Conditions for approval
18. Packaging
19. References and request for literature should be made to:
20. Name and address of manufacturer or importer
The contents of product safety information are reviewed by a review team and a risk manager during approval review, and after approval, they are revised based on the consultation between PMDA and MAH based on the information collected in post-marketing surveillance.

Based on the consultation with PMDA, MAHs notify the package insert including product safety information to PMDA electronically via the Internet and then the package insert is published on the PMDA website.
PMDA English website

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