

Electronic Submission of ADR Report and Use of MedDRA/J

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Safety Division

Pharmaceutical and Food Safety Bureau MHLW

Toshihito Ikeda

Issuance of Doctor-letter

- Olanzapine : (Psychotropic agents)
Diabetic ketoacidosis and Coma
- Ticlopidine hydrochloride: (Thrombolytics)
TTP, Agranulocytosis, Serious Hepatic disorder
- Gefitinib: (Anti-non-small cell lung cancer agent)
Acute Lung disorder, Interstitial pneumonia
- Edaravone: (Agent for improvement of symptoms in acute phase of cerebral infarction)
Renal failure acute
- Quetiapine fumarate: (Psychotropic agents)
Diabetic ketoacidosis and Coma

Strengthening Safety Measures in Post-marketing phase

(Revision of Pharmaceutical Affairs Law)

Main points of the Revision

- To mandate Establishment of the division for Safety Measures in licensing of the drug
- To mandate appointment of the person responsible for Safety measures in licensing of the drug
- To require periodic Report on Infection in addition to ADR report, Submission of Reexamination and Reevaluation materials (in case of biologics)
- To clarify obligation to operate Safety Measures in the Industries and to prompt positive execution of the Safety Measures

Trend of ADR Reports

| Year | Industry | Hospital | Total |
|------|----------|----------|--------|
| 1995 | 14,288 | 1,859 | 16,147 |
| 1996 | 16,831 | 1,914 | 18,745 |
| 1997 | 17,504 | 3,730 | 21,234 |
| 1998 | 18,466 | 4,882 | 23,348 |
| 1999 | 20,031 | 5,502 | 25,533 |
| 2000 | 22,326 | 5,297 | 27,623 |
| 2001 | 22,451 | 4,094 | 26,545 |

ICH Topics on Safety Measures of PMS

- V1: PSUR (Periodic Safety Update Report)
Supplement to E2C Guideline
(Step 2 , September 2002 Washington)
- V2: Good Case Management Practices
GCMP DRAFT
(For Step 2, February 2003 Tokyo)
- V3: Prospective Planning of Pharmacovigilance
PPP: Adopted as a Topic (September 2002 Washington)
(Guideline drafting Start February 2003 Tokyo)

Periodic Safety Report

- Format of Periodic Safety Report and How to fill up the Document

(Notification from Director, Safety Division and Director, Evaluation and Licensing Division :11 November 2002)

1. Description of ADR and Infection from “Drug use results surveys” should be based on MedDRA/J
2. Description of AE from “Drug use results surveys”, “Special surveys” and “Post-marketing clinical trial” should be based on MedDRA/J
3. Description of ADR and Infection in “Individual ADR and Infection case report” should be based on MedDRA/J

Electronic Reporting of ADR

- ICH-E2B: Guideline (Step 4 ; July 1997)
- ICH-M2: Electronic Standards for the Transfer of Regulatory Information and Data (Reached consensus ; October 1999)
- Notifications
 - “Use of the Japanese Medical Dictionary for Regulatory Activities Terminology (MedDRA/J)” ; December 1999
 - “Specifications for messages and data items for transmitting individual cases safety reports” ; March 2001,
 - “ Specifications for messages and data items for transmitting individual cases safety reports for marketed drugs” ; May 2002

Status of FDA and EMEA

- FDA

Pharmaceutical Industries Implemented (5)

Bristol-Myers Squibb

GlaxoSmithKline

Johnson & Johnson

Merck

Roche

- EMEA

Implement January 2003 ?

Status of MedDRA Implementation

- Japan (as of June 2002)
 - Approximate 30% of Total Reports in MedDRA/J
 - Approximate 100 industries Implemented
 - Made Mandatory from October 2003
- FDA
 - Several industries report in MedDRA
 - Others report in COSTART
 - Full Implementation not fixed yet
- EMEA
 - Made Mandatory from January 2003

Steps for Implementation in Japan

- Large scale Test Trial (155 Industries Participated)
- Symposium (End of November 2002)
- Cipher code and Attestation
- Development of ICSR Transmission System
- Test by MHLW just before Implementation
- Development of Data base