and to assess how the product is used in relation to terms of licence of marketing approval.

Methods: A post-marketing surveillance study using the observational cohort technique of Modified-Prescription Event Monitoring (M-PEM) is ongoing. Patients were identified from prescriptions (Rx) issued by primary care doctors from September 2008. Questionnaires sent 12 months after patient's first Rx capture demographic, drug utilisation and event data. Summary descriptive statistics were calculated; 'off label' use was defined according to the summary of product characteristics (SPC) at time of study.[1]

Results: 10 848 M-PEM forms were sent, 5986 (55.2%) were returned of which 3276 (54.7%) were reviewed at interim, giving a valid cohort of 2236. Median age was 43 yrs (IQR 33-56), 915 (40.9%) patients were male; 11 (0.5%) were aged <18 yrs and 280 (12.5%) were aged >65 yrs. Licensed primary indications of BD, schizophrenia and depression were reported for 52.1% of the cohort (1165/2236). [Primary indication refers to 1st reported indication (not in order of clinical importance)]. Non-licensed primary indications included anxiety (n = 166, 7.4%), personality disorder (n = 82, 3.7%), and dementia (n = 57, 2.6%). 68.8% of the cohort were prescribed a start dose of 50-300mg/day, as per the SPC. There were 835 reasons for stopping Seroquel XL reported for 683 pts; most frequently reported event/clinical events were 'not effective' (n = 129, 15.4%) and drowsiness/sedation (n = 57, 6.8%). 5 pregnancies were reported.

Conclusions: The interim results of this post-marketing surveillance study indicate there is some prescribing of Seroquel XL outside the terms of licence, including SPC recommendations for age and indication.

Reference

1. AstraZeneca UK Limited. Summary of product characteristics: Quetiapine (Seroquel XL) 2010 August 26 [online]. Available from URL: http://www.medicines.org.uk/EMC/medicine/21175/SPC/Seroquel+XL+50+mg%2c+150mg%2c+200+mg%2c+300+mg%2c+400+mg+prolonged-release+tablets/

PP078. FDA Final Rule on IND Safety Reporting: Impact to Your Clinical Studies

S. Van Doren
BioSoteria, Inc., Emeryville, CA, USA

The FDA announced changes to the regulations on IND safety reporting, which went into effect on March 28, 2011, (although it may not be enforced until September 29, 2011).

This final rule which codifies the FDA's expectations for timely review, evaluation, and submission of relevant and useful safety information of drug and biologic products subject to an investigational new drug (IND) application. The final rule amends parts 312 and 320 of FDA regulations by revising the requirements for IND safety reporting and for bioavailability and bioequivalence studies. The IND regulation changes involve: clarification of several definitions, what safety information to report and when (including additional safety information required for expedited reporting) and various other clarifications related to IND safety reporting.

The new rule requires that certain safety information now be reported within 15 days of becoming aware of an occurrence. These reports include findings from clinical or epidemiological studies that suggest a significant risk to study participants; serious suspected adverse reactions that occur at a rate higher than described in the IB; and SAEs from bioavailability and bioequivalence studies, among other changes. Along with this final rule, the FDA issued a draft guidance for industry and investigators that provides information and advice about the new requirements. Dr. Van Doren will review how these regulatory changes may impact your ongoing and future clinical trials.

References

1. Federal Register, September 29, 2010, p59936

2. U.S. Code of Federal Regulations (CFR) sections 312 and 320. "Guidance to Industry and Investigators: Safety Reporting Requirements for IND and BA/BE Studies"

PP079. Reliability of the Reported Ingested Dose of Acetaminophen for Predicting the Risk of Toxicity in Acetaminophen Overdose Patients

S.H. Zyoud,[1] *R. Awang,*[1] *S. Syed Sulaiman*[2] and *S.W. Al Jabi*[2]
1 WHO Collaborating Centre for Drug Information, National Poison Centre, Universiti Sains Malaysia (USM), Penang, Malaysia; 2 Clinical Pharmacy Program, School of Pharmaceutical Sciences, Universiti Sains Malaysia (USM), Penang, Malaysia

Objectives: The present study examines the relationship between the dose of acetaminophen reported to have been ingested by patients and the occurrence of serum acetaminophen levels above the 'possible toxicity' line in patients presenting at the hospital after acetaminophen overdose. The prognostic value of patient-reported dosage cut-offs of 8 g, 10 g and 12 g was determined.

Methods: This retrospective cohort study included patients admitted to the emergency department or hospital within 24 hours of acetaminophen ingestion. Serum acetaminophen concentrations were considered to be the gold standard, and specificity, sensitivity, and positive/negative predictive values were calculated from the reported ingested dose, to predict toxicity using the Rumack–Matthew nomogram (i.e. the 'possible toxicity' treatment line) and standard equations.[1,2]

Results: Of 305 patients identified, 291 met the study inclusion criteria, and 121 (41.6%) had serum acetaminophen concentrations above the 'possible toxicity' treatment line. The range of patient-reported acetaminophen ingested was 1–75 g, with 185 patients (63.6%) reporting ≥8 g. 118 patients (97.5%) who reported ingesting ≥8 g had serum acetaminophen concentrations above the '150-line', compared with only 3 patients (2.5%) who reported ingesting < 8 g ($p < 0.001$). The positive predictive value of a patient-reported dose ≥8 g for predicting serum acetaminophen concentrations above the 'possible toxicity' treatment line was 63.78%, with a negative predictive value of 97.17%. The sensitivity of patient-reported doses ≥8 g was high (97.52%), but with low specificity (60.59%). The sensitivity of patient-reported doses ≥10 g was also high (89.26%) with low specificity (65.29%), while the sensitivity of ≥12 g dose was low (61.16%) with high specificity (86.47%).

Conclusions: Patient-reported doses of acetaminophen are good risk indicators for acetaminophen overdose patients in Malaysia. Patient-reported ingestion of ≥8 g (as a cutoff dose) had a higher sensitivity than ≥10 g or ≥12 g. The results of this study have important implications for toxicity risk evaluations in areas with poor serum acetaminophen assay availability.

References

1. Rumack BH, Matthew H. Acetaminophen poisoning and toxicity. Pediatrics 1975; 55: 871-6

2. Rumack BH, Peterson RC, Koch GG, et al. Acetaminophen overdose. 662 cases with evaluation of oral acetylcysteine treatment. Arch Intern Med 1981; 141: 380-5