Background

The Specialist Cohort Event Monitoring (SCEM) registry study design is a new methodology developed parallel with the new legislative requirement for pharmaceutical companies to undertake a Risk Management Plan as part of post-authorisation safety monitoring. (9)

Sycrest® (asenapine) is a novel atypical antipsychotic agent launched January 2012 in the UK used in the treatment of moderate to severe manic episodes associated with bipolar I disorder in adults. 12 OBSERVA aims to monitor short term (up to 12 weeks) safety and drug utilisation of asenapine prescribed to patients by psychiatrists in the mental health care setting in England and Wales.

Objectives

1. To present the design and rationale of the OBSERVA study;
2. To discuss opportunities for pharmacists to expand their professional roles.

Methods

Design:
A single exposure new user observational design to collect exposure and outcome data on a cohort of evaluable patients prescribed asenapine over 2 years (Figure 1).

Figure 1. OBSERVA SCEM registry study outline

Asenapine approved, DSRU decides to monitor drug

Prescribers in secondary care enrolled to study, consent obtained from patients started treatment in secondary care setting and simple baseline questionnaire completed

12 week questionnaires completed by prescribers irrespective if patient stopped. Questionnaires returned, data entered.

Data reviewed by Research Fellow.

Events of interest followed up. Confidentiality & security carefully maintained.

Study objectives:
Primary: To describe the incidence of selected identified risks.
Secondary: To advance the understanding of the patient population, describe off-label prescribing and use outside of the approved indication and/or populations with special label precautions.
Exploratory: To describe reported non-compliance (with 10-minutes abstinence label precautions.

Data source and variables:
There are no specific exclusion criteria. Patients will be identified via specialist

Resources:
OBSERVA -The Observational Safety Evaluation of Asenapine
Observational Safety Evaluation of Asenapine registry study: rationale and design

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References:

Methodological considerations

Selection Bias
The desire is to study asenapine use in a more heterogeneous population than those observed in clinical trials. However, a potential weakness of this (and any observational study) is selection bias arising because of certain patient characteristics which influence the probability of being treated.

In comparison to studies conducted in the primary care setting, by identifying new users within the secondary care setting, risk estimates are likely to be less subject to the influence of:

Selection bias arising from treatment survivors and inclusion of patients likely to be less complex in terms of underlying disease, co-morbidities and concomitant medications than in the general disease population.

Immortal time bias arising not only from misclassification of person-time exposed to the new medication but also from under-ascertainment of events related to the start of treatment.

Selection bias may also be introduced by external factors such as clinical setting, the physician’s natural caution for adopting new medicines or recruiting patients with more severe mental health conditions who may have difficulty in providing consent/participation in research and influences on prescribing and policy (e.g. expert committee guidelines).

Confounding
The design does not include an internal counterfactual comparator for estimating strength of association between exposure to asenapine and acute transient events associated with administration in such a diverse study population. Therefore the self controlled case series method will be employed. (5) This method is increasingly being used in pharmacoepidemiology because as a case only design it is: efficient relative to a standard cohort design, self-controlled in terms of fixed (time invariant) confounders (known and unknown) which are controlled for implicitly, with the emphasis on comparing time windows periods associated with high risk (i.e. after starting treatment) with low risk periods when acute events are unlikely to occur.

Pharmacists in Research
Pharmacists play important roles in influencing drug policy, use and outcomes through collaboration with other health care professionals (HCPs). Pharmacists’ involvement in developing treatment guidelines, pharmaceutical care practices, health screening and monitoring (e.g. for issues related to treatment concordance) means that they are well placed to provide a positive contribution in pharmacoepidemiological research. Clinical pharmacists could improve the success of SCEM studies by contributing to: methodological aspects at the design stage; implementation of signalling processes to alert study investigators of eligible patients (referral of patients to study investigators); methodological assessment of data analyses; monitoring and reporting adverse events.

Results
A positive ethics opinion was received August 2011. Since November 2012, 16 investigative sites have engaged with full Research & Development approval. OBSERVA has been adopted by the Mental Health Research Network in England and Wales (Figure 2), who collaborate in multi-site enrolment of investigative sites and patient recruitment (initially where the product has been adopted on the prescribing formulary), plus maintain engagement. Thus potential obstacles affecting recruitment such as lack of engagement of psychiatrists are likely to be minimised.

Conclusions
Well designed observational studies and registries are an important and valuable approach to monitoring the post-marketing safety of new treatments.

The SCEM design provides a framework suitable to evaluate the safety of newly marketed medicines in the secondary care setting. Identifying appropriate strategies during study design may help overcome recruitment challenges. This is anticipated to be of particular value given increasing legal demands for post-authorisation Pharmacovigilance.

Conflict of Interest Statement: The Drug Safety Research Unit is an independent charity (No. 327206), which works in association with the University of Portsmouth. It receives unconditional donations from pharmaceutical companies. The companies have no control on the conduct or the publication of the studies conducted by the DSRU. The Unit has received such funds from the manufacturer of asenapine (Merck).