Rosemary Cantwell
Sent via email: request-100758-e4d04b77@whatdotheyknow.com

Date 13th February 2012

Ref: FOI 12/024

Dear Ms Cantwell,

Freedom of Information request: Clozapine and Amisulpride

Thank you for your recent Freedom of Information request concerning clozapine and amisulpride. It may be helpful if I firstly provide some background information regarding the MHRA and the work we carry out.

The Medicines and Healthcare products Regulatory Agency (MHRA) is the executive Agency of the Department of Health that acts on behalf of the Ministers to protect and promote public health and patient safety by ensuring that medicines, healthcare products and medical equipment are used safely and meet appropriate standards of safety, quality, performance and effectiveness. The MHRA assesses the balance of risks and benefits of all medicines at the time of initial licensing and throughout their use in clinical practice. Where appropriate, the MHRA seeks advice from the independent Commission on Human Medicines (CHM).

The Yellow Card Scheme is the UK system for collecting and monitoring information on suspected Adverse Drug Reactions (ADRs). The Scheme is run by the MHRA and currently relies on voluntary reporting of suspected ADRs by health professionals and patients. There is also a legal obligation for pharmaceutical companies to report serious ADR reports to their drugs. The purpose of the Scheme is to provide an early warning that the safety of a product may require further investigation.

In your request you have asked for the number of people who have died as a result of taking clozapine or amisulpiride in 2011 or where these two medicines were a contributory factor. It is important to note that the number of reports of suspected ADRs received via the Yellow Card Scheme does not directly equate to the number of people who suffer adverse reactions to drugs for a number of reasons. The scheme is associated with an unknown level of under-reporting, ADR reporting rates may be influenced by the seriousness of reactions, their ease of recognition, extent of use of a particular drug, promotion and publicity about a drug, and the existence of patient monitoring schemes (as for clozapine).

The Clozaril Patient Monitoring Scheme (CPMS) has been successful in reducing the mortality and morbidity associated with clozapine-induced agranulocytosis and is recognised to be one of the most stringent safety monitoring schemes applied to any medicine in the UK. In terms of ADR reporting it means that MHRA not only receives a report for every serious blood-related ADR associated with clozapine, it also means that patients who receive treatment with clozapine are generally more closely monitored than patients who receive other medicines – and this increases the chance that other types of adverse reactions are detected and reported to us more frequently for clozapine than for other medicines.

In 2011, the MHRA received a total of 3259 UK reports of suspected ADRs for clozapine. Of these, 515 cases were associated with a fatal outcome and 644 reported cardiac related disorders. During the same time period, the MHRA received a total of 73 UK reports of suspected ADRs for amisulpride. Of these, 9 cases were associated with a fatal outcome and 23 reported cardiac related disorders. Please find attached copies of the Drug Analysis Prints (DAPs) for clozapine and amisulpride for 2011 which provide a breakdown of all UK spontaneous suspected ADRs reported to the MHRA. Please refer to the information sheet included for guidelines on how to interpret the print.

When interpreting this data, it is particularly important to note that causality has not been established. Healthcare professionals and members of the public are asked to report even if they only have a suspicion that the medicine may have caused the event. It is therefore not possible to determine the numbers of patients who developed heart conditions on account of taking these medications from this data. The fact that an adverse reaction has been reported does not necessarily mean that the medicine has been proven to cause the reaction. Many factors have to be taken into account in assessing the relationship between a drug and suspected reaction including how long after taking the suspected drug the reaction occurred, the possible contribution of other drugs being taken, and the underlying disease.

A number of the deaths reported for clozapine were due to cancer or cancer progression, which were unrelated to treatment with clozapine. In addition it is recognised that schizophrenia is associated with mortality rates that are 2-3 times higher than in the general population. Studies suggest that this excess of mortality is accounted for by a combination of an increased risk of suicide, in particular in young male patients soon after diagnosis, and more importantly, a higher number of natural deaths (largely due to cardiovascular disease). Indeed, some of the most frequently reported causes of death in the MHRA ADR database for clozapine are suicide and cardiovascular disease.

Further to your request for the number of people taking Clozapine in 2011 who were removed from the clozapine monitoring schemes, unfortunately we do not have the breakdown of data from the clozapine monitoring schemes (there are 3 different schemes in the UK). You will need to approach the Licence holders directly for this information.

I hope this information is of use to you. If you are unhappy with our response, you may ask for it to be reviewed. That review will be undertaken by a senior member of the Agency who has not previously been involved in your request. If you wish to pursue that option please write to the Communications Directorate, Area 4-T, Medicines and Healthcare products Regulatory Agency, at the above address quoting reference FOI 12/024. After that, if you remain dissatisfied, you may ask the Information Commissioner to make a decision on whether or not we have interpreted the FOIA correctly in withholding some information from you.

Yours sincerely,

Edward Stone
Pharmacovigilance Information Scientist
Pharmacovigilance Information Unit

Vigilance and Risk Management of Medicines

cc: - Ms Sarah Cumber, Therapeutic Group Co-ordinator

Copyright notice
The information supplied in response to your request is the copyright of MHRA and/or a third party or parties, and has been supplied for your personal use only. You may not sell, resell or otherwise use any information provided without prior agreement from the copyright holder. For full details on our copyright policy please visit:

http://www.mhra.gov.uk/home/Idcplg?IdcService=SS_GET_PAGE&nodeId=412
or email the MHRA Information Centre" "