MHRA PUBLIC ASSESSMENT REPORT

Pseudoephedrine and ephedrine: managing the risk of misuse of medicines

July 2010 update

PLAIN LANGUAGE SUMMARY

Background
The Medicines and Healthcare products Regulatory Agency (MHRA) is the government agency responsible for regulating medicines and medical devices in the UK. We continually review the safety of all medicines in the UK and inform healthcare professionals and the public of the latest updates. In our public assessment reports we discuss safety issues associated with a particular medicine or group of medicines. The following report presents a review of the impact of measures introduced to control the potential misuse of medicines containing pseudoephedrine (PSE), and ephedrine (EPH), in the manufacture of the Class A controlled drug methylamphetamine. These measures were introduced in 2007–2008, and their impact first reviewed in 2009.

PSE and EPH are nasal decongestants[a] contained in many cough and cold medicines sold over-the-counter (OTC) in UK pharmacies. There is concern that PSE and EPH can be extracted from these medicines and used in the illegal manufacture of the Class A controlled drug methylamphetamine[b] – a highly addictive drug which affects the central nervous system and can cause serious physical and psychological harm. This concern prompted a public consultation in 2007, following which the Commission on Human Medicines[c] (CHM) advised that a number of measures should be introduced to control the supply of OTC medicines containing PSE and EPH. These measures included reducing the pack size for OTC products containing PSE and EPH, and a restriction on sale to one pack per transaction.

CHM also advised that a working group be set up to monitor the effectiveness of the pharmacy controls, and to advise the CHM on other measures that should be put in place to minimise the misuse of OTC medicines containing PSE or EPH in the illicit manufacture of methylamphetamine. The Working Group was established in September 2007. Based on recommendations from CHM, the following legal sales restrictions were put in place on April 1st 2008:

- It became illegal to sell or supply any product that contains more than 720 mg PSE or 180 mg EPH without a prescription
- It became illegal to sell or supply a combination of products that between them add up to more than 720 mg PSE or 180 mg EPH without a prescription
- It became illegal to sell or supply a product that contains PSE and a product that contains EPH in one transaction

In addition the Royal Pharmaceutical Society of Great Britain (RPSGB) issued guidance that the sale and supply of products containing PSE or EPH must only be made by pharmacists or suitably trained pharmacy staff under the supervision of a pharmacist.

Impact of restrictions and CHM recommendations
In July 2009, the Working Party presented to CHM an update on the impact of these measures to control the misuse of PSE or EPH-containing medicines. The evidence showed that the measures were helping to contain the potential problem of misuse, and that sales of PSE and EPH products had reduced. A public assessment report giving full details of the evidence, and the CHM's conclusions in July 2009, is available on our website: MHRA Public Assessment Report: Controlling the risk of misuse of medicines containing pseudoephedrine and ephedrine.

[a] Drugs which help to clear a blocked nose
[b] Commonly known as 'methamphetamine', 'crystal meth' or 'ice'
[c] An independent body who gives advice to government Ministers about the safety, quality, and efficacy of medicines

In light of recommendations from the CHM, stakeholders including the pharmacy profession, the Home Office, the Association of Chief Police Officers (ACPO) and the Serious Organised Crime Agency (SOCA) have continued to take measures to minimise the misuse of medicines containing PSE and EPH. They report that these measures are continuing to be successful, and have recently provided updated information on the impact of these measures, such as:

- The RPSGB, the National Pharmacy Association (NPA), the Company Chemists Association (CCA) and the Proprietary Association of Great Britain (PAGB) continue to raise awareness in the pharmacy profession of the indirect abuse potential of medicines containing PSE or EPH.

- In a survey conducted in June 2010 of 347 NPA members, 98% were aware of the rules regarding sales of PSE.

- Sales figures provided by the PAGB show that sales of PSE products declined by 7% from April 2009 to April 2010.

- The number of registered methylamphetamine addicts remains small. The ACPO's assessment, based on findings to date, is that there is low availability of methylamphetamine across the UK.

Conclusions
In July 2010, the CHM considered the above feedback from stakeholders and concluded that the regulatory measures implemented in 2009 to manage the risk of misuse of OTC medicines containing PSE or EPH were continuing to be successful. The CHM recommended that:

- the existing levels of monitoring, education and awareness measures by pharmacists should be maintained

- liaison with stakeholders including the Home Office, the Association of Chief Police Officers (ACPO) and the Serious Organised Crime Agency (SOCA) should continue

- the Working Group should be reconstituted as necessary to review the situation if any new concerns arise.

The CHM also commended the pharmacy profession for their significant contribution towards helping to keep the situation under control. They noted that implementation of the measures introduced to regulate sales, together with the additional voluntary actions overseen by the profession, had so far been effective and were much appreciated.

1. INTRODUCTION

(See glossary for explanation of medical terms)

The Medicines and Healthcare products Regulatory Agency (MHRA) is the government agency responsible for regulating medicines and medical devices in the UK. We continually review the safety of all medicines in the UK and inform healthcare professionals and the public of the latest updates. The following MHRA Public Assessment Report presents a review of the impact of measures introduced to control the potential misuse of medicines that contain pseudoephedrine (PSE)) and ephedrine (EPH), in the manufacture of the Class A controlled drug methylamphetamine.

2. BACKGROUND

PSE and EPH are nasal decongestants contained in many cough and cold medicines sold OTC in UK pharmacies. There has been increasing concern that PSE and EPH can be extracted relatively easily from over-the-counter (OTC) medicines and used in the illicit manufacture of methylamphetamine (commonly known as "methamphetamine", "crystal meth" or "ice"). Methylamphetamine was reclassified on 18 January 2007 by the Home Office as a Class A controlled drug, based on the recommendation of the Advisory Council on the Misuse of Drugs[a] (ACMD).

Because of this concern, a public consultation was carried out in March 2007 on minimising the risk of misuse of medicines containing PSE or EPH in the manufacture of methylamphetamine. In this consultation, the MHRA sought views on restricting the availability of these medicines by changing their legal status from pharmacy (P) to prescription-only medicines (POM), together with a restriction in their pack size.

In July 2007, the Commission on Human Medicines (CHM; an independent body who give advice to government Ministers about the safety, quality, and efficacy of medicines) considered the responses to the consultation. They advised that the legal status of medicines containing (PSE) and ephedrine (EPH) should be reclassified from P to POM in July 2009, unless the risk of misuse of these OTC medicines in the illicit manufacture of methylamphetamine was contained. The CHM provided advice on pack size restrictions and other measures to control supply of OTC medicines containing PSE and EPH, and advised that a Working Group should be set up to advise on implementation of the measures (see press release and weblinked minutes). Accordingly, the CHM Working Group on PSE and EPH (Working Group) was established in September 2007 to advise the CHM on the implementation of measures that should be put in place to minimise the misuse of OTC medicines containing PSE or EPH in the illicit manufacture of methylamphetamine.

Following CHM advice to restrict pack sizes of PSE and EPH, a further public consultation in October 2007 considered specific amendments to the Prescription Only Medicines Order 1997 (POM Order) to make the sale and supply of products containing more than 720 mg of PSE or 180 mg EPH prescription-only. This legislation (SI 2008/464) was established on 1st April 2008:

- It became illegal to sell or supply any product that contains more than 720 mg PSE or 180 mg EPH without a prescription.
- It became illegal to sell or supply a combination of products that between them add up to more than 720 mg PSE or 180 mg EPH without a prescription
- It became illegal to sell or supply a product that contains PSE and a product that contains EPH in one transaction

[a] An independent expert body that advises the government on drug-related issues in the UK

Professional guidance was also issued by the Royal Pharmaceutical Society of Great Britain (RPSGB) for PSE or EPH-containing products to be supplied personally by a pharmacist or a trained staff member under the supervision of a pharmacist (see section 3.1 below).

In July 2009, CHM considered the impact of measures which had been put in place to minimise the risk of misuse of PSE and EPH-containing products and recommended that: the existing levels of monitoring education and awareness measures by pharmacists should be maintained; liaison with stakeholders including the Home Office (HO), Association of Chief Police Officers (ACPO) and the Serious Organised Crime Agency (SOCA) should continue; the Working Group should be reconstituted as necessary, and in any case to review the situation on a yearly basis.

A public assessment report published in July 2009 giving full details of the measures and the CHM's conclusions is available on our website: MHRA Public Assessment Report: Controlling the risk of misuse of medicines containing pseudoephedrine and ephedrine. An article on this issue was also published in the September 2009 issue of *Drug Safety Update*, the MHRA monthly bulletin for health professionals on the safety of medicines.

3. UPDATE ON IMPLEMENTATION OF MEASURES

In light of the CHM's recommendations above, stakeholders have continued to take measures to help minimise the misuse of OTC medicines containing PSE or EPH in the illicit manufacture of methylamphetamine. Information provided recently is summarised below.

3.1 Pharmacy supervision plus education and awareness initiatives

The Working Group established close links with the RPSGB, the Pharmaceutical Society of Northern Ireland (PSNI) the National Pharmacy Association (NPA) the Company Chemists Association (CCA) and the Proprietary Association of Great Britain (PAGB). These organisations have provided updated information to the MHRA on the continuing measures to maintain awareness by the pharmacy profession of the indirect abuse potential of medicines containing PSE or EPH.

The RPSGB is committed to supporting pharmacists in relation to the misuse of PSE or EPH and is planning to issue further communications to members to ensure they maintain vigilance with these products. In particular, guidance will be issued in time for the autumn cough and cold season.

The RPSGB has reported on development of a module on the sale of a PSE product for the 'Simulated Patient Project'. This is a type of clinical audit which aims to improve the quality of advice provided when pharmacists and pharmacy staff interact with patients. The module is designed to review skills demonstrated during a consultation in areas such as information gathering, provision of advice and outcome of consultation, then assess these against a set of pre-set standards (minimum, above average, and gold).

The PSNI has placed guidance on its website relating to PSE sales. Monitoring the website shows there is constant access of this information by either professionals or the public. The PSNI liaises with the Department of Health, Social Services and Public Safety (DHSSPS) and its pharmaceutical inspectorate, and there is no current

evidence of any problem issues with the sale and supply of PSE-containing products in Northern Ireland.

The NPA continues to maintain and develop an awareness training resource for members to download from the NPA website. It is now available in various formats to suit the users, eg, group training or individual learner. The NPA reminds members at intervals to ensure that newly appointed staff are made aware of the current rules, by means of superintendent email alerts, the carrier sheet of the NPA member magazine and press releases. In a survey conducted in June 2010 of 347 members, 98% of members responded that they are aware of the rules regarding sales of PSE-containing products.

The CCA continues to operate the MethGuard UK awareness training programme, although numbers completing the programme have decreased, possibly because the vast majority of members have now developed their own in-house resource, including several major high-street pharmacy stores. Some major pharmacy chains have also developed/are developing a till system to limit sales to one pack.

3.2 Pharmacy reporting of suspicions

The 'Reporting Your Suspicions' card continues to be available on the RPSGB website. The RPSGB inspectorate reported one or two instances of unusual quantities of PSE being requested; these were informal reports, which were dealt with locally via liaison with the Controlled Drug Liaison Officer (CDLO) or local intelligence networks.

3.3 Sales monitoring for evidence of use of over-the-counter medicines in the manufacture of methylamphetamine

The PAGB provided sales figures for PSE and phenylephrine (PE) products, which show a decline in PSE and PE sales of 7% and 6%, respectively, during the financial year April 2009–April 2010. PAGB have commented that PSE unit sales are declining at a faster rate than PE-containing products compared to the previous year, and also that there has been an overall decline in sales of these products during 2009/2010. However, this may be partly due to the lack of a cough/cold season (which is a driving force for sales of these products).

3.4 Triggers for a review of the availability of pseudoephedrine or ephedrine over-the-counter medicines

In June 2008, the CHM agreed with Working Group proposals on factors which act as potential triggers for a review of the pharmacy/OTC availability of PSE or EPH-containing medicines. The ACPO, SOCA and the Home Office have provided updated information in these areas which is summarised below:

The number of methylamphetamine laboratories found (and scale: eg, personal use only or quantities with intention to supply) using OTC PSE or EPH to manufacture methylamphetamine has not increased since the last confirmed report in London in 2008.

SOCA and ACPO have reported that there have been no significant events concerning OTC-sourced PSE or EPH used in the manufacture of methylamphetamine.

Reports of suspicious requests for OTC PSE or EPH-containing medicines by pharmacists to RPSGB/SOCA are documented via the reporting system (the 'Reporting Your Suspicions' card). There were three reports in 2009, but in 2010 there were no formal reports of customers behaving suspiciously when attempting to purchase quantities of PSE or EPH. In addition, there have been no reported pharmacy 'break ins' where PSE or EPH-containing products were stolen. Data from the last five years

do not indicate a significant increase in the number of methylamphetamine users, and the numbers of registered methylamphetamine addicts remains small[a].

3.4.5 Actual seizures of methylamphetamine manufactured using non-OTC PSE or EPH remains low, illicit drug laboratories found by police are rare, and numbers of individuals in treatment remains limited. The main supply continues to be import rather than local manufacture, with bulk precursor chemical purchases still the easiest source of PSE and EPH. Based on findings to date, the ACPO's assessment is that there is low availability of methylamphetamine across the UK.

Liaison with relevant stakeholders including ACPO, SOCA, and the RPSGB will continue to provide the above information as it arises. Overall, SOCA and ACPO have indicated that the issue of methylamphetamine abuse in the UK is under control.

4. INTERNATIONAL POSITION

An update of available information on international measures to minimise the risk of misuse of PSE or EPH-containing medicines is provided below.

Europe
Previously, the ***Czech Republic*** had been identified as having significant problems with abuse of PSE. From May 2009 the Czech Regulatory Authority (SUKL) switched PSE products to a new category – 'OTC with a sales restriction'. Dispensing is limited as follows:

- One pack containing a maximum of 720 mg PSE per person per week
- A maximum quantity of 1800 mg per person per month
- Pharmacies must enter sales in a central register to verify that the product has not been sold to that particular person in the same week
- The purchase of these products over the internet or by mail order is prohibited.

The action taken in the Czech Republic appears to have had a significant impact on the supply of PSE and EPH.

There are no reports of significant problems in other European countries.

Australia
The measures put in place to control the potential misuse of PSE-containing products are continuing. A pharmacist must be involved in each sale, and all preparations containing more than 720 mg PSE require a doctor's prescription. Patients have to provide photographic identification, and pharmacists have to log purchases onto a real-time online database, which alerts them to previous purchases by the same individual.

New Zealand
Methylamphetamine abuse in New Zealand is a significant problem and the police close down several hundred manufacturing laboratories per year. While the majority of PSE is sourced via illegal importation, police estimate that one-third of all clandestine laboratories detected contain PSE that has been obtained from pharmacies. Concerns about the use of PSE as a precursor for the manufacture of methamphetamine led to the reclassification of pseudoephedrine in 2003 as a Class C controlled drug (Schedule 3 of the Misuse of Drugs Act 1975). PSE preparations containing not more than 60 mg per unit dose (or 240 mg for a slow-release formulation), and supplied in packages containing not more than 1800 mg, may be sold by pharmacies without a prescription.

[a] Data from the UK Home Office

All other doses require a prescription. There are also voluntary schemes in place to move PSE and EPH products behind the counter, and seek photographic identification of people purchasing these products.

America & Mexico
There have been no changes in the marketing of PSE in the USA in recent years. Following the Combat Methamphetamine Epidemic Act of 2005, the following restrictions to PSE sales were introduced by the Food and Drug Administration:

- PSE has to be stored behind the counter or in locked cabinets (in pharmacies and non-pharmacy outlets)
- Purchasers have to provide identification
- Retailers must keep a written record of the sale
- Pack sizes are limited to 1·8 g and transactions limited to one pack
- The quantity purchased per day is limited to 3·6 g a day (two packs)
- No more than 9 g can be purchased per month (five packs)

Some states, for example Oregon, have more stringent requirements including prescription-only status for this drug.

Mexico is the primary foreign source of methylamphetamine to the USA and has become one of the largest producers since a suppression of laboratories in the USA. From February 2009, the sale of PSE has been banned in Mexico and Guatemala.

5. DISCUSSION

The feedback from stakeholders is that the regulatory measures recommended by the CHM to help minimise the risk of misuse of OTC medicines containing PSE or EPH are continuing to be implemented successfully.

The pharmacy representative organisations are maintaining their support and encouragement of education and training by pharmacists and pharmacy staff, to ensure awareness of misuse of PSE and EPH and the links to methylamphetamine misuse.

There have only been a couple of reports from pharmacies of suspicious requests for unusual quantities of OTC PSE and these have been handled locally.

The factors that would trigger a review of continued OTC PSE or EPH availability have been reviewed and there are no significant issues of concern. SOCA has reported that no new meth labs have been found.

Internationally, there is evidence that those countries where there was a problem are now taking steps better to manage the risk of misuse.

6. RECOMMENDATIONS AND CONCLUSIONS

After reviewing the updated information summarised in this report, the CHM agreed that the measures implemented from 2007 are continuing to successfully control the supply of OTC PSE and EPH-containing products. The CHM recommended that:

- the existing level of monitoring and the education and awareness measures by pharmacists should be maintained
- liaison with stakeholders including the Home Office, ACPO and SOCA should continue
- the Working Group should be reconstituted as necessary to review the situation should any new evidence of concern arise
- A further update report should be considered by CHM in 2011.

The CHM also commended the pharmacy profession for their significant contribution towards helping to keep the situation under control. They noted that implementation of the measures introduced to regulate sales, together with the additional voluntary actions overseen by the profession, had so far been effective and were much appreciated.

7. GLOSSARY

Class A controlled drugs
In the UK, certain drugs are designated as controlled substances (ie, only certain designated persons may manufacture, supply and possess them) and are divided into three classes: A, B and C. Those categorised as Class A are considered to be the most likely to cause harm (see http://webarchive.nationalarchives.gov.uk/20100419081707/http:/drugs.homeoffice.gov.uk/drugs-laws/misuse-of-drugs-act/ for more information)

Clinical Audit
A process performed by the UK's National Health Service that seeks to improve patient care and outcomes by reviewing performance in the Service

Decongestant
A drug that helps to clear a blocked nose

Ephedrine
A drug that narrows blood vessels and widens airways, used mainly as a nasal ***decongestant***

Illicit
Illegal

Legislation
A proposed law or group of laws

Methylamphetamine
A Class A controlled drug that is illegal to possess, supply or manufacture. It is a **stimulant** that causes feelings of exhilaration

Misuse (of medicines)
Using a drug for improper purposes (ie, not for treating a condition or disease)

Over-the-counter
Medicines that can be sold to a customer without a prescription

Pharmacy (referring to medicine classification)
Medicines that can only be sold to a customer by a trained pharmacist

Phenylephrine
A drug that narrows blood vessels, used mainly as a nasal ***decongestant***

Precursor (chemical)
A chemical that is required in the process of making a drug, which becomes part of the end-product

Prescription Only Medicine
Medicines that can only be sold to a customer if they have a valid prescription from a doctor

Pseudoephedrine
A drug that narrows blood vessels, used as a nasal ***decongestant***

Public Consultation
A process that seeks the public's input on matters that affect them

Stakeholders
A person, group, organisation or system which affects, or can be affected by, an organisation's actions

Stimulant
A substance that causes increased activity in the body, particularly in the nervous system, and the heart and circulatory system