



Risk of patient harm from an interaction between miconazole and coumarin anticoagulants

To: General practitioners, dentists, non-medical prescribers, nurses and pharmacists.

For information: All NHS Wales Chief Executives, Medical Directors, Directors of Nursing, Chief Pharmacists, Medication Safety Officers, Patient Safety Teams; Medical, Nursing and Pharmacy Directors in independent hospitals; residential and nursing care homes.

Coroner's Report

A Regulation 28 Report was issued by HM Coroner to Welsh Government on 7 March 2016 regarding the death of a patient from intracerebral haemorrhage (stroke). In this particular incident, the patient was regularly prescribed warfarin for treatment of atrial fibrillation and was concomitantly prescribed miconazole oral gel for the treatment of oral thrush by a dentist. On admission to hospital the patient was found to have a significantly raised International Normalised Ratio (INR) and subsequently died from an intracerebral haemorrhage. The coroner considered that the combined use of warfarin and miconazole may have been a contributory factor in the death of this patient.

The coroner is concerned that:

- There appears to be a lack of knowledge of the interaction of warfarin and miconazole amongst health professionals; and/or
- It is not clear which sources of information health professionals should use to check possible interactions.

The purpose of this notice is to ensure that health professionals who prescribe and supply medicines in Wales are aware of the potential for interactions to occur between miconazole, including topical preparations, and coumarin anticoagulants (warfarin, acenocoumarol, phenindione); and to highlight readily accessible sources of information regarding drug-drug interactions.

Actions

Who: All hospitals and community services (general practices, dental practices, pharmacies, community nurses) where miconazole containing products are prescribed, dispensed, supplied or administered.

When: As soon as possible but no later than June 10 2016.

1. Circulate this notice to all medical, dental, nursing, pharmacy and non-medical prescribing staff.
2. Identify if the co-prescribing of miconazole containing products and coumarin anticoagulants has or could occur in your organisation.
3. Consider if immediate action needs to be taken locally and ensure that an action plan is put in place, if required, to minimise the risks of these incidents occurring.
4. Before prescribing any miconazole containing products, prescribers must check the patient's medical and drug history (using electronic records and/or questioning the patient/relatives), in particular the current use of coumarin anticoagulants.
5. Before dispensing or selling miconazole containing products, pharmacy staff must check the patient's medical and drug history (using electronic records and/or questioning the patient/relatives), in particular the current use of coumarin anticoagulants.



Background

Interaction between miconazole and coumarin anticoagulants

Miconazole is an imidazole antifungal administered orally, topically and vaginally to treat oropharyngeal candidiasis, skin infections and vaginal candidiasis respectively.¹ Miconazole containing products can be prescribed by healthcare professionals and/or purchased over-the-counter from pharmacies.

Miconazole interacts with some medication through its inhibitory action on cytochrome enzymes responsible for the metabolism of many drugs.² A clinically significant drug interaction exists between miconazole containing products and coumarin anticoagulants (warfarin, acenocoumarol and phenindione).² Miconazole inhibits the metabolism of the coumarin anticoagulants, resulting in increased anticoagulant effects.

Miconazole is systemically absorbed when administered topically, vaginally and orally (including as oral gel).² Consequently, patient harm and/or death has been reported from bleeding complications following the concomitant administration of coumarin anticoagulants and miconazole (oral, topical or vaginal) products.²

The interaction between miconazole and coumarin anticoagulants is a well established serious drug interaction.

Sources of information regarding drug-drug interactions

Details of interactions are listed in appendix one of the British National Formulary (BNF). The interaction between miconazole and coumarin anticoagulants is listed in "Antifungals, Imidazole" and "Coumarins" sections of appendix one of the BNF. Specifically, the BNF states that "miconazole" enhances the anticoagulant effect of coumarins (miconazole oral gel and possibly vaginal and topical formulations are absorbed)".¹

Print copies of the BNF are distributed annually to hospitals, GP practices, dental practices and community pharmacies across Wales. Unrestricted access to the most recent version of the online BNF is available through the NHS evidence website: www.evidence.nhs.uk/formulary/bnf/current

In print copies of the BNF, interactions which are potentially serious will have the symbol • placed against the name of the relevant interacting drug. In online versions, potentially serious interactions are shown in bold against a pink background.

The concomitant use of drugs involved in potentially serious interactions should be avoided.

- Healthcare professionals prescribing, supplying and administering miconazole containing products must check for drug interactions using an appropriate resource (e.g. British National Formulary, electronic Medicines Compendium) and take appropriate action to ensure patient safety.

Share any learning from local investigations or locally developed good practice resources by emailing: ImprovingPatientSafety@Wales.gsi.gov.uk

Technical Notes

Stakeholder engagement

The notice was adapted in collaboration with the Medication Safety Officer network within Wales.



Further information on drug interactions is also available in the Summary of Product Characteristic (SPC) for each medication which can be accessed from the electronic Medicines Compendium (eMC):

www.medicines.org.uk/emc/

Relevant professional standards

Doctors, dentists, pharmacists and nurses are reminded of their professional obligations:

*General Medical Council Good Medical Practice*³

"Check that the care or treatment provided for each patient is compatible with any other treatments the patient is receiving, including (where possible) self-prescribed over-the-counter medications."

*General Dental Council Guidance on Prescribing Medicines*⁴

"You must provide good quality care based on current evidence and authoritative guidance. Prescribing medicines is an integral aspect of many treatment plans... You must have an understanding of your patient's current health and medication, including any relevant medical history, in order to prescribe medicines safely."

*General Pharmaceutical Council Standards of Conduct, Ethics and Performance*⁵

"Get all the information you require to assess a person's needs in order to give the appropriate treatment and care... Do your best to provide medicines and other professional services safely and when patients need them."

*Nursing and Midwifery Council Standards for Medicines Management*⁶

"You must know the therapeutic uses of the medicine to be administered, its normal dosage, side-effects, precautions and contra-indications... You must administer or withhold in the context of the patient's condition and co-existing therapies. You must contact the prescriber or another authorised prescriber, without delay, where contraindications to the prescribed medicine are discovered..."

Situations where concomitant use of interacting medicines cannot be avoided

Coumarin anticoagulants interact with a variety of medicines. Sometimes, the concomitant use of interacting medicines is unavoidable. National Patient Safety Alert 18 '*Actions that make anticoagulant therapy safer*' requires that organisations:



“Promote safe practice for prescribers co-prescribing one of more clinically significant interacting medicines for patients already on oral anticoagulants; to make arrangements for additional INR blood tests and to inform the anticoagulant service that an interacting medicine has been prescribed. Ensure that those dispensing clinically significant interacting medicines for these patients check that these additional precautions have been undertaken.”⁷

Implications for practice

A variety of topical miconazole preparations can be prescribed by doctors, dentists, non-medical prescribers and sold over the counter from pharmacies. The healthcare professional prescribing or supplying miconazole (for example a dentist or pharmacist) may be different to the person prescribing and monitoring a patient's anticoagulant therapy. Prior to prescribing or supplying topical miconazole preparations, prescribers and pharmacy staff must confirm whether a patient takes a coumarin anticoagulant and take steps to reduce the risk of potentially serious adverse events occurring as a result of their concomitant use.

Further guidance on the management of dental patients taking anticoagulants and antiplatelet medicines is available from the Scottish Dental Clinical Effectiveness Programme.⁸



References

- ¹ British National Formulary. www.evidence.nhs.uk/formulary/bnf/current [accessed 28th April 2016]
- ² Stockley's Drug Interactions. www.medicinescomplete.com/mc/stockley/current/login.htm?uri=https%3A%2F%2Fwww.medicinescomplete.com%2Fmc%2Fstockley%2F2010%2F [accessed 28th April 2016]
- ³ General Medical Council. Good Medical Practice. www.gmc-uk.org/guidance/good_medical_practice.asp [accessed 28th April 2016]
- ⁴ General Dental Council. Guidance on Prescribing Medicines. 2013. www.gdc-uk.org/Dentalprofessionals/Standards/Documents/Guidance%20Sheet%20Guidance%20on%20Prescribing%20Medicines%20September%202013%20v2.pdf
- ⁵ General Pharmaceutical Council. Standard of Ethics, Conduct and Performance. 2014. www.pharmacyregulation.org/sites/default/files/standards_of_conduct_ethics_and_performance_july_2014.pdf
- ⁶ Nursing and Midwifery Council. Standards for Medicines Management. www.nmc.org.uk/globalassets/sitedocuments/standards/nmc-standards-for-medicines-management.pdf
- ⁷ NPSA. NPSA/2007/18. Actions that Make Anticoagulant Therapy Safer. 2007. www.nrls.npsa.nhs.uk/resources/?entryid45=59814
- ⁸ Scottish Dental and Clinical Effectiveness Programme. Management of Dental Patients Taking Anticoagulants or Antiplatelet Drugs. 2015. www.sdcep.org.uk/wp-content/uploads/2015/09/SDCEP-Anticoagulants-Guidance.pdf