From the Chief Medical Officer
Dr Michael McBride

HSS (MD) 19/2012

Department of
Health, Social Services and Public Safety
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Date: 28 May 2012

For Action:
All General Practitioners
(for cascade to practice nurses and pharmacists)
GP Locums
Family Practitioner Service Leads, HSC Board
(for cascade to GP Out of Hours services)
Medical Directors of HSC Trusts
(for cascade to transplant specialists)
Directors of Nursing of HSC Trusts
(for cascade to all nursing staff)
All Community Pharmacists
Heads of Pharmacy & Medicines Management, HSC Trusts

For information:
Chief Executive, Health and Social Care Board
Chief Executives, HSC Trusts
Director of Integrated Care, Health and Social Care Board
Chief Executive, Public Health Agency
Executive Medical Director/Director Public Health, Public Health Agency
Director of Nursing, Public Health Agency
Professor Patrick Johnston, Dean, School of Medicine, Dentistry & Bio-medical Sciences, QUB
Dr Clare Loughrey, NIMDTA
Professor Linda Johnston, Head of School of Nursing & Midwifery, QUB
Dr Owen Barr, Head of School of Nursing, University of Ulster
Glynis Henry, NIPEC
The Regional Medicines and Poisons Information Service, Belfast HSC Trust
Mr Joe Brogan, Asst Dir of Commissioning, Pharmacy and Medicines Management, HSC Board

Dear Colleague

Oral tacrolimus products should be prescribed and dispensed by brand name only to avoid the risk of medication errors - Letter from Sir Gordon Duff, Chairman of the Commission on Human Medicines

This communication is to draw you attention to updated advice that all oral tacrolimus products should now be prescribed and dispensed **by brand name only**. This is to minimise the risk of inadvertent switching between products, which has been associated with reports of toxicity and graft rejection.

This updated advice follows a review by the Commission on Human Medicines (CHM) on the safer use of oral tacrolimus products. The CHM review concluded that in light of the growing number of tacrolimus products, to ensure maintenance of therapeutic response on a particular brand and to minimise the risk of medication errors from any unintended switching between

different products, oral tacrolimus products should be prescribed and dispensed by brand name only.

All tacrolimus products in the UK, including generics, are approved with a brand name.

If a prescriber considers that switching to another tacrolimus brand would be of benefit to the patient, careful therapeutic monitoring under the supervision of a transplant specialist is required.

Current regional guidelines in Northern Ireland on medicines not suitable for generic prescribing and dispensing including tacrolimus attached.

This recommendation does not imply that a patient's treatment cannot be changed to a different tacrolimus pharmaceutical form or brand if the prescriber considers this appropriate. However, any changes between brands (which may or may not involve changes in dosing regimen) should be accompanied by careful therapeutic monitoring under the supervision of an appropriate specialist.

Advice for healthcare professionals and patients

- Prescribers should prescribe oral tacrolimus products by brand name only. When prescriptions have previously been written using the generic name, the brand on which the patient is stabilised should be established to ensure that the patient is supplied with the same product.
- If a prescriber intends to switch between any tacrolimus brands, careful medical supervision by an appropriate specialist and therapeutic monitoring are required.
- Pharmacists should always dispense the exact brand prescribed. They should contact the prescriber if the prescription is not clear or if the requested brand is unavailable to ensure the appropriate medicine is dispensed.
- Patients should be advised to take careful note of the name of their usual tacrolimus brand and should check with their doctor or pharmacist if they receive a different brand or if they have any other questions about the prescription, e.g. about the dose.

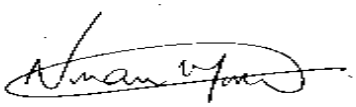
This advice will remain in place until any further advice by CHM is issued.

Please report suspected adverse reactions to any medicine or vaccine through the Yellow Card Scheme (www.mhra.gov.uk/yellowcard).

Further information is provided in the attached letter and Question and Answers document and is also available at www.mhra.gov.uk and in the current edition of the BNF.

Yours sincerely

Dr Michael McBride
Chief Medical Officer



Dr Norman Morrow
Chief Pharmaceutical Officer

Mrs Angela McLernon
Acting Chief Nursing Officer

This letter is available on the DHSSPS website at
www.dhsspsni.gov.uk/cmo_communications.htm

COMMISSION ON HUMAN MEDICINES
CHAIRMAN: SIR GORDON W. DUFF

23 May 2012

Oral tacrolimus products should be prescribed and dispensed by brand name to avoid the risk of medication errors

Dear Colleague,

I am writing to inform you of updated advice on oral tacrolimus products. These should be prescribed and dispensed by brand name to minimise the risk of inadvertent switching between products, which has been associated with previous reports of toxicity and graft rejection.

This action follows further review by the Commission on Human Medicines (CHM) on the safe use of oral tacrolimus products. The CHM review concluded that in light of the growing numbers of tacrolimus products, and to ensure maintenance of therapeutic response when a patient is stabilised on a particular brand, oral tacrolimus products should be prescribed and dispensed by brand name only. This supersedes previous advice regarding the prescribing and interchangeability of different tacrolimus products.

This updated recommendation does not preclude patients changing to a different tacrolimus brand if the prescriber considers this to be of benefit to the patient. However, any changes between brands should always be accompanied by careful therapeutic monitoring.

All tacrolimus products in the UK, including generics, are approved with a brand name.

Advice for healthcare professionals and patients

- Prescribers should prescribe oral tacrolimus products by brand name only. When prescriptions have previously been written using the generic name, the brand on which the patient is stabilised should be established to ensure that the patient is supplied with the same product.
- If a prescriber intends to switch between any tacrolimus brands, careful medical supervision and therapeutic monitoring are required.

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- Pharmacists should always dispense the exact brand prescribed. They should contact the prescriber if the prescription is not clear to ensure the appropriate medicine is dispensed.
- Patients should be advised to take careful note of the name of their usual tacrolimus brand and should check with their doctor or pharmacist if they receive a different brand or if they have any other questions about the prescription, e.g. about the dose.

Background

Tacrolimus is a drug with a narrow therapeutic index, and even minor differences in blood levels have the potential to cause transplant rejection or adverse reactions.

The three different pharmaceutical forms of oral tacrolimus products are shown below, together with brand names of currently approved products.

- Immediate release capsule taken twice a day (including the following brands - Adoport, Aletris, Capexion, Evenil, Miloprosan, Prograf, Tacni, Takon, Taliximun, Tamitect and Vivadex)
- Prolonged release capsule taken once daily (Advagraf)
- Granules for oral solution taken twice daily (Modigraf).

In 2008 there were reports of unintended switching of pharmaceutical forms that led both to toxicity and to graft rejection reactions. This prompted the publication in 2009 of the advice on the requirement for close supervision when changing tacrolimus products and the need for great care when prescribing and dispensing oral tacrolimus. Following the introduction of the first generic oral immediate release tacrolimus products, and to minimise the risk of medication errors, further advice was issued in May 2010. This advice stressed the need to provide the full information (pharmaceutical form, strength, dose and dose frequency) in the prescription of tacrolimus, or the alternative of prescribing by brand name.

The CHM has now completed a further review on the safe use of tacrolimus products. The CHM considered that the risk of medication errors between the different oral pharmaceutical forms may increase as more tacrolimus products are approved in the UK. Therefore, as a precautionary measure, the CHM has updated its advice on the safe use of oral tacrolimus products and recommends

that to avoid confusion for patients and prescribers, and to avoid inadvertent switching of product from different suppliers, all oral tacrolimus products should be prescribed by brand name only.
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This recommendation does not imply that a patient's treatment cannot be changed to a different tacrolimus pharmaceutical form or brand if the prescriber considers this appropriate. However, any changes between brands (which may or may not involve changes in dosing regimen) should be accompanied by careful therapeutic monitoring under the supervision of an appropriate specialist.

This advice will remain in place until any further advice by CHM is issued.

Please report suspected adverse reactions to any medicine or vaccine through the Yellow Card Scheme (www.mhra.gov.uk/yellowcard).

Further information is available at www.mhra.gov.uk.

Yours faithfully,

Items Unsuitable for Generic Prescribing

Health and Social Care Board

Nov 11

The following list provides examples of drugs/preparations which the Medicines Management Advisors would NOT recommend for generic prescribing. However, this list is guidance only and practices may wish to add other categories of their own depending on practice policy. For further information refer to the BNF or contact your Medicines Management Advisor. Please note: The list of brand names given as examples is not exhaustive.

Medicine Category	Generic name / group	Examples	Comments
Drugs with a **narrow therapeutic index**.	**Aminophylline**	e.g. Phyllocontin Continus®	There may be differences in the bioavailability of the preparations and/or the difference between therapeutic and toxic plasma concentrations. Therefore the brand name should be prescribed. However, where bioequivalence is not so significant e.g. pain control, brand prescribing is not necessary.
	Lithium	e.g. Priadel®, Camcolit®, Liskonum®	
	Theophylline	e.g. Nuelin SA®, Slo-Phyllin®, Uniphyllin Continus®	
or certain indications e.g. epilepsy, renal transplant etc.	**Carbamazepine**	e.g. Tegretol®, Carbagen®, Epimaz®	
	Levetiracetam	e.g. Keppra®	
	Lamotrigine	e.g. Lamictal®	
	Phenytoin	e.g. Epanutin®	
	Sodium valproate	e.g. Epilim®, Epilim Chrono®	
	Topiramate	e.g. Topamax®	
	Ciclosporin	e.g. Neoral®, Sandimmun® Deximune®	
	Tacrolimus	e.g.Prograf®, Advagraf®	
	Mycophenolate	e.g.CellCept®, Arzip®, Myfenax®	
Certain **modified-release preparations**	**Diltiazem**	e.g. Angitil XL®, Zemtard®, Slozem®, Adizem XL®, Tildiem LA®	The BNF states that the brand names should be specified in certain instances as different versions of these modified-release (m/r) preparations may not have the same clinical effect.
	Mesalazine	e.g. Asacol MR®, Pentasa®	
	Nifedipine	e.g. Adipine MR or XL®, Coracten SR or XL®, Adalat Retard®,	
	Methylphenidate	e.g.Concerta XL®, Equasym XL®, Medikinet XL®	
Certain **Controlled Drugs** including patches (Schedule 2 and 3)	**Buprenorphine**	e.g. BuTrans®, Transtec®	Caution due to differing dosage regimes for SR and XL preparations. The BNF states that dosage should be reviewed if brand altered.
	Fentanyl (transdermal)	e.g. Mezolar®, Durogesic DTrans®, Fentalis®, Matrifen®, Tilofyl®	
	Morphine	e.g. MST®, MXL®, Zomorph®, Morphgesic SR ®, Sevredol®	
	Oxycodone	e.g. Oxycontin®, Oxynorm®	
Certain **inhaler devices**	**CFC Free Beclometasone** (+/- Formoterol)	Qvar®, Clenil® Fostair®	Always state the type of device e.g. accuhaler, turbohaler. Caution should be exercised when changing from CFC containing aerosol to Qvar or Fostair (dose adjustment required).
	Dry powder devices	Accuhaler®, Easyhaler®, Turbohaler®, Pulvinal®, Clickhaler®, Foradil® etc.	
Multi-ingredient products	**See examples →**	Stalevo®	Generic prescribing may not be practical or may cause confusion due to multiple ingredients. Some combination products are appropriate for generic prescribing using an approved 'co-' prefix e.g. co-codamol, co-amilofruse, etc.
		Hormone replacement therapy	
		Oral contraceptives	
		Multi-ingredient GI preps. e.g. Peptac®, pancreatin, rehydration salts, laxatives etc.	
		Multi-ingredient ENT preparations	
		Creams, bath oils, antiseptics, liquids or gels	
		Bowel cleansing solutions	
Specific brands for **specific indications**	**Duloxetine**	e.g. Yentreve® or Cymbalta®	
	Sildenafil	e.g. Viagra® or Revatio®	
	Buprenorphine	e.g. Subutex® or Temgesic®	
	Midazolam	e.g. Buccolam®, Epistatus®	
Miscellaneous	**See examples →**	Antipsychotic depot injections	These should be prescribed using the brand name to avoid confusion / aid product identification. Generic prescribing for these drugs may affect clinical response or contribute to administration incidents.
		Stoma care products & appliances	
		Wound products	
		Insulin	
		Nutritional products	
		Vaccines	
		NRT	
		Calcium salts – Natecal D3®, Adcal®,	
		Pre-filled injectables – e.g. Adrenaline, somatropin, apomorphine, erythropoietin,etc	

Note: Please also refer to the HSCB guidance on using specified brands that are cost effective choices for the HSC.

Oral tacrolimus products: Updated CHM advice (May 2012)

Questions and answers

What is oral tacrolimus and what is it prescribed for?

Tacrolimus is a medicine that helps control the body's immune system. "Oral" tacrolimus medicines are prescribed after a liver, heart and kidney transplant operation, to prevent the body from rejecting the new organ. It is also used for the treatment of transplant rejection when other immune treatments have failed.

What are the main risks with this medicine?

If a patient is under dosed there is a risk of loss of the transplanted organ, because of 'rejection' by the body's immune system. On the other hand if the patient is overdosed undesirable effects may be more likely to occur. For this reason, patients need to be carefully monitored so the correct drug level in the blood is maintained. Changes in drug blood levels, even minor, may lead to under dosing or overdosing.

Where can I find out about the potential side effects of my tacrolimus medicine?

Your medicine comes with a Patient Information Leaflet, which describes how to take the medicine and provides advice and information on potential side effects.

What is MHRA recommending?

The MHRA is recommending that to mini mise the risk of medication errors caused by inadvertent switching between brands , prescribers should prescribe tacrolimus products by brand name only. Pharmacists should always dispense the exact brand prescribed, and should contact the prescriber if in doubt, to ensure that the correct brand is dispensed.

Why is MHRA making this recommendation now?

There are a growing number of oral tacrolimus medicines available in the UK and the Commission on Human Medicines (CHM) has conducted a review on the safe use of tacrolimus medicines. The conclusion of the review is that there is a potential risk for confusion leading to patients receiving the wrong medicine.

How will the MHRA recommendation affect me?

If you are currently taking an oral tacrolimus medicine you should continue to do so without any changes, as instructed by your doctor. You should take a careful note of the brand name of your usual tacrolimus medicine (see full list below of currently approved products). If you are ever given a tacrolimus medicine with a different brand name you should check straight-away with your pharmacist or doctor that you have been given the correct medicine.

Do I need to be particularly aware regarding my tacrolimus prescription?

Yes, you should be told and should try to remember the ex act name of your tacrolimus medicine. T he name of the medicine is stated on the label of the medicine and on the patient information leaflet that is supplied with the medicine. If you notice any changes in your prescription or if you are dispensed a different tacrolimus brand or the dosage instructions are different, you should immediately consult your pharmacist or doctor.

How many different brands are there?

There are currently thirteen brands of oral tacrolimus approved in the UK and each one has a unique name, so called brand name.

The three different pharmaceutical forms of oral tacrolimus products are shown below, together with brand names of currently approved products.

- Immediate release capsule taken twice a day (including the following brands - Adoport, Aletris, Capexion, Evenil, Miloprosan, Prograf, Tacni, Takon, Taliximun, Tamitect and Vivadex)

- Prolonged release capsule taken once daily (Advagraf)

- Granules for oral solution taken twice daily (Modigraf).

What if a brand became unavailable?

If a particular brand is not available and a patient has been receiving that particular brand he or she may be switched to an alternative brand. However, this change of brand should only be done under medical supervision and additional tests should be conducted to check the amount of tacrolimus in the blood after the change.

What should a doctor state on a tacrolimus prescription?

A doctor should state the brand name of the particular medicine together with the dose (e.g. 20 mg) and the frequency it should be given (e.g. once a day).

Would the pharmacist have to dispense the same tacrolimus brand stated in the prescription?

Yes, the pharmacist should dispense the particular brand specified in the prescription. If there is any doubt regarding the prescription (for example, the intended brand, or dose), the pharmacist should consult the prescribing physician before dispensing the medicine.

Is it OK if my doctor changes me from one brand of tacrolimus to another?

Yes, you may have a change in the brand of tacrolimus but this should be done only under medical supervision and additional tests should be conducted to check the amount of tacrolimus in the blood after the change.

What should I do if I've forgotten the brand name of my usual medicine?

Your doctor should know the exact brand you are taking so you should check with your doctor first. If are unable to discuss it with your doctor speak to your pharmacist.