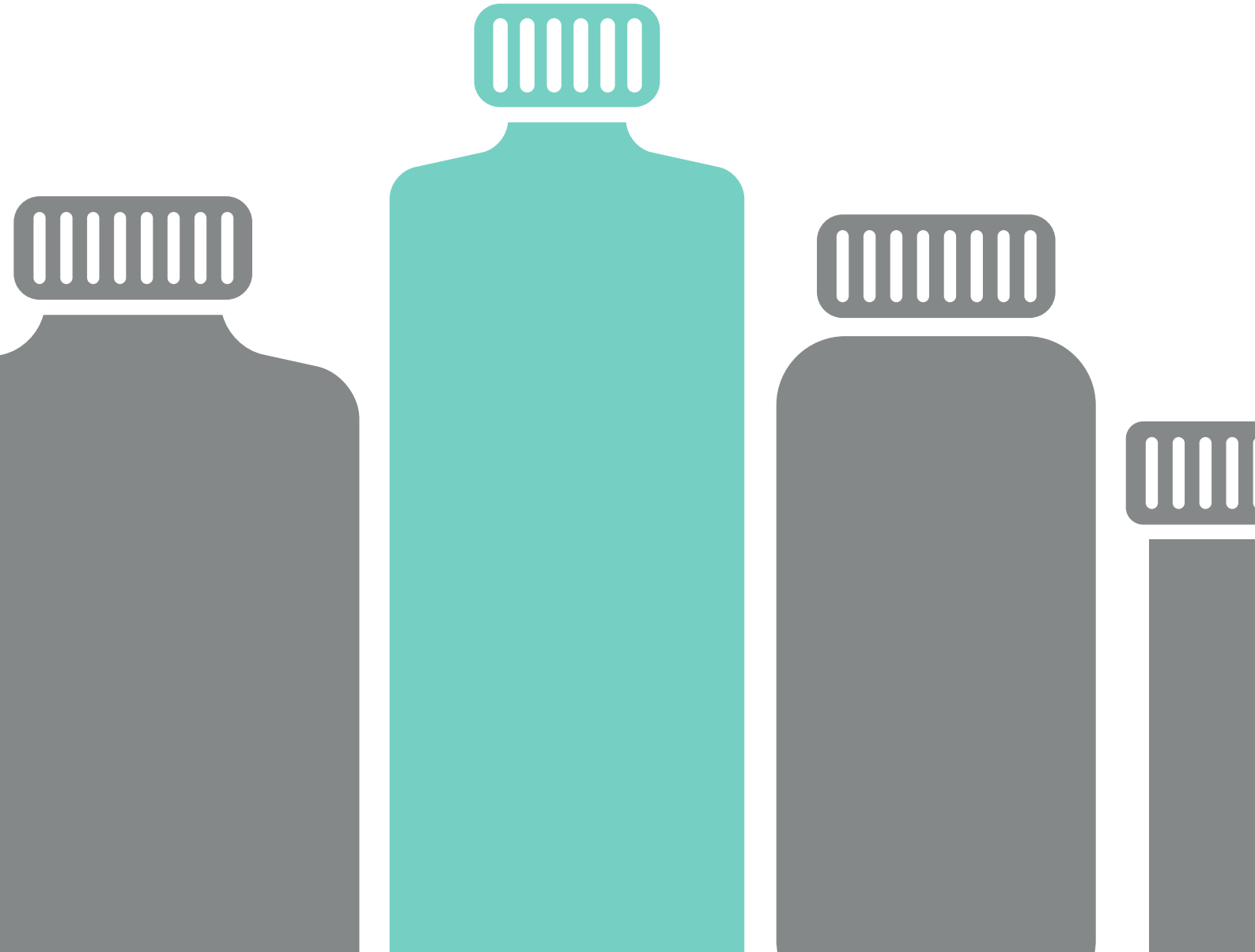
Greater Manchester
Commissioning Support Unit

Medicines Management

Generic Prescribing Guidelines

Greater Manchester Medicines Management Group (GMMMG) Guidance



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Generic Prescribing Guideline

Executive Summary:

- A generic medicine contains the same quantity of active substance(s) as the proprietary medicine that originally received marketing authorisation (i.e. the reference medicine).
- Generic medicines are, overall, much less expensive to the NHS. Their appropriate use instead of branded medicines delivers considerable cost savings.
- Across Greater Manchester CCGs the annual potential savings range from £123,700 to £252,800
- It is good practice to prescribe drugs generically using their approved, International Non-proprietary Name (INN) (i.e. as described in the BNF) and not specify the manufacturer or supplier, except where a change to a different manufacturer's product may compromise efficacy or safety
- List prices for some 'branded generics' may be lower than the reimbursement price for equivalent generics. However, any cost savings achieved by their use may be unsustainable by the manufacturer and may not necessarily be cheaper, or in the best interests of the NHS in the longer term.
- If a generic medicine is granted a license, the regulatory authority has considered it equally safe and clinically equivalent to the reference branded medicine when used at the same dose to treat the same condition. There is little clinical evidence to suggest that interchanging branded and generic medicines causes any adverse clinical consequences.
- There are a few circumstances when it is appropriate to prescribe a specific manufacturer's product (branded or generic). These include:

– drugs with a narrow therapeutic index
– certain modified- or controlled-release drugs
– certain administration devices
– multiple ingredient products
– 'biosimilar' medicines
– ensuring adherence to long-term medications, where differences in appearance between manufacturer's products might cause confusion and anxiety

1. Background

1.1. The Department of Health continues to support the increased use of generic medicines in a way that is less prescriptive and acceptable to patients, recognising that there are still some more cost savings to be made in this area.

1.2. Presently, if a specific brand-name drug is prescribed in primary care, a pharmacist is obliged to supply this even if an equivalent generic version is available. Reimbursement is made using the manufacturer's list price for the branded product.

1.3. When a generic name is written, a branded or generic version can be supplied, but the pharmacist is reimbursed at the generic rate. The reimbursement price to dispensers of generic medicines includes a significant margin to fund the UK community pharmacy contract and encourage price competition between generic medicine suppliers.

1.4. This is due, among other things, to the larger discount generally offered to dispensers on the average generic medicine. The difference between the discounted price that the pharmacy

buys medicines for and what they are reimbursed by the NHS, forms part of the funding for the community pharmacy contract.[7]

1.5. If this community pharmacy margin is undermined by a large change in prescribing practice, e.g. a whole population switch to a branded item from a generic medicine, the result would be a drop in reimbursement to the national pharmacy contract, which is set annually. This loss in community pharmacy earnings will need to be found from elsewhere in the prescribing budget e.g. by increasing the reimbursement of other generic items.

1.6. Hence a change in one area of prescribing may look like a saving to the prescribing budget but over the year the national amount recouped from prescribing of generic items will remain fixed.

1.7. Some generic medicines have been given a brand name by the manufacturer for marketing reasons; these products are referred to as '**branded generics**'. List prices for branded generics may be lower than the list price for equivalent generics (Drug Tariff Part VIII), and some Primary Care Organisations have adopted policies promoting selected branded generics to achieve cost savings. However, these savings may be unsustainable by the manufacturer and overall may not necessarily be cheaper, or in the best interests of the NHS in the longer term[7].

2. Scope

2.1. This guidance applies to all services contracted by or delivered by the NHS across Greater Manchester, including: GPs, any other prescribers, Acute Hospitals, NHS community providers, and Out Patient clinics who provide NHS prescriptions which are dispensed in a pharmacy.

2.2. This covers the provision of prescriptions to a patient registered on the list of a general medical practitioner, or temporary resident.

2.3. It does not cover the provision of private services or prescriptions to members of the public who are not registered with the practice.

3. Benefits of Generic Prescribing

3.1 Many medicines are available in both generic and branded forms. However, generic medicines are, overall, much less expensive to the NHS.

3.2 Generic prescribing can reduce the risk of prescribing or dispensing error as each drug has only one approved name, rather than many brand names.

3.3 Generic Prescribing allows patients to recognise the medicine International Non-proprietary Name (INN) on their prescription. This will reduce expectation that a particular brand should be used when a situation occurs where a different product needs to be supplied. Examples of these situations could be patent expiry or a brand becoming unavailable or obtaining supply from abroad or a hospital or different dispensary than the patient's usual one.

3.4 Generic prescribing allows any suitable generic (or equivalent branded product) to be dispensed, reduces the number of items to be stocked in the pharmacy and can potentially reduce delays in supplying medicines to the patient (e.g. when a particular brand is not stocked)

3.5 Where non-proprietary ('generic') titles are given, they should be used in prescribing, except in the circumstances detailed in section 4This will enable any suitable product to be dispensed, thereby saving delay to the patient and sometimes expense to the health service. The only exception is where there is a demonstrable difference in clinical effect between

each manufacturer's version of the formulation, making it important that the patient should always receive the same brand; in such cases, the brand name or the manufacturer should be stated. Non-proprietary titles should **not** be invented for the purposes of prescribing generically since this can lead to confusion, particularly in the case of compound and modified-release preparations.[6]

4. When should a Specific Manufacturers Product be Prescribed?

4.1 A specific manufacturer's product could be either branded or generic.

4.2 **Drugs with a narrow therapeutic index -** there is no good quality evidence for any clinically significant difference between bioequivalent medicines containing drugs with a narrow therapeutic index. However, in view of the concerns and potentially serious consequences of losing therapeutic control, patients should be maintained on the same manufacturer's product for drugs with a narrow therapeutic index.

Examples: phenytoin; carbamazepine; ciclosporin; lithium

4.3 **Anti-epileptics (where used in epilepsy only) -** There is no robust evidence that switching products adversely affects seizure control and not all anti-epileptics have a narrow therapeutic index. However NICE CG137 The Epilepsies states

"Consistent supply to the child, young person or adult of a particular manufacturer's AED preparation is recommended, unless the prescriber, in consultation with the child, young person, adult and their family and/or carers as appropriate, considers that this is not a concern. Different preparations of some AEDs may vary in bioavailability or pharmacokinetic profiles and care needs to be taken to avoid reduced effect or excessive side effects. Consult the summary of product characteristics (SPC) and British national formulary on the bioavailability and pharmacokinetic profiles of individual AEDs, but note that these do not give information on comparing bioavailability of different generic preparations."

Therefore, pragmatically, it is reasonable to err on the side of caution and specify the preparation by brand name (or as a generic from a particular manufacturer) to maintain continuity of supply, particularly for seizure free and stabilised patients, regardless of the antiepileptic drug being prescribed.

a. Where newer antiepileptics are prescribed that are only currently available as the branded product care should be taken to ensure that prior to generic alternatives becoming available all prescriptions for control of epilepsy are changed to brand to avoid inadvertent generic switch once generics are available.

b. Patients should be considered as individual cases and if a patient has poor control then switching to a generic product may bnot inadvertnatly affect seizure control.

c. Where antiepileptic drugs are used for control of conditions other than epilepsy (e.g. neuropathic pain, migraine prophylaxis etc) products should be prescribed generically where available.

4.4 **Certain modified- or extended-release products -** Drug release and bioavailability profiles may differ considerably between modified-release or extended-release formulations of drugs, primarily because of different formulation approaches taken by manufacturers.

The MHRA recommends that all modified-release preparations should be prescribed by their brand name, but the BNF warns against changing brands only where there is the possibility of significant clinical impact (e.g. loss of clinical control or increased risk of adverse effects).

In many instances, variation that results from non-bioequivalence is likely to have a smaller effect than other factors that determine absorption and distribution of the drug (e.g. not taking the medicine exactly on time and varying the time of taking the medicine with respect to food). For these reasons the BNF does not highlight the need to keep to the same brand for every modified-release drug.[3]

Examples: modified-release diltiazem, nifedipine and mesalazine; transdermal strong opioids, tacrolimus

4.5 **Certain drug administration devices -** Technique may be an important component of drug delivery, and brand name prescribing is appropriate where administration devices, such as metered dose inhalers, have different instructions for use and patient familiarity with the same product is important. The MHRA has advised healthcare professionals that CFC-free beclometasone inhalers (Qvar® and Clenil Modulite®) are not interchangeable and should be prescribed by brand name.[4] These products have different designs and provide different quantities of the active drug to the lungs

4.6 **Multiple ingredient products -** Generic titles may not always exist for many multiple ingredient products, and prescribing a specific brand or manufacture's product is necessary for identification and ensuring that the correct product is dispensed.

Examples: oral contraceptives; emollient creams. Non-proprietary titles should not be invented for the purpose of prescribing generically

4.7 **Different licensed indications for the same drug -**
Example: Cymbalta®▼ is licensed for treatment of depression, diabetic peripheral neuropathic pain in adults, and generalised anxiety disorder, whereas Yentreve®▼ is licensed for stress urinary incontinence in women (both contain duloxetine▼).

4.8 **Biosimilar products -** A biological medicine is a medicine that contains one or more active substances made by or derived from a biological source[1] A biosimilar medicine is a biological medicine that is developed to be similar to an existing biological medicine (the 'reference medicine'). Biosimilars are not the same as generics, which have simpler chemical structures and are considered to be identical to their reference medicines.

The active substance of a biosimilar and its reference medicine is essentially the same biological substance, though there may be minor differences due to their complex nature and production methods. Subtle differences between biosimilar medicines from different manufacturers and the reference product may not be fully apparent until greater experience in their use has been established.

Biosimilar medicines are not viewed as being interchangeable with the originator product in the UK. In 2008, the Medicines and Healthcare products Regulatory Agency recommended that it is good practice to prescribe biological products by brand name to ensure that automatic substitution of a biosimilar product does not occur when the medicine is dispensed.[8] A recent EU directive requires the brand name to be included in the medical prescription of all biological products.[9]
Therefore, in order to support pharmacovigilance monitoring, the specific biological medicinal product given to the patient should be clearly identified, and **prescribing should refer to a specific manufacturer's product**.

Examples: Six biosimilar medicinal products are currently marketed in the UK—three versions of filgrastim (Nivestim, Tevagrastim and Zarzio), two versions of epoetin (Binocrit and Retacrit) and one version of somatropin (Omnitrope).

Applications for biosimilar versions of follitropin alfa and infliximab are under evaluation by the European Medicine's Agency (EMA) Committee for Medicinal Products for Human Use. In the future there may also be biosimilar versions of insulins, recombinant vaccines, interferons and monoclonal antibodies such as rituximab and trastuzumab.
It is estimated that about 50% of the current UK market for biological medicines by spend may be subject to biosimilar competition by 2019. An up to date list of biosimilar products licensed by the EMA is available on their website[10]. It is recommended that patients commencing biosimilars are prescribed a preparation likely to be less expensive in the longer term but switching between biosimilars is not recommended.

4.9 **Different excipients-** Inactive formulation ingredients (excipients) may differ between products (branded and generic). Where an individual patient is intolerant to an excipient, it may be reasonable to prescribe a specific brand or generic product that does not contain the troublesome component.

4.10 **Differences in appearance-** For conditions requiring long-term medication, differences in appearance between manufacturer's products might cause confusion and anxiety, and this may affect adherence. This may be of most concern among the elderly, those with learning disabilities, mental health patients, non-English speaking patients and those with low-levels of 'health literacy'. Where it is not possible to allay patients' concerns effectively, it may be appropriate for a specific brand or manufacturer's generic to be prescribed. Recommendations about how healthcare professionals can support patients to adhere to their prescribed medicine can be found in NICE clinical guideline 76.[11]

4.11 A table of "Items Unsuitable for Generic Prescribing" is available in Appendix 1 based on an original version by Health and Social Care Board of Northern Ireland; July 2008.

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12th September 2013

Appendix 1

Items Unsuitable for Generic Prescribing

The following list provides examples of drugs/preparations which the GMMMG would NOT recommend for generic prescribing. This list is guidance only. For further information refer to the BNF. Refer to GM Formulary for preferred brands where applicable.

BNF	Drug or drug class	Reason for considering brand-name prescribing	Specific references
Chapter 1			
1.1.2	Antacids preparations containing simeticone	To aid identification. Products contain multiple ingredients.	-
	Compound alginates and proprietary indigestion preparations	To aid identification. Products contain multiple ingredients.	-
1.5.1	Mesalazine oral preparations	The delivery characteristics of oral mesalazine preparations may vary; these preparations should not be considered interchangeable	BNF
1.6.4	Macrogols (polyethylene glycols)	To aid identification. Products contain multiple ingredients.	-
1.9.4	Pancreatin supplements	To aid identification. Products contain multiple ingredients.	-
Chapter 2			
2.6.2	Diltiazem Standard Formulations 60mg modified release preparations	These formulations are licensed as generics and there is no requirement for brand name dispensing. Although their means of formulation has called for the strict designation 'modified-release' their duration of action corresponds to that of tablets requiring administration 3 times daily	BNF
2.6.2	Diltiazem Longer-Acting Formulations >60mg modified release preparations	Different versions of modified-release preparations containing more than 60 mg diltiazem hydrochloride may not have the same clinical effect. To avoid confusion between these different formulations of diltiazem, prescribers should specify the brand to be dispensed	BNF
2.6.2	Nifedipine modified release preparations	Different versions of modified-release preparations may not have the same clinical effect. To avoid confusion between these different formulations of nifedipine, prescribers should specify the brand to be dispensed. Modified-release formulations may not be suitable for dose titration in hepatic disease.	BNF
Chapter 3			

BNF	Drug or drug class	Reason for considering brand-name prescribing	Specific references
3.1.1	Dry powder inhalers	Patient familiarity with one brand is important; instructions for use vary between preparations.	-
3.1.3	Theophylline modified release preparations	The rate of absorption from modified-release preparations can vary between brands. If a prescription for a modified-release oral theophylline preparation does not specify a brand name, the pharmacist should contact the prescriber and agree the brand to be dispensed. Additionally, it is essential that a patient discharged from hospital should be maintained on the brand on which that patient was stabilised as an in-patient. Theophylline has a narrow therapeutic index.	BNF
3.1.3	Aminophylline modified release preparations	MR preparations have different release characteristics and are not interchangeable. Aminophyline has a. narrow margin between therapeutic and toxic dose	BNF
3.2	Beclometasone dipropionate CFC-free pressurised metered dose inhalers	*Qvar* and *Clenil Modulite* are not interchangeable. *Qvar* has extra-fine particles and is approximately twice as potent as *Clenil Modulite* and CFC-containing beclometasone inhalers. The MHRA has advised that CFC-free beclometasone inhalers should be prescribed by brand name. This applies also to combination products.	BNF, MHRA
3.2	Beclometasone dry powder inhalers	Patient familiarity with one brand is important; instructions for use vary between preparations.	-
3.2	Beclometasone and formoterol CFC-free metered dose inhalers	See beclometasone CFC-free metered dose inhalers, above.	BNF, MHRA
3.4.3	Adrenaline pre-filled syringes	Patient familiarity with one brand is important; instructions for use vary between preparations.	-
Chapter 4			
4.2.3	Lithium preparations	Preparations vary widely in bioavailability. Changing the preparation requires the same precautions as initiation of treatment. Lithium has a narrow therapeutic index.	BNF
4.4	Methylphenidate modified release preparations	MR preparations contain different proportions of immediate-release and modified-release methylphenidate.	-
4.7.2	Buprenorphine transdermol	BuTrans/Transtec are different strengths, have different indications and drug release rates.	-

BNF	Drug or drug class	Reason for considering brand-name prescribing	Specific references
4.7.2	Morphine oral modified release preparations	MR preparations have different release characteristics; Patient familiarity with one brand is important.	PCF3
4.7.2	Fentanyl patches	Patches are available as matrix and reservoir formulations; Patient familiarity with one brand is important. Reservoir patches (e.g. *Fentalis®, Tilofyl®*) must not be cut because damage to the rate-limiting membrane can lead to a rapid release of fentanyl resulting in overdose. If the prescriber intends the patch to be cut (although this is unlicensed and not recommended by the MHRA) then the prescription must specify a brand of matrix formulation patch (e.g. *Durogesic DTrans*, *Matrifen*).	PCF3 MHRA
	Oxycontin/oxycodone	A number of errors have been reported where the wrong preparation has been dispensed or administered when this drug was prescribed generically.	Controlled drug reports to accountable officer
4.8.1	Antiepileptic medicines	Loss of seizure control has been reported in patients after switching brands of antiepileptic medicines. Continuity of the same brand, or the same generic preparation is recommended for patients with seizure disorders. (For individual antiepileptic agents, see below.)	NICE Epilepsy Action
4.8.1	Carbamazepine	Different preparations may vary in bioavailability; to avoid reduced effect or excessive side-effects, it may be prudent to avoid changing the formulation Carbamazepine has a narrow therapeutic index. (See also 'Antiepileptic medicines' above.)	BNF
4.8.1	Lamotrigine	Generic and branded products are bioequivalent. See also 'Antiepileptic medicines' above.	MHRA
4.8.1	Phenytoin	On the basis of single dose tests there are no clinically relevant differences in bioavailability between available phenytoin sodium tablets and capsules but there may be a pharmacokinetic basis for maintaining the same brand of phenytoin in some patients. Phenytoin has a narrow therapeutic index. (See also 'Antiepileptic medicines' above.)	BNF

BNF	Drug or drug class	Reason for considering brand-name prescribing	Specific references
4.8.1	Sodium valproate	Modified release preparations should be prescribed by brand but the pharmacological effects of sodium valproate may not be clearly correlated with the total or free plasma valproate acid levels.	Epilim 200 SPC
4.8.1	Topiramate	Generic and branded products are bioequivalent. See also 'Antiepileptic medicines' above.	MHRA
4.9.1	Apomorphine pre-filled syringe	Patient familiarity with one brand is important; instructions for use vary between preparations.	-
4.9.3	Botulinum toxin type A	Preparations are not interchangeable due to differences in potency.	BNF
Chapter 6			
6.1.1	Insulin	Patient familiarity with the same brand is important; training is required in the use of specific devices for self-injection.	-
6.4.1	Hormone replacement therapy oral preparations	Different brands of the same formulation are available. Patient familiarity with one brand is important.	-
6.4.1	Estradiol transdermal patches	Different brands of the same formulation are available. Patient familiarity with one brand is important.	-
6.5.1	Somatropin injection cartridges	Patient familiarity with the same brand is important and training is required in the use of specific devices for self-injection. Some somatropin preparations are licensed as 'biosimilar' medicines.	-, BNF
Chapter 7			
7.3.1	Combined oral contraceptive	Different brands of the same formulation are available. Patient familiarity with one brand is important.	-
7.3.2	Progestogen only oral contraceptive	Different brands of the same formulation are available. Patient familiarity with one brand is important. In addition the advice for action following a missed pill differs between brands so important to keep to the same brand.	-
7.4.5	Alprostadil injection	Patient familiarity with one brand is important; instructions for use vary between preparations.	-
Chapter 8			

BNF	Drug or drug class	Reason for considering brand-name prescribing	Specific references
8.2.1	Mycophenolate	Generic mycophenolate is considered bioequivalent to *CellCept*; but it may be prudent not to change formulation except on the advice of a transplant specialist. Mycophenolate mofetil and mycophenolic acid preparations are not interchangeable.	BNF,
8.2.2	Ciclosporin	Preparations are not interchangeable and should be prescribed by brand-name to avoid inadvertent switching. It is important not to change formulation except on the advice of a transplant specialist. Ciclosporin has a narrow therapeutic index.	BNF MHRA
8.2.2	Tacrolimus	Preparations are not interchangeable; care should be taken to ensure the correct preparation is prescribed and dispensed. It is important not to change formulation except on the advice of a transplant specialist. Tacrolimus has a narrow therapeutic index.	BNF, MHRA
8.2.4	Interferon pre-filled disposable injection devices Peginterferon pre-filled disposable injection devices	Patient familiarity with one brand is important; instructions for use vary between preparations.	
Chapter 9			
9.1.3	Erythropoietin	Patient familiarity with the same brand is important and training is required in the use of specific devices for self-injection. Some epoetin preparations are licensed as 'biosimilar' medicines.	BNF, UKMi
9.1.6	Pegfilgrastim Filgrastim	Patient familiarity with the same brand is important and training is required in the use of specific devices for self-injection. Generic filgrastim has been approved as a 'biosimilar' medicine.	BNF, UKMi
9.2.1	Oral rehydration salts	To aid identification. Products contain multiple ingredients.	-
9.5.1	Calcium salts	To aid identification. Products contain multiple ingredients.	-
Chapter 12			
12.1-12.3.5	ENT preps	To aid identification. Products contain multiple ingredients. Steroid nasal sprays could be prescribed generically unless brand has lowest acquisition cost.	

BNF	Drug or drug class	Reason for considering brand-name prescribing	Specific references
12.3.5	Saliva replacement products	To aid identification. Products contain multiple ingredients.	-
Chapter 13			
13.1-13.10	Preparations for skin and scalp conditions containing multiple ingredients	To aid identification. Products contain multiple ingredients. Also, potency of topical corticosteroids preparations is a result of the formulation as well as the corticosteroid.	-