Which medicines should be considered for brand-name prescribing in primary care?

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Background

Medicines may be prescribed by 'brand' (proprietary) or 'generic' (recommended International Non-proprietary Name, rINN) name.

In primary care, if a medicine is prescribed by brand name, the pharmacist may dispense only the specified brand and is reimbursed for doing so. If a medicine is prescribed by generic name, the pharmacist may dispense any suitable generic or branded product and is reimbursed at a set price, listed in the Drug Tariff [1]. Proposals for 'generic substitution' whereby community pharmacists would be allowed to supply a generic preparation even if a branded product were prescribed have been rejected in England [2]. Since 2013, legislation has allowed generic substitution in Ireland for medicines on an 'interchangeable list' maintained by the Health Products Regulatory Agency (formerly the Irish Medicines Board) [3].

Advantages of generic prescribing are that it is generally more cost-effective than prescribing by brand name and, because it allows any suitable product to be dispensed, can reduce delays in supplying medicines to the patient [4,5]. Increasing the level of generic prescribing in the UK has long been encouraged. A measure of the generic prescribing of twenty medicines in primary care in England ('Potential Generic Savings Report') is reported as a prescribing comparator [6].

Although generic prescribing is encouraged, there are some circumstances in which it is preferable to prescribe by brand name. Broadly, these circumstances are where continuity of the same brand is important due to differences in bioavailability, where patient training differs between products and for biological medicines [4,7]. The NHS Dictionary of Medicines and Devices (dm+d) and NHS Prescription Service Common Drug Reference database annotate medicines not recommended for generic prescribing [7,8]. Prescribing decision-support software may also indicate medicines for which brand-name prescribing is preferred.

Answer

Medicines should be prescribed by brand name in the following situations:

1. Where there is a difference in bioavailability between brands of the same medicine, particularly if the medicine has a narrow therapeutic index. In these circumstances, lack of clarity over which preparation is intended when prescribing can lead to the patient receiving a sub-therapeutic or toxic dose. Examples include ciclosporin, lithium, CFC-free beclometasone metered dose inhalers and some antiepileptic medicines [4].

2. Where modified-release (MR) preparations are not interchangeable, particularly if the medicine has a narrow therapeutic index. This avoids confusion between formulations with different release characteristics. Examples include aminophylline and methylphenidate [4].

3. Where there are important differences in formulation between brands of the same medicine. For example, fentanyl patches, which are available as matrix formulations and reservoir formulations. Reservoir patches must not be cut because damage to the rate-limiting membrane can lead to a rapid release of fentanyl resulting in overdose [9]. If the prescriber intends the patch to be cut (although this is unlicensed and not recommended by the Medicines and Healthcare Regulatory Agency (MHRA) [10]) then the prescription must specify a brand of matrix formulation patch.

4. Where administration devices have different instructions for use and patient familiarity with one product is important. Examples include dry powder inhalers and adrenaline auto-injectors [4,8].
5. Where the product is a biological rather than chemical entity. Many such agents are licensed as biosimilar medicines. Examples include erythropoietin and somatropin (growth hormone) preparations [4].

Brand-name prescribing may also be preferred:

- Where products contain more than one ingredient and brand-name prescribing aids identification. This can be useful when prescribing products with multiple ingredients (e.g. pancreatin supplements and skin or scalp preparations) [11].
- Where branded and generic preparations have different licensed indications. Generic preparations are licensed on the basis of bioequivalence with the branded product and it can be argued that brand-name prescribing is not necessary. It can also be argued that a medicine should not be used 'off-label' for an unlicensed indication when a licensed alternative exists. In March 2015, NHS guidance was issued recommending pregabalin be prescribed by brand name (*Lyrica*) as far as reasonably possible, when used for neuropathic pain; for all other indications, pregabalin should be prescribed generically [12,13]. At the time *Lyrica* was the only pregabalin preparation licensed for neuropathic pain. From July 2017, that guidance was withdrawn and replaced with new advice allowing pregabalin to be prescribed generically for all indications [14].
- For some patients, where differences in product name, presentation, appearance or taste may lead to anxiety, confusion, dosing errors and reduced adherence. Difficulties for patients with autism, learning difficulties or mental health problems should be considered [15].

Table 1 lists medicines that may be considered for brand-name prescribing in primary care. It does not list all biologics, self-administration devices or medicines with multiple ingredients. Please consider the bullet points above.

Note: This Medicines Q&A does not imply branded preparations are superior to generics. Where brand-name prescribing is recommended, it is a means of ensuring the patient consistently receives the same product. It is similarly possible to prescribe a branded generic, or to specify the manufacturer of a generic preparation on the prescription. The intention is to avoid inadvertent switching between preparations where this may have a detrimental effect on patient care.

The table has been compiled using a number of sources; specific references for individual medicines are included where appropriate. Entries are listed by BNF chapter.

Table 1. Medicines that may be considered for brand-name prescribing in primary care.

Drug or drug class	Reason for considering brand-name prescribing
Chapter 1	
Mesalazine oral preparations	The BNF states there is **no evidence** that any one oral preparation of mesalazine is more effective than another; however, delivery characteristics of mesalazine preparations may vary [4]. If switching to a different brand of mesalazine, advise the patient to report any changes in symptoms [16].

Drug or drug class	Reason for considering brand-name prescribing
Chapter 2	
Diltiazem MR preparations >60mg	Different versions of diltiazem MR preparations containing more than 60mg may not have the same clinical effect [4].
Nifedipine MR preparations	Different versions of nifedipine MR preparations may not have the same clinical effect [4].
Chapter 3	
Dry powder inhalers	Patient familiarity with one brand is important; instructions for use vary between preparations and patient training is required [8]. Generic prescribing of inhalers should be avoided as this can lead to people with asthma being given an unfamiliar inhaler device with resultant problems of usage and compliance [17].
Theophylline MR preparations	Theophylline has a narrow therapeutic index and bioavailability differs between brands of oral MR theophylline. Patients should be maintained on the same brand [4, 17]. If a prescription for an oral theophylline MR preparation does not specify a brand name, the pharmacist should contact the prescriber and agree the brand to be dispensed [4].
Aminophylline MR preparations	Aminophylline has a narrow therapeutic index and bioavailability differs between brands. Patients should be maintained on the same brand [4]. If a prescription for an oral aminophylline MR preparation does not specify a brand name, the pharmacist should contact the prescriber and agree the brand to be dispensed [4].
Beclometasone dipropionate-containing CFC-free pressurised metered dose inhalers	Beclometasone dipropionate CFC-free pressurised metered-dose inhalers are **not** interchangeable and should be prescribed by brand name; *Qvar* has extra-fine particles, is more potent than traditional beclometasone dipropionate CFC-containing inhalers, and is approximately twice as potent as *Clenil Modulite* [4,18].
Adrenaline (epinephrine) pre-filled syringes	Patient familiarity with one brand is important; instructions for use vary between preparations and patient training is required [8]. To ensure patients receive the auto-injector device that they have been trained to use, prescribers should specify the brand to be dispensed [4].
Chapter 4	
Lithium preparations	Lithium has a narrow therapeutic index and preparations vary widely in bioavailability. Changing the preparation requires the same precautions as initiation of treatment [4].

Drug or drug class	Reason for considering brand-name prescribing
Chapter 4 continued	
Buprenorphine patches	Buprenorphine patches are available as 72-hourly, 96-hourly and 7-day formulations [4,9]. Brand name prescribing is recommended to reduce the risk of confusion and error in dispensing and administration [9,19].
Fentanyl patches	Fentanyl patches are available as matrix and reservoir formulations. Reservoir patches must not be cut because damage to the rate-limiting membrane can lead to a rapid release of fentanyl resulting in overdose [9]. If the prescriber intends the patch to be cut (NB: unlicensed and not recommended by the MHRA) then the prescription must specify a brand of matrix formulation patch. Brand name prescribing is recommended to reduce the risk of confusion and error in dispensing and administration [9,19].
Methylphenidate MR preparations	Methylphenidate MR preparations contain both immediate-release (IR) and MR methylphenidate. The proportion of IR and MR methylphenidate differs between brands; different preparations may not have the same clinical effect [4].
Morphine oral MR preparations	Oral morphine MR preparations are available in 12-hourly and 24-hourly formulations. Dosage requirements should be reviewed if the brand of morphine MR is altered [4]. The pharmacokinetic profiles of MR products differ; to minimise the risk of mistakes, it is best to keep individual patients on the same MR brand [9]. Including the brand name on the prescription and dispensing label will aid in identification of the correct formulation to be dispensed or administered [20].
Oxycodone oral MR preparations	Oral oxycodone MR preparations are available in 12-hourly and 24-hourly formulations [4]. Brand-name prescribing is recommended to reduce the risk of confusion and error in dispensing and administration [9,21].
Tramadol oral MR preparations	Oral tramadol MR preparations are available as 12-hourly or 24-hourly formulations [4]. Brand-name prescribing is recommended to reduce the risk of confusion and error in dispensing and administration [9].

Drug or drug class	Reason for considering brand-name prescribing
Chapter 4 continued	
Antiepileptic drugs (when used for epilepsy)	The MHRA has classified antiepileptic drugs (AEDs) into three categories of risk, based primarily on their therapeutic index and physiochemical characteristics (in particular solubility and permeability across membranes) to help healthcare professionals decide whether it is necessary to maintain continuity of a specific manufacturer's product [22]: Category 1: Specific measures are necessary to ensure consistent supply of a particular product (which could be either a branded product or a specified manufacturer's generic product). Category 2: NB: By default, this category includes all AEDs not listed in categories 1 or 3. The need for continued supply of a particular manufacturer's product should be based on clinical judgement and consultation with patient and/or carer. It is necessary to consider clinical factors such as seizure frequency, treatment history and the potential implications for the individual of having a breakthrough seizure. Category 3: Therapeutic equivalence between branded and generic products (and between generics) can be assumed. For these drugs, it is usually unnecessary to ensure that patients are maintained on a specific manufacturer's product unless there are specific reasons such as patient anxiety and risk of confusion or dosing errors. The MHRA acknowledges factors other than therapeutic equivalence are important. Differences between products (e.g. product name, packaging, appearance and taste) may be perceived negatively by patients or carers and may lead to dissatisfaction, anxiety, confusion, dosing errors and reduced adherence. Difficulties for patients with autism, learning disability or mental health problems should be considered [15]. NICE recommends consistent supply (of the same brand, or the same generic preparation), for patients with seizure disorders, unless the prescriber, in consultation with the patient and their family or carers, considers this not to be a concern [23]. (For individual antiepileptic agents, see below.)
Carbamazepine	MHRA Category 1 (see 'Antiepileptic drugs' above)
Ethosuxamide	MHRA Category 3 (see 'Antiepileptic drugs' above)
Gabapentin	MHRA Category 3 (see 'Antiepileptic drugs' above)
Lacosamide	MHRA Category 3 (see 'Antiepileptic drugs' above)

Drug or drug class	Reason for considering brand-name prescribing
Chapter 4 continued	
Antiepileptic drugs (when used for epilepsy) continued	
Levetiracetam	MHRA Category 3 (see ‘Antiepileptic drugs’ above)
Phenobarbital	MHRA Category 1 (see ‘Antiepileptic drugs’ above)
Phenytoin	MHRA Category 1 (see ‘Antiepileptic drugs’ above)
Pregabalin	MHRA Category 3 (see ‘Antiepileptic drugs’ above) NHS guidance effective from July 2017 advises pregabalin can be prescribed generically for all indications [14]. Previous guidance issued in March 2015 recommended pregabalin be prescribed by brand name as far as reasonably possible, when used for neuropathic pain [12,13]. That guidance has now been withdrawn.
Primidone	MHRA Category 1 (see ‘Antiepileptic drugs’ above)
Tiagabine	MHRA Category 3 (see ‘Antiepileptic drugs’ above)
Vigabatrin	MHRA Category 3 (see ‘Antiepileptic drugs’ above)
Chapter 6	
Insulins	Patient familiarity with one brand is important; instructions for use vary between preparations and patient training is required [8].
Chapter 8	
Mycophenolate (when used to prevent transplant rejection)	Switching between a brand and generic formulation, or between generic formulations, should be initiated only by a transplant specialist [24].
Ciclosporin (when used to prevent transplant rejection)	Ciclosporin must be prescribed and dispensed by brand name. Patients should be stabilised on a particular brand of oral ciclosporin because switching between formulations without close monitoring may lead to clinically important changes in blood-ciclosporin concentration [25]. Switching between a brand and generic formulation, or between generic formulations, should be initiated only by a transplant specialist [24].

Drug or drug class	Reason for considering brand-name prescribing
Chapter 8 continued	
Tacrolimus (when used to prevent transplant rejection)	Inadvertent switching between oral tacrolimus products has been associated with reports of toxicity and graft rejection. 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 [26]. Switching between a brand and generic formulation, or between generic formulations, should be initiated only by a transplant specialist [24].
Chapter 13	
Preparations for skin and scalp conditions containing multiple ingredients	To aid identification where products contain multiple ingredients [11]. Also, potency of topical corticosteroid preparations is a result of the formulation as well as the corticosteroid [4].

Summary

Prescribing medicines by generic rather than brand name can improve cost-effectiveness and is encouraged. However, there are some circumstances in which continuity of the same product is important for patient safety and prescribing a specific manufacturer's product (brand or generic) is preferred. These include:

- Where there is a difference in bioavailability between brands of the same medicine, particularly if the medicine has a narrow therapeutic index.
- Where modified-release preparations are not interchangeable.
- Where there are important differences in formulation between brands of the same medicine.
- Where administration devices (e.g. inhaler or self-injection) have different instructions for use and patient familiarity with one product is important.
- Where the product is a biological rather than chemical entity.
- Where products contain multiple ingredients and brand-name prescribing aids identification.
- Where there are differences in licensed indications.

Limitations

This list of medicines is not comprehensive. It does not list all biologics, self-administration devices or medicines with multiple ingredients. Please consider the bullet points in the main text.

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Search strategy
In-house enquiries [Search terms: "generic substitution", "therapeutic equivalency"]
BNF [Search terms: generic, interchangeable, brand]
NICE Evidence Search [Search terms: "generic prescribing"]
Internet search [including Irish Medicines Board, NHS Business Services Authority]