University Hospitals Bristol NHS
NHS Foundation Trust

# M4: Policy for Prescribing of Medicines Used Outside the Scope of a Product Licence

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|---|---|
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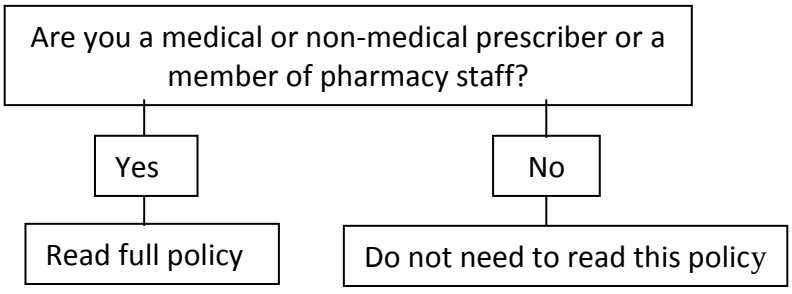
| **Document Abstract** | |

Whenever possible, prescribing of medicines should be for indications for which the medicine is licensed. However, there are clinical situations when the use of unlicensed medicines or use of medicines outside the terms of the licence i.e. 'off-label' may be judged by the prescriber to be in the best interest of the patient on the basis of available evidence. This policy lists the type of situations when an unlicensed medicine may be used and details the prescriber's responsibility to the patient in assessing the patient's needs for alternatives to the use of an unlicensed medicine and ensuring that the patient is fully aware of the use of an unlicensed medicine.

Who should read this document?




[1] Divide number of words (2532) by 240 for average reading time and add 25% for specialist content.

| Document Change Control | | | | |
|---|---|---|---|---|
| **Date of Version** | **Version Number** | **Lead for Revisions** | **Type of Revision** | **Description of Revision** |
| 17.01.13 | 2 | Director of Pharmacy | Major | Review, update and re-format into new approved trust format. |
| May 2016 | 3 | Director of Pharmacy | Minor | Review and Update. |
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## Table of Contents

# 1. Introduction

1.1 Whenever possible, prescribing of medicines should be for indications for which the medicine is licensed. However, there are clinical situations when the use of unlicensed medicines or use of medicines outside the terms of the licence i.e. 'off-label' may be judged by the prescriber to be in the best interest of the patient on the basis of available evidence. Such practice is particularly common in certain areas of medicine: for instance, in paediatrics where difficulties in the development of age-appropriate formulations means that many medicines used in children are used off-label or are unlicensed.

1.2 Healthcare professionals may regard it necessary to prescribe or advise on the use of an unlicensed medicine (through the 'specials' regime when no licensed suitable alternative is available, or when a medicine is prepared in a pharmacy by, or under the supervision of, a pharmacist), or the use of a licensed medicine outside the terms defined by the licence e.g. outside defined indications, doses, routes of administration, contrary to listed warnings or use in pregnancy.

1.3 Unlicensed or Off label use commonly includes the use of:

a) A medicine by its licensed route, to treat a disease not included in its licensed indications, or to treat a patient group not included in these licence specifications.

b) A medicine by an unlicensed route or in a manner not included in the data sheet recommendations.

c) An unlicensed medicine, in the absence of any suitable licensed formulation.

1.4 In each of these situations, the prescriber should be fully aware that his/her professional responsibility is increased. The prescriber has a duty to take reasonable care and act in a manner consistent with the practice of a responsible body of his/her peers of similar professional standing.

1.5 The Trust indemnity cover applies to any clinicians who prescribe in such a responsible manner. Practice in any other way may result in the prescriber being personally accountable for any injury caused to the patient. (Advice on the use of medicines in unlicensed indications may be obtained from the pharmacy).

1.6 Licensed medicines must therefore be prescribed, and administration of these medicines undertaken according to the Summary of Product characteristic recommendations, unless the patient has special needs that are not met by this course of action.

1.7 Medical and non-medical independent prescribers and supplementary prescribers acting in accordance with the clinical management plan are permitted to prescribe unlicensed or off label medicines providing that they are acting within the boundaries of their individual clinical competence; the professional codes and ethics of their statutory bodies; and the prescribing policies of UHBristol.

1.8 The responsibility that falls on healthcare professionals when prescribing an unlicensed medicine or a medicine off-label may be greater than when prescribing a licensed medicine within the terms of its licence. Prescribers should pay particular attention to the risks associated with using unlicensed medicines or using a licensed medicine off-label. These risks may include: adverse reactions, low product quality; or discrepancies in product information or labelling (e.g. absence of information for some unlicensed medicines, information in a foreign language for unlicensed imports, and

potential confusion for patients or carers when the Patient Information Leaflet is inconsistent with a medicine's off-label use).

## 2. Purpose and Scope

2.1 The purpose of this policy is to identify the scenarios when an unlicensed medicine is most likely to be used and to define the prescriber's responsibilities in the use of an unlicensed medicine.

## 3. Definition

### 3.1 *Licensed medicine*

(a) A licensed medicine is a medicine that holds a marketing authorisation or product licence. A marketing authorisation or product licence defines a medicine's terms of use: its Summary of Product Characteristics outlines, among other things, the indication(s), recommended dose(s), contraindications, and special warnings and precautions for use on which the licence is based, and it is in line with such use that the benefits of the medicine have been judged to outweigh the potential risks. Furthermore, a licensed medicine has been assessed for efficacy, safety, and quality; has been manufactured to appropriate quality standards, and when placed on the market is accompanied by appropriate product information and labelling.

### 3.2 *Unlicensed medicine*

(a) An unlicensed medicine is a medicine which either;

i. Does not hold a marketing authorisation in the UK.

ii. Is a 'special'; that is a medicine that is specially manufactured or imported to the order of a doctor, dentist, nurse independent prescriber, pharmacist independent prescriber or supplementary prescriber for the treatment of an individual patient. (MHRA, https://www.gov.uk/government/publications/supply-unlicensed-medicinal-products-specials).

(b) The term unlicensed medicine is often used to indicate off-label use of a licensed medicine.

### 3.3 *Off-label use of a licensed medicine*

(a) Off label use of a licensed medicine is the use of a licensed medicine outside the scope of its product licence. This may be in an unlicensed patient group e.g. the use in a child when the medicine is licensed for adults only, or the use of a different dose, route or for a different indication to that detailed in the marketing authorisation.

## 4. Duties, Roles and Responsibilities

### 4.1 *Director of Pharmacy*

(a) The Director of Pharmacy will ensure that all unlicensed medicines issued by pharmacy are issued in accordance with the pharmacy standard operating procedures for dispensing unlicensed medicines.

## 4.2 *Prescribers*

(a) Prior to prescribing an unlicensed medicine, prescribers will be satisfied that an alternative licensed medicine will not meet the patient's needs.

(b) Prior to prescribing an off-label medicine, prescribers will be satisfied that such use would better serve the patient's needs than an appropriately licensed alternative.

(c) Before prescribing an unlicensed medicine or using a medicine off-label, prescriber's will:

i. Be satisfied that there is a sufficient evidence base and/or experience of using the medicine to show its safety and efficacy

ii. Take responsibility for prescribing the medicine and for overseeing the patient's care, including monitoring and follow-up

iii. Record the medicine prescribed and, where common practice is not being followed, the reasons for prescribing this medicine. Record the fact that you have informed the patient that the medicine is not licensed or being used off label.

(d) Prescribers will:

i. Give patients, or those authorising treatment on their behalf, sufficient information about the proposed treatment, including known serious or common adverse reactions, to enable them to give informed consent. Where current practice supports the use of a medicine outside the terms of its licence, it may not be necessary to draw attention to the licence when seeking consent. However, it is good practice to give as much information as patients or carers require or which they may see as relevant.

ii. Explain the reasons for prescribing a medicine off-label or prescribing an unlicensed medicine where there is little evidence to support its use, or where the use of a medicine is innovative

## 4.3 *Pharmacy Staff*

(a) Pharmacy staff are responsible for the accuracy and quality of the preparation when a medicine has been specially prepared for a patient.

(b) Pharmacy staff are responsible for accurately dispensing an unlicensed medicine in accordance with pharmacy department standard operating procedures.

## 4.4 *All Healthcare professionals*

(a) Healthcare professionals have a responsibility to help monitor the safety of medicines in clinical use through submission of suspected adverse drug reactions to the MHRA and CHM via the Yellow Card Scheme. Such reporting is equally important for unlicensed medicines or those used off-label as for those that are licensed.

# 5. Policy Statement and Provisions

## 5.1 *Use of licensed medicines outside the scope of a product licence (off-label use)*

(a) In circumstances where the patient category or disease is not included in the product licence, the prescriber is responsible for the clinical effects of the medicine. He/she must therefore be fully aware of this responsibility and consider the benefits and risks before prescribing.

(b) If the benefits of using a product outside the scope of the licence are appreciable, this may be the more appropriate practice.

(c) If there is good published data on dosage and efficacy of a medicine in a required situation, it may be prescribed outside the scope of its product licence. In this situation, the General Practitioner may be asked to assume prescribing responsibility. The GP may request prescribing information and guidance in such circumstances and the resulting communication should be undertaken speedily to avoid inconvenience to patients.

(d) Prescriptions must always be clear and complete, hence must provide specific details of the administration of a medicine. For example, for intravenous infusions, the dose, infusion fluid, volume, rate and route must be specified. In circumstances where the prescriber wishes to administer the drug outside the scope of the licence, he/she must again consider the benefits and risks prior to prescribing and will be responsible for the clinical effects of the preparation.

## 5.2 *Use of Unlicensed Medicines*

(a) Where a licensed equivalent is available, it should be used unless the patient's requirements are not met by the use of the licensed product.

(b) Where a licensed product is unavailable although the ingredients are recognised as standard. In such circumstances, the pharmacy may prepare or purchase unlicensed preparations, for example:

i. Re-formulating licensed drugs into a different pharmaceutical presentation to aid administration to specific patient groups (e.g. oral suspensions for paediatric patients).
ii. Developing novel formulations using recognised pharmaceutical ingredients to treat specialist patient groups (e.g. individually prepared topical dermatology formulations).

(c) The prescriber should consider that supplies of unlicensed medicines may not be consistent or guaranteed, particularly if the unlicensed medicines has to be specifically imported for use.

## 5.3 *Where novel formulations of unconventional ingredients are required*

(a) Occasionally, novel formulations may be purchased or developed locally for individual patients which contain unconventional ingredients (i.e. they do not appear in a current Pharmacopoeia). Where such therapy may be regarded as research, proposals to prescribe

such medicines must be submitted to the Research Ethics Committee, prior to use in patients.

(b) In circumstances where a prescriber considers the use of such novel formulations is essential and urgent, informed written consent must be obtained from the patient or guardian.

(c) As with other unlicensed medicine use, the manufacturer is responsible for the accuracy and quality of preparation and the prescriber is responsible for the clinical effects of the preparation.

### 5.4 *Compassionate Use of medicines prior to marketing authorisation*

(a) On some occasions, new medicines are made available for individual patients on a compassionate basis, often prior to receiving a marketing authorisation in the United Kingdom.

(b) This poses an ethical dilemma, and it has been agreed that the compassionate use of such drugs would be ethical as long as the patient was offered treatment and gave informed consent for that treatment on the basis that the duration of therapy may be limited. It would not then be unethical to stop giving the drug once it was no longer free, if no funding had been agreed.

## 6. Standards and Key Performance Indicators

### 6.1 *Applicable Standards*

(a) Prescribers will consider the suitability of available licensed products before deciding to prescribe an unlicensed medicine.

(b) Prescribers will assume increased responsibility for the clinical action of the medicine when they have prescribed an unlicensed medicine.

### 6.2 *Measurement and Key Performance Indicators*

(a) Only the following staff groups will prescribe unlicensed medicines:

Doctors, dentists, nurse independent prescribers, pharmacist independent prescribers, optometrist independent prescribers and supplementary prescribers acting in accordance with the clinical plan.

## 7. References

MHRA. Informal consultation paper on the review of unlicensed medicines. Accessed on 18/12/12. Available at http://www.mhra.gov.uk/Publications/Consultations/Medicinesconsultations/Othermedicinesconsultations/CON046465

MHRA. Medicines that do not need a license (exemptions from licensing). Accessed on 18/12/12. Available at http://www.mhra.gov.uk/Howweregulate/Medicines/Doesmyproductneedalicence/Medicinesthatdonotneedalicence/index.htm

## 8. Associated Documentation

8.1 Pharmacy department unlicensed medicines standard operating procedure.

8.2 Patient Information Leaflet. Use Of Unlicensed Medicines Supplied By The Pharmacy Production Department

8.3 Patient Information Leaflet. The Use Of Unlicensed Medicines And Medicines For Unlicensed Conditions Information For Patients And Carers

8.4 Patient Information Leaflet. The Use Of Unlicensed Medicines And Medicines For Unlicensed Indications Information For Older Children

## 9. Appendix A – Monitoring Table for this Policy

9.1 The agreed aspects of the policy, including the standards and KPIs will be monitored every 24 months and tabled as an agenda item at Medicines Governance Group.

Unlicensed medicines will be included when audits of prescribing standards are completed in line with chapter 2 of the medicines code, the prescribing policy.

## 10. Appendix B – Dissemination, Implementation and Training Plan

10.1 The following table sets out the dissemination, implementation and training provisions associated with this Policy.

| Plan Elements | Plan Details |
|---|---|
| **The Dissemination Lead is:** | Director of Pharmacy |
| **This document replaces existing documentation:** | Yes |
| **Existing documentation will be replace by:** | Superseding existing document and removal from DMS |
| **This document is to be disseminated to:** | All prescribers, medical and non-medical |
| **Training is required:** | No |

| Plan Elements | Plan Details |
|---|---|
| **The Training Lead is:** | N/A |

| Additional Comments |
|---|
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## 11. Appendix C – Document Checklist

11.1 The checklist set out in the following table confirms the status of 'diligence actions' required of the 'Document Owner' to meet the standards required of University Hospitals Bristol NHS Foundation Trust Procedural Documents. The 'Approval Authority' will refer to this checklist, and the Equality Impact Assessment, when considering the draft Procedural Document for approval. All criteria must be met.

| Checklist Subject | Checklist Requirement | Document Owner's Confirmation |
|---|---|---|
| **Title** | The title is clear and unambiguous: | Y |
| | The document type is correct (i.e. Strategy, Policy, Protocol, Procedure, etc.): | Y |
| **Content** | The document uses the approved template: | Y |
| | The document contains data protected by any legislation (e.g. 'Personal Data' as defined in the Data Protection Act 2000): | N |
| | All terms used are explained in the 'Definitions' section: | Y |
| | Acronyms are kept to the minimum possible: | Y |
| | The 'target group' is clear and unambiguous: | Y |
| | The 'purpose and scope' of the document is clear: | Y |
| **Document Owner** | The 'Document Owner' is identified: | Y |
| **Consultation** | Consultation with stakeholders (including Staff-side) can be evidenced where appropriate: | Y |
| | The following were consulted: | Medicines Governance Group members and prescriber representatives |
| | Suitable 'expert advice' has been sought where necessary: | Y |

| Checklist Subject | Checklist Requirement | Document Owner's Confirmation |
|---|---|---|
| **Evidence Base** | References are cited: | Y |
| **Trust Objectives** | The document relates to the following Strategic or Corporate Objectives: | N/A |
| **Equality** | The appropriate 'Equality Impact Assessment' or 'Equality Impact Screen' has been conducted for this document: | Y |
| **Monitoring** | Monitoring provisions are defined: | Y |
| | There is an audit plan to assess compliance with the provisions set out in this procedural document: | Y |
| | The frequency of reviews, and the next review date are appropriate for this procedural document: | Y |
| **Approval** | The correct 'Approval Authority' has been selected for this procedural document: | Y |