

ESSEX PARTNERSHIP UNIVERSITY NHS FOUNDATION TRUST

THE USE OF UNLICENSED MEDICINES

(use of medicines without a marketing authorisation “licence” or licenced medicines used outside the terms of the marketing authorisation “licence”)

1. INTRODUCTION

- 1.1. In order to minimise the risk to patients and the legal liability of healthcare professionals, the use of unlicensed medicines, and licensed medicines for unlicensed indications should only occur in line with procedures set out in this document.
- 1.2. In the UK, no medicine can be marketed for human use without a ‘marketing authorisation’ (formerly called a product licence) issued by the MHRA (Medicines and Healthcare products Regulatory Agency) or by the EMA (European Medicines Agency) if it has been authorised via the EU-wide procedure. The marketing authorisation (MA) is intended to guarantee the quality, safety and efficacy of the medicine, and states the clinical indication(s), recommended dose, and route of administration by which the medicine may be used; contraindications, special warnings and other particulars for the safe use of the drug will also be included, such as the age group to which it can be given.
- 1.3. Provided a medicine is used within the terms of its MA, the manufacturer will usually carry full liability for any unforeseen adverse consequences that are directly attributable to the medicine.
- 1.4. When a drug does not have a MA, the drug is said to be ‘unlicensed’. When a drug does have a MA, but is used in a way or for an indication which is not set out within the MA, the drug is said to be used ‘off-label’. Although the terms are clearly defined, in reality, ‘unlicensed’ is often used to describe both situations.
- In the USA this is termed “Off-Label” and this term is increasingly used in the UK.
- 1.5. For a variety of good clinical reasons, the use of unlicensed medicines and licensed medicines for unlicensed indications or in unlicensed doses is widespread in palliative care and in the treatment of children.

Mixing of two, or more, licenced injectable medicines in a syringe, for administration via a syringe driver, produces an unlicensed medicine. Administration of that mixture may be, for some individual component medicines, also be an unlicensed route of administration.

In such circumstances, it is judged by the prescriber to be in the best interests of the patient based on the available evidence. Were this practice to be curtailed the treatment of many patients would be impeded. It is therefore important that prescribers, supplying pharmacists and administering nurses are

aware of the associated medico-legal implications. Such prescribing may carry an increased level of risk for the patient, and may expose the prescriber and the Trust to liability for any adverse consequences that arise from the treatment.

- 1.6. Whilst licensed medicines are subject to stringent control by the MHRA, neither prescriber nor pharmacist can make the same assumptions of quality, safety and efficacy about unlicensed medicines.
- 1.7. The purpose of this procedural guideline is to provide a framework within which the Trust can assess the use of unlicensed medicines and off-label indications or doses, thereby safeguarding patients against the risk of injury and minimising the likelihood of claims against individual practitioners or the Trust.
- 1.8. The Trust recognises that:
 - 1.8.1. Prescribers may select medicines for treatment of individual patients or groups of patients when an licenced alternative may not be clinically appropriate or suitable
 - 1.8.2. Practitioners may be expected in the standard course of their duties to administer unlicensed medicines prescribed by prescribers both within and outwith the Trust (e.g.: hospital or hospice prescribers)

Where that use takes place within the provisions of this Procedural Guideline, then vicarious liability covers those activities

2. USE OF MEDICINES OUT-OF-LICENCE / OFF-LABEL

- 2.1. The use of licensed medicines for indications, or at doses, that are outside the terms of the MA is widespread: Examples include the use in children of medicines that are only licensed for use in adults; and medicines in syringe drivers administered by continuous subcutaneous infusion.
- 2.2. Clinicians may be unaware that a medicine is not licensed for a particular indication or at a particular dose, especially if the drug is widely used in this way. Nevertheless, the manufacturer is unlikely to be found liable for any harm resulting from prescribing for an unlicensed indication unless the product itself can be shown to have been defective.
- 2.3. It is often not apparent from the prescription that a medicine is being used in an unlicensed way, and the Trust cannot maintain a fully comprehensive system for monitoring such situations.
- 2.4. The Medicines Management Group will attempt to identify, as far as is possible, the well-established unlicensed uses for which licensed medicines are being used within the Trust as part of its formulary development role.
- 2.5. Medicines Management Group will maintain a register of medicines identified as used out-of-licence / off-label.
- 2.6. Prescribers wishing to use licensed medicines for unlicensed indications are required to ensure that there is published clinical information on safety and

efficacy in use, even if this evidence is of lower-grade; where this is absent, to seek approval from the Medicines Management Group, particularly if the dosage exceeds that recommended for licensed indications. This should be done using the Unlicensed Medicine Request Form in [Annex 1](#).

Where there is any doubt over safety and efficacy in clinical use, prescribers or nurses/staff administering shall seek advice from the Community Health Services Pharmacy Lead or a Medicines Information (MI) Centre (contact details can be found on the inside front cover of the BNF).

3. UNLICENSED MEDICINES

3.1. The Medicines Act permits clinicians to prescribe unlicensed medicines (i.e. ones that do not have a MA) provided they:

- act responsibly and with reasonable skill and care, consistent with a reasonable body of their peers of similar professional standing.
- do so knowingly.
- obtain patient consent where possible, ensuring that the patient is aware of the unlicensed status of the drug and that its effects may be less well understood than those of a licensed product.

3.2. Unlicensed medicines will usually fall into one of the following broad categories:

3.2.1. Medicines purchased on a named patient/named doctor basis. These include medicines without a UK license but which are licensed abroad and can be imported.

3.2.2. Medicines for which the UK license has been suspended, revoked or not renewed, but which the manufacturer continues to make available for certain categories of patient.

3.2.3. Medicines for which a MA has not been applied, or for which the MA has not yet been approved.

3.2.4. Clinical trial medicines; these will usually be covered by a clinical trials exemption certificate.

3.2.5. Admixtures of licensed medicines, for example in a syringe driver.

3.3. Responsibility for the use of an unlicensed medicine rests with the prescriber, and the Trust is required to have a system in place to ensure that a prescriber knows that a medicine is unlicensed and that he is aware of his responsibilities, and has made other clinicians aware eg: nurses and practitioners administering.

3.4. Provided the unlicensed medicine (as in sections [3.2.1](#), [3.2.2](#) and [3.2.4](#), but excluding [3.2.5](#)) has been approved by the Medicines Management Group (see section [7](#)), the pharmacy department will obtain a supply, taking the necessary steps to ensure the quality of the product.

4. RESPONSIBILITIES OF PRESCRIBERS

- 4.1. Prescribers should be aware of the licence status of medicines that they use, and before prescribing an unlicensed medicine be satisfied that an alternative licensed medicine would not meet the patient's needs.
- 4.2. Additionally, before prescribing a medicine off-label the prescriber should be satisfied that such use would better serve the patient's needs than an appropriately licensed alternative.
- 4.3. 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; product quality; or discrepant 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).
- 4.4. Prescribers should remember that whenever an unlicensed medicine is prescribed, or a licensed medicine is prescribed outside the terms of its licence, the prescriber is professionally and clinically accountable and may be called upon to justify their actions.
- 4.5. Supplementary prescribers may prescribe in accordance with a clinical management plan (CMP) in a tripartite arrangement with a doctor or dentist, the patient and the supplementary prescriber. A supplementary prescriber, when acting under and in accordance with the terms of a CMP, may prescribe unlicensed medicinal products
- An Independent Prescriber may prescribe unlicensed medicinal products
- 4.6. The prescriber should be satisfied that there is a sufficient evidence base to show its safety and efficacy, and take responsibility for monitoring and follow-up. MHRA guidelines recommend that:
- the reason(s) for prescribing are recorded and that the content of the requisite conversation, regarding an unlicensed medicine, with the patient and/or carers is also recorded. This conversation should give sufficient information to allow patients (and/or their carers) to make an informed decision about the proposed treatment.
 - as for licensed medicines, health care professionals should report suspected adverse drug reactions to an unlicensed medicine to the MHRA via the Yellow Card Scheme.
- 4.7. Before prescribing, prescribers shall complete an 'Unlicensed Medicines Request Form' for submission to the Medicines Management Group for unlicensed medicines not previously used in the Trust.

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- 4.8. Where a consultant requests an unlicensed medicine, s/he should confirm whether junior medical staff will be permitted to prescribe it.
- 4.9. Prescribers must liaise with the relevant hospital Pharmacy to ensure continuity of supply for outpatients receiving unlicensed medicines. General Practitioners should not be asked to assume prescribing responsibility for unlicensed medicines.
- 4.10. Prescribers must consult fully with general practitioners before asking them to take on the responsibility for the prescribing of a licensed medicine outside the terms of its product licence. A general practitioner is not obliged to prescribe in such circumstances.

5. RESPONSIBILITIES OF PHARMACISTS

- 5.1. Pharmacists must ensure that the prescriber, and nurses or other authorised registered practitioners administering are aware whenever a requested medicine is only available as an unlicensed product
- 5.2. Where an unlicensed medicine is to be ordered for the first time pharmacy must obtain a completed 'Unlicensed Medicines Request Form', unless in urgent circumstances, where discussion is adequate.
- 5.3. The pharmacy department will ensure that if a licensed medicine is available it is purchased in preference to an unlicensed product, wherever possible.
- 5.4. As purchaser, the pharmacy department will take responsibility for the quality of medicines obtained from manufacturers with a Specials Manufacturing Licence. Items purchased should be produced in accordance with a product specification provided by the local Pharmacy Quality Assurance Service.
- 5.5. Incoming unlicensed medicines should be quarantined and segregated from storage of licensed medicines. Certificates of Analysis of Conformity must be forwarded to the Pharmacy Quality Assurance Service who may request that further testing be carried out before the medicine can be released from quarantine.
- 5.6. Pharmacy will maintain appropriate records of receipts and issues of unlicensed medicines and a list of unlicensed medicines, currently being purchased and used within the Trust.
- 5.7. As purchaser, pharmacy will ensure that there are no breaches in patient confidentiality, when providing information to external suppliers of unlicensed medicines.

6. RESPONSIBILITIES OF STAFF ADMINISTERING UNLICENCED MEDICINES AND MEDICINES OUT-OF-LICENCE

- 6.1. Registered healthcare practitioners may be expected to administer unlicensed medicines and medicines out-of-licence as part of their general duties

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- 6.2. Practitioners administering medicines have a duty of care to satisfy themselves that they have sufficient information to administer a medicine prescribed out-of-licence/off-label safely and, wherever possible, that there is acceptable published evidence for the safe use of that product and efficacy for the intended indication.
- 6.3. Medication which is licensed but used outside its licensed indications (commonly known as 'off-label') may be administered under a patient group direction only where such use is exceptional justified by best practice. This shall be included within PGDs developed in the Trust

7. RESPONSIBILITIES OF THE MEDICINES MANAGEMENT GROUP

- 7.1. It is the responsibility of the Trust's Medicines Management Group (MMG) to manage the unlicensed use of medicines within the Trust.
- 7.2. Where a prescriber wishes to initiate treatment with an unlicensed medicine the group will receive and assess a completed 'Unlicensed Medicine Request Form'. In some situations (see section [5.2](#)) this will be retrospective to the commencement of prescribing.
- 7.3. The minutes of the MMG meeting will record approval for use. Decisions by the MMG to monitor use will be communicated to the requesting consultant. Reports on outcomes may be required.

8. REQUESTING AN UNLICENSED MEDICINE

- 8.1. The Trust requires that all unlicensed medicines prescribed within the organisation have been approved by the Medicines Management Group. In order to achieve this, clinicians wishing to use an unlicensed medicine are required to complete an 'Unlicensed Medicine Request Form', (see [Annex 1](#)). Copies of the form can be downloaded from the Medicines Management web pages of the EPUT intranet.
- 8.2. The clinician should complete Section 1 of the request form and liaise with the appropriate Community Health Services Pharmacy Lead to enable completion of Section 2. The completed form should then be signed and sent to the Chief Pharmacist who will ensure that the request is discussed at the next available meeting of the Medicines Management Group.
- 8.3. When there is no urgency to obtain a supply of the unlicensed medicine the request will be considered at the next meeting of the Medicines Management Group. If the group gives approval for use pharmacy will then order a supply or a prescription may be issued.
- 8.4. When an unlicensed medicine is urgently required the Community Health Services Pharmacy Lead or Chief Pharmacist may arrange for a supply to be obtained, if its need has been authorised by the MMG Chair. However, approval for continued use must still be sought by submitting a completed request form.

- 8.5. Where there is disagreement between a requesting consultant and Community Health Services Pharmacy Lead or Chief Pharmacist on either the need for an unlicensed medicine or the urgency of the request, the matter should be discussed with the Medical Director.

9. INDEMNITY

- 9.1. NHS bodies owe a duty of care to patients receiving treatment or undergoing tests. NHS indemnity covers negligent harm caused to these patients in the following circumstances:

- Whenever they are receiving an established treatment, whether or not in accordance with an agreed guideline or protocol.
- Whenever they are receiving a novel or unusual treatment which in the clinical judgement of the health professional is appropriate for the particular patient.
- Whenever they are subjects of clinical research, whether as patients hoping to derive therapeutic benefit or as healthy volunteers. (Research projects must have the approval of the Trust's Research Governance Group.
- NHS indemnity will normally cover the use of unlicensed medicines and the use of licensed medicines outside the terms of their product licence.

- 9.2. In such instances the Trust will normally carry full legal liability for any claims of negligence arising from harm to patients from the unlicensed use of medicines providing the requirements set out in this procedure have been followed.

10. FURTHER INFORMATION

- 10.1. Further information on the off-label or unlicensed use of medicines can be obtained from the MHRA website (Drug Safety Update April 2009) <http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON087990>



UNLICENSED MEDICINE REQUEST FORM

Section 1 DRUG DETAILS (to be completed by the consultant)

Product (name, form, strength):	
Manufacturer / Supplier (if known):	
Clinical indication for use:	
Dose and frequency:	
What treatment (medicine or other) would previously have been prescribed for this indication?:	
Give reason(s) for preferred use of the requested product:	
If a patient information sheet is to be used, please attach a copy (NB – most unlicensed products do not have English-language package inserts). If an information sheet is not being used, please give reason(s).	

Section 2 PRODUCT AVAILABILITY DETAILS (to be completed jointly by consultant and pharmacist)

Does this product have a product license or marketing authorisation in another country?	YES / NO
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If YES:

Manufacturer and country of origin:	
Licensed indication(s) for the product in that country:	
Is the product licensed in the country for the intended indication given in Section 1?	YES / NO
Obtain a Summary of Product Characteristics and attach a copy	

If NO

Is there a product manufactured in the UK?	YES / NO
If yes, state manufacturer:	
Is the manufacturer a pharmaceutical company?	YES / NO
Is the product intended for HUMAN use?	YES / NO

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Patient's status (informal/compulsorily detained) (2nd opinion required if compulsorily detained)

Consultant / Prescriber Name:	Signature:	Date:
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By signing above you confirm that you have investigated the benefits and risks associated with the use of the unlicensed medicine specified in Section 1. Attach a copy of the patient consent form. If not, please give reason(s) below

Pharmacist Name:	Signature:	Date:
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Notes:

This product is not covered by a UK medicinal Marketing Authorisation (MA). Unlicensed medicines have not usually been subjected to the rigorous independent assessment of efficacy and safety that applies to licensed medicines and their use may carry a higher level of risk to patients.

In the event of harm to a patient, the manufacturer of an unlicensed medicine is only likely to be found liable if the harm results from a defect in the product. The manufacturer carries no legal responsibility for unlicensed use, putting greater liability on the prescriber and the Trust. A clinician directing the supply of an unlicensed product retains liability for any adverse consequences arising from use of the product; this applies even for products licensed within other EU countries.

When proposing the use of an unlicensed medicine it is the responsibility of the consultant to:

- Take special care to investigate and assess the risks and benefits. If necessary, the proposed use of the product should be discussed with a specialist to ensure that there is a reasonable body of medical opinion supporting the use of the medicine as proposed.
- Obtain informed consent from the patient whenever practical.
- Be appropriately insured.
- Complete an 'Unlicensed Medicine Request Form' and supply information supporting the use of the product to the Medicines Management Group (MMG), for each patient requiring the unlicensed medicine, unless exempted from this requirement by the MMG.
- Write the first prescription for each patient. Thereafter, another doctor working under that consultant can continue to prescribe the unlicensed medicine, unless the MMG requires 'consultant-only' prescribing.
- Report any serious adverse drug reactions using the 'Yellow Card' system.
- Inform the patient's GP in writing of any unlicensed prescribing that will be continued on discharge from hospital. Prescribing of unlicensed medicines should usually be continued by the hospital.

Prescribers wishing to use an unlicensed drug for the first time should complete an 'Unlicensed Medicine Request Form', which will require information from the supplying pharmacy. Completed forms and supporting information should be sent to the Community Health Services Pharmacy Lead or Chief Pharmacist to be added to the MMG agenda.

MMG approval will normally be required before the pharmacy will be authorised to purchase an unlicensed medicine, and the consultant will be notified of the date of the MMG meeting at which their request is to be considered. In exceptional circumstances the MMG Chair can authorise purchase prior to MMG approval; in this event, all prescriptions must be written by the consultant.