

Policy & Procedure for Use of Unlicensed Medicines

Policy

1. The Trust wishes to operate a system to control the use of medicines outside of their 'licence' (Marketing Authorisation). It aims to recognise such use as common and necessary in good medical practice but also to promote awareness of, and safety in, the use of unlicensed medicines. It distinguishes between uses of medicines that are documented in an authoritative source ('established but unlicensed' uses) and those that are not.
2. If any medicine is licensed for a disorder, then the Trust wishes a licensed medicine to be preferred for treatment over an unlicensed medicine, unless there is good reason to do otherwise (e.g. previous adverse reaction).
3. The Trust
 - a. wishes to encourage patients/carers to participate as much as they can in treatment decisions as informed individuals. It also wishes to protect its staff who abide by this system from litigation directed against them, so far as it can.
 - b. therefore expects that a patient's informed consent to the use of any unlicensed medicine will be obtained (wherever possible) and noted in the medical record, and that an information leaflet will be provided where the use of the medicine is not documented in an authoritative source.
4. The Trust works in partnership with primary care, and therefore wishes general practitioners to be given an explanation of the choice of an unlicensed medicine, without taking for granted their willingness to continue the treatment.
5. The Trust
 - a. believes it is in line with best practice in the management of medicines for it to be aware how its staff use unlicensed medicines and to restrict their use to situations where the likely benefits outweigh the likely risks.
 - b. therefore, via the Medicines Committee, will keep a register of those uses for medicines that are outside the terms of their licence but that it has approved. The register will note the approved groups of patients, indications for use, route of administration and dose.
6. The Medicines Committee may limit the use of an unlicensed medicine by:
 - a. restricting it to particular prescribers
 - b. making its use dependent on use of a guideline
 - c. declining to approve it.

In emergency situations, the Medicines Committee may reach a rapid provisional decision by 'chairman's action'. If the committee declines to approve a medicine, the applicant may appeal to the Chief Executive.

The Medicines Committee will not approve the administration of an unlicensed medicine under a Patient Group Direction.

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7. The use of an medicine outside its licence, or without a licence, need not be registered if:
 - a. that use is noted without adverse comment in the British National Formulary (BNF).
 - b. a specialty has agreed with the Medicines Committee to exempt it from recording requirements because it would be burdensome to record every example, and because the specialty nominates at least one authoritative and accessible reference source other than the BNF that its members will use for guidance. If no such source is available, a general statement of principle in the spirit of this policy signed by all consultants in the specialty may be accepted.
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Procedure for registering an unlicensed use of a medicine

1. **Either:** Prescribers are asked to complete a form (Appendix) describing the present or proposed use of the medicine and the evidence for it. The form will be submitted for approval to the Trust Medicines Committee.
Or: In clinical areas where so many medicines are used outside their licensed indications that this procedure is not practical (e.g. Cancer Services and Paediatrics) a statement will need to be submitted listing sources regarded as offering authoritative guidance on the use of medicines in that area, or in some other way meet the spirit of this policy.
 2. The Medicines Committee shall create a register from the data submitted from the above and this shall be available to the staff of the Trust and included in the annual Medicines Management report to the Trust Board.
 3. This process is separate and distinct from the Policy for the Introduction of New Drugs, but where a proposed new drug is to be used in a way that is unlicensed, approval will require compliance with both policies.
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Summary of action points

Prescribers

- ✓ Especially for unusual medicines or diseases, check in the BNF or elsewhere if you might be prescribing an unlicensed medicine. Choose a licensed medicine if you can.
- ✓ When using an unlicensed medicine, obtain informed patient consent (so far as you can) and record what was said in the notes.
- ✓ Discuss prescriptions for unlicensed medicines with those who may be asked to administer them.
- ✓ Use the form (Appendix here) to apply to register in the Trust any unlicensed use not in the BNF or some other agreed source.
- ✓ Supply information to the pharmacy about medicines you wish them to obtain on a 'named patient' basis.
- ✓ If it would help for the GP to continue this treatment, explain why you chose it, describe how the responsibility for any monitoring will be arranged, and ask to be notified if they do not wish to do so. Hospital supply will be better for rarely used and the more toxic medicines.

Pharmacists

- ✓ Contact the prescriber before dispensing any prescription likely to be an unlicensed use of a medicine recorded neither in the BNF, nor in another agreed source, nor in the Trust's register of approved uses.
- ✓ If the prescriber cannot be contacted before administration of the medicine, assess the risk and consider delaying dispensing or advising the relevant nurse/midwife in charge.

Nurses and midwives

- ✓ If you are concerned about being asked to administer a medicine that seems unusual, first check the BNF and the Trust's register of unlicensed uses, then discuss with the prescriber, or, if unavailable, a pharmacist.

Background

The licensing of medicines

The terms used in the licensing of medicines have changed in recent years. Formerly, the Medicines Control Authority issued a Product Licence. Now the Licensing authorities award a Marketing Authorisation. The Licensing Authority may now be either the Medicines and Healthcare products Regulatory Agency (MHRA) for the UK, or the European Commission for the EU, advised by the Committee for Medical Products for Human Use (CHMP). The effect is much the same, and the principle remains that a manufacturer provides evidence of use of specified doses of the medicine for certain conditions in particular groups of people, and the evidence for safety and efficacy is judged by an expert and lay panel. When an 'authorisation' is given, it is given for specific doses, for certain indications in the same sort of people. These are set out in the Summary of Product Characteristics (SPC, formerly the Data Sheet) and popular sources of information like the BNF use words consistent with this.

The purpose of the licensing system is to protect the public by preventing the promotion or sale of substances as medicines without independent expert scrutiny of their safety and effectiveness. It also provides prescribers and pharmacists with an independently approved source of technical information (the SPC) on the approved uses of the medicine, and the patient with similar non-technical information (the Patient Information Leaflet). An incidental effect is to make the manufacturer liable for harm that comes from any defect in the product – but only when the medicine is used as specified in the Marketing Authorisation – which is known as strict liability under the Consumer Protection Act (1987).

The licensing system is thus valuable, but it is not ideal. To provide a Licensing Authority with the information it needs is expensive, and a company would never recover the cost of seeking approval for use of a medicine in a rare disorder, or in one that occurs mainly in poor countries that buy few medicines. There may be no commercial value in licensing a new use found for an old medicine. Ethical reservations have impeded clinical trials in children, and to some extent in emergency conditions, and the perverse result is that children and severely ill patients are most likely to receive medicines about which key information is not available, and which have no marketing authorisation. These limitations are common knowledge, but they have been addressed only partially, and provide the main reasons why the prescribing of unlicensed medicines is commonplace and seldom either dangerous or negligent, and why the authoritative British National Formulary sometimes refers to unlicensed use of medicines.

Unlicensed use of medicines and authoritative support

Most medicines used in the Trust are used within the terms of their 'licence'. Unlicensed use is most often prescribing a medicine that has a Marketing Authorisation for one purpose but using it instead for a different disease, in a different dose, by a different route or in a different group of patients. This is increasingly referred to as "off-label" use. Off-label use of a medicine is a little less safe - it has not been approved after independent expert scrutiny, prescriber and patient have some information but the information is not written with their circumstances in mind. In addition, the prescriber, and so the Trust, is liable if (as rarely occurs) there is a defect in the medicine itself, even though there was no clinical negligence.

Some medicines are routinely prescribed, but have no licence for any use. Thalidomide, the medicine that caused many fetal abnormalities in the 1960s, which resulted in the

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licensing system being set up, illustrates two examples of this. Thalidomide has been known for some years to be valuable in treating reactions that occur early in the treatment of leprosy, which is noted in the BNF as appropriate when employed by experts in this field. It is also used in the treatment of sarcoidosis resistant to common treatments, which has sound evidence to support it, but no official recommendation. Only the first of these is an ‘unlicensed but established’ use.

Unlicensed medicines are also used in clinical trials. In evaluating the risks involved the Research Ethics Committee (REC) will usually have expert advice from the MHRA, which issues a Clinical Trials Licence to new medicines that have some evidence of safety. The REC will not allow any trial with an unlicensed medicine unless the prescribers have indemnity against actions for damages by a patient harmed by the experimental medicine, so legally this is a different situation.

It is commonly said that some medicines used for many years ‘have no licence’. It is true that they have never had the rigorous pre-marketing scrutiny of new medicines, but the manufacturers have ‘Licences of Right’ issued when the licensing system began. If new evidence of hazard appears, the MHRA can modify or withdraw their licence.

The legal position is thus that any unlicensed use of a medicine makes the Trust liable for ‘product defect’, but that this is too rare to require any measure beyond ensuring that an unlicensed medicine is used only if no licensed medicine is suitable. Far more likely is a situation in which a patient is harmed by an unlicensed medicine and seeks damages for negligence. It would then be far easier to defend an ‘unlicensed but established’ use than one without authoritative support. As for uses that are not already ‘established’, which may be new or unusual but in the best interests of patients, these would be easier to defend if they have been approved in advance after due consideration by the Trust. This provides the rationale for the policy set out above.

Communication

With patients: This background is not easy to explain to patients, few of whom will be aware of the licensing system for medicines. “In order to treat you, I should let you know that we will have to look outside the drugs officially approved for your problem,” would represent one approach. It may be possible to add reassurance that, “.... but we can still use one of the drugs experts generally recommend”, if it is an established (= documented in an authoritative source) use. For uses that are not established, it should normally be said that there is a serious problem in finding a suitable treatment, and summarising the evidence for risk and benefit of the treatment proposed, backed up by an information leaflet. Many national bodies have published advice and one provides useful general information leaflets.

Royal College of Paediatrics and Child Health, general information leaflets

[Information for older children](http://www.rcpch.ac.uk/publications/formulary_medicines/Patient_Information_One.pdf) [CTRL + click to follow link]

http://www.rcpch.ac.uk/publications/formulary_medicines/Patient_Information_One.pdf

[Information for Parents and Carers](http://www.rcpch.ac.uk/publications/formulary_medicines/Patient_Information_Two.pdf) [CTRL + click to follow link]

http://www.rcpch.ac.uk/publications/formulary_medicines/Patient_Information_Two.pdf

A general leaflet that can be issued by Newham University Hospital NHS Trust staff can be found in the appendix.

With pharmacists: Prescribers are often unaware whether a medicine is or is not licensed for the purpose for which they intend to use it, and if a current BNF is not available, they may be unable to check. If in doubt, it is better to raise the matter with a pharmacist than hope for the best, as the pharmacist is put in a difficult position if there is an appreciable risk in the use of an unlicensed drug, and the prescriber cannot easily

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be contacted. The pharmacist who finds a prescription for an unlicensed medicine which is not in accord with this policy will always first try to contact the prescriber, before having to consider whether to delay in dispensing the medicine, or to contact the nurse or midwife responsible for administering it.

With nurses and midwives: The administration of medicines is not a routine and mechanical act, and the Nursing and Midwifery Council makes it clear that nurses and midwives are expected to be aware of its clinical and ethical context. They should be satisfied that they have enough information to administer the medicine safely, and wherever possible that there is acceptable evidence for its use, and (for an unlicensed medicine) appropriately informed consent. If it is evident that this policy has been adhered to, then it is easier for them to fulfil this duty. It is sensible for the prescriber to discuss the prescription of an unlicensed medicine with the senior nursing staff on duty at the time, and at other times it is expected that they may seek further information from the prescriber, or, if unavailable, from a pharmacist.

With general practitioners: If a hospital doctor wishes to ask a GP to continue an unlicensed treatment, an explanation of the treatment choice is needed in the discharge note or clinic letter also essential. Some PCTs have advised their GPs not to prescribe unlicensed medicines. In Newham it is a matter between the individual GP and the hospital, but with no assumption that the GP will automatically take over prescribing. It is particularly important to clarify how any monitoring of the desired and adverse effects will be carried out, and how the prescriber will be informed of the results. For established uses, it is reasonable to ask GPs to say if they do not wish to continue such treatment. For rare and for potentially very toxic drugs, hospital supply may be preferable.

Newham University Hospital NHS Trust

Application for Registration of a Medicine for an Unlicensed Use

Registration is **not** required for 'established' uses of medicines – i.e. listed in the BNF or another source agreed by a specialty. It **is** required for any unlicensed use not documented in this way, and perhaps new or unusual, even if the medicine has a licence for another use. A separate form is needed to apply for a drug new to the Trust.

Please submit your request for such a medicine or use by completing Section 1 below and sending to the pharmacy at Newham General Hospital. Please indicate if the request is urgent, in which case Chairman's action may be taken.

SECTION 1: *To be completed by the Consultant with responsibility for the patients.*

It is my clinical judgement that

Name, form and strength of medicine

would benefit patients under my care who suffer from

Indication for use of medicine

Proposed dose, frequency and route of administration

Duration of therapy

Known side effects / adverse reactions / toxicity

References to published work or other evidence for this treatment choice

Other therapy which will usually be tried first

I attach a copy of the patient information I will give to the patients and that lists possible risks and side effects about which the patient will be informed. I will also follow the Trust procedure on obtaining informed consent.

Consultant's signature: _____ **Date:** ____/____/____

Name in block capitals: _____

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SECTION 2: *To be completed by a Pharmacist where an unlicensed medicine has been prepared within the Trust Pharmacy or purchased by the Trust Pharmacy [where not applicable mark N/A]*

Preparation / Formula:
Manufacturer / Supplier:
Grade of ingredients:
Formula Reference:
Stability:
Report by Quality Assurance on non-pharmacopoeial standard ingredients:
Potential harmful impurities:
Proposed shelf life and reasons:

Pharmacist's signature: _____ **Date:** ____/____/____

Name in block capitals: _____

SECTION 3: *To be completed by the Chairman of the Trust Medicines Committee*

Date application received:

Recommendation:

Chairman's signature: _____ **Date:** ____/____/____

Name in block capitals: _____

Newham University Hospital

NHS Trust

This leaflet is about the information you get with your medicines

Please read it carefully

What information should I normally expect?

A manufacturer must obtain a licence from the government's Medicines and Healthcare products Regulatory Agency before selling a new medicine. The license tells us how the medicine can be used, the conditions it can be used to treat, the doses to be used and the age of the patient it is given to and so on.

Manufacturers have to include with their medicines a patient information leaflet. The information in it must, by law, describe the licensed use.

Most medicines prescribed by your doctor or brought over the counter from a pharmacist are licensed as described above.

Why have I been given this leaflet?

It is often necessary for doctors to prescribe medicines for use that is not in the license. This is true for a lot of medicines used for children or in special circumstances, such as in cancer care, or as part of a clinical trial or, as is often the case,

the medicine is used in only a small number of patients and the manufacturer cannot afford to get a license.

If you are given this leaflet it is because you have been prescribed medicine for use outside of its license. You can tell this because the information from the manufacturer in the box will not mention the reason you have been prescribed the medicine.

Is it safe?

If you are prescribed any medication at Newham University Hospital NHS Trust, whether licensed or not, your doctor will have carefully thought about the best care for you. Even if the medicine is used outside the license, we make sure there is good evidence of the benefits and you can be sure that any other similar doctor would also prescribe it.

What if I have more Questions?

Your doctor or pharmacist will be happy to help more if you want.

The Hospital telephone number is 020 7476 4000

The Medicines Information line in the Pharmacy Department is 020 7363 8048