Northamptonshire Healthcare
NHS Foundation Trust

MMP006

Unlicensed Medicines

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Why we need this Policy

The Marketing Authorisation (MA), formerly the Product Licence, granted by the Medicines and Healthcare Products Regulatory Authority (MHRA) defines the therapeutic purposes (clinical indications) for which a product may be marketed and how it should be used. This is done in accordance with the Human Medicines Regulations 2012 (SI 2012/1916). The manufacturer may then promote and sell the product for these purposes. These clinical indications are based on data submitted by the manufacturer as part of the MA application. The MHRA also considers other data to approve the manufacturing processes, shelf-life, etc.

The Trust recognises that there will be occasions when the prescribing of a drug without marketing authorisation (unlicensed) or for indications which are not covered by the marketing authorisation (off-label) is necessary for the treatment of patients.

What the Policy is trying to do

This policy describes the responsibilities of those practitioners involved and the procedures to be followed when prescribing and seeking approval to use a drug without marketing authorisation.

This Policy is NOT intended to cover:

- Medicines used in Clinical Trials.
- Products prepared under Sections 9, 10 or 11 of the Medicines Act 1968.
- Drugs used/mixed within syringe drivers in palliative care
- Licensed Medicines prescribed or administered outside of their product licence (see MMP001-Control of medicines policy section 6.3.11)
- Repacked Medicines
- Unlicensed herbal remedies supplied under regulation 3(6) of the Human Medicines Regulations 2012.
- Unlicensed homeopathic medicines (prepared in a pharmacy)
- Investigational medicinal products
- Intermediate products intended for further processing by an authorised manufacturer
- Medicinal products for export to countries outside of the European Economic Area
- Products prepared in a pharmacy under regulation 4 of the Human Medicines Regulations 2012
- Products prepared by a doctor or dentist under regulation 3(5) of the Human Medicines Regulations 2012.
- Reconstituted IV additives and CIVAS products (prepared in a pharmacy)
- Products supplied for compassionate use in accordance with Article 83 of Regulation (EC) 726/2004
- Temporarily- authorised medicinal products supplied in response to the spread of pathogenic agents, toxins, chemical agents or nuclear radiation any of which could cause harm (in accordance with Article 5(2) of Directive 2001/83/EC)

Which stakeholders have been involved in the creation of this Policy

Medicines Management Committee

Any required definitions/explanations

Licensed Medicines

A UK licensed medicine is one that has been granted a marketing authorisation (MA) (previously known as a product licence PL), and can be 'placed on the market' in the UK for the treatment of medical conditions as defined in its MA (i.e. its licensed indications). When prescribed within the terms of the marketing authorisation the manufacturer is likely to be found liable for any harm caused by that medicine.

Unlicensed Medicines

A medicine that does not hold a UK marketing authorisation

Unlicensed medicines can fall into the following categorise

- Products for which a licence has yet to be granted in the United Kingdom; a licence may exist elsewhere.
- Products that no longer have a licence because license has been abandoned, suspended, revoked or not renewed.
- Products manufactured for export
- Products undergoing clinical trials
- Extemporaneously prepared medicines, e.g.
    - Products made from licensed medicines, e.g. low dose formulations for children/elderly; liquid formulations for elderly or those unable to swallow

- Re-packed Medicines
    - When a medicine is removed from its original container (manufacturer packaging) and re-packed, e.g. during normal dispensing or repacking of medication into compliance aids, it technically becomes 'unlicensed

Licensed Medicines Used for Unlicensed Indications ("off-label")

The Summary of Product Characteristics (SPC) lists: indications, dose ranges, methods of administration, age restrictions, contra-indications and storage conditions. Any use not in accordance with the SPC is "off-label" or an unlicensed use.

If a prescriber uses a licensed medicine for an unlicensed indication i.e. in breach of the terms of its marketing authorisation then the manufacturer is unlikely to be found liable for any harm caused by the medicine, unless harm is directly attributed to a defect in it. The ultimate responsibility for prescribing rests with the prescriber who signs the prescription and is professionally accountable for his/her action. The Trust may also be liable.

Where this "off-label" prescribing is well established clinical practice or recommended in accredited guidelines then no additional paperwork is required to be completed. However, where this is the introduction of new practice, or an obscure, individualised prescription in unorthodox clinical circumstances, then this should be discussed with and approved by either the Clinical Director or Chief Pharmacist prior to prescribing.

Where a practitioner administers a licensed medicine outside the terms of the marketing authorisation e.g. Subcutaneous cyclizine, vaccines stored outside of 2°C - 8°C, or oral sodium valproate for bipolar disorder, they should be satisfied that they have sufficient information to administer the medicine safely and that there is acceptable evidence for the use of the medicine in this way. This should be done by seeking information from the prescriber and other appropriate sources.

Off-label use commonly occurs in paediatrics, palliative care and mental health.

Prescriber
Doctor, dentist or independent and supplementary non-medical prescribers who are authorised to prescribe off-label and unlicensed medicines.

Key duties

Medicines Management Committee
- Will approve the policy prior to being ratified by the Policy Board.
- Is responsible for the implementation and dissemination of this policy
- Will review and approve requests for use of unlicensed medicines

Prescribers responsibilities
- To prescribe licensed medicines whenever possible.
- Should a licenced product become unavailable, it may be necessary for an unlicensed equivalent to be supplied. This should be seen as a temporary measure until supplies of the licensed product can be resumed.
- To prescribe unlicensed medicines knowingly and only after careful consideration. To be satisfied that there is a sufficient evidence base and/or experience of using the medicine to demonstrate its safety and efficacy.
- To document the reasons for choosing the medicine.
- To be professionally accountable for prescribing all medicines including unlicensed medicines.
- To discuss with the patient the medicine's licence status and explain that for an unlicensed medicine its effects may be less well understood than those of a licensed product. To discuss with the patient the risks and benefits of use of the unlicensed medicine so that a collaborative decision can be reached regarding use of the unlicensed medicine
- To obtain agreement for use of the unlicensed medicine from the patient and complete the Agreement form ()
- To give the patient the patient information leaflet (Copy available on intranet
- When recommending the use of an unlicensed product to other prescribers taking over the care of the patient ensure any supporting evidence including information on availability and supply are available. Other prescribers are not obliged to prescribe in such circumstances.
- To review treatment if appropriate licensed medication becomes available.

Administering nurses responsibilities
- To be aware of the unlicensed status of the medication
- To seek appropriate advice/information regarding administration

Clinical pharmacist responsibilities
- To inform prescribers of unlicensed status of medicines and provide the appropriate documentation for completion. (Appendix 1).

Supplying pharmacy's responsibilities
The Pharmacy Departments supplying unlicensed medicines for use in inpatient areas are providing Pharmacy Services via a contracted third party arrangement and therefore will procure, receive, store and supply these products in accordance with their own standard operating procedure on the Use of Unlicensed Medicines. These pharmacy departments will only supply an unlicensed medicine following:

1) Receipt of a completed Request and risk assessment form for unlicensed medicines (Appendix 1)
2) Authorisation from a Senior member of the NHFT Clinical Pharmacy Team or Medical Director

Process for prescribing unlicensed medicines

Unlicensed medicines can be prescribed by doctors, dentists, independent non-medical prescribers and supplementary prescribers (within a clinical management plan) to fulfil a "special need" of an individual patient. This need must relate to a clinical need of an individual patient, and does not include reasons of cost, convenience or operational needs.
Furthermore, pharmacists can dispense such medicines and practitioners can administer them to patients.

Should a patient suffer harm as a result of the effects of an unlicensed medicine then the manufacturer is not liable (unless the medicine was shown to be defective). Any legal action would also involve the Trust as a result of employer's vicarious liability.

The MHRA uses the following Risk Hierarchy for the use of unlicensed medicines

- An unlicensed product should not be used where a product available and licensed within the UK could be used to meet the patient's "special need"
- Although the MHRA does not recommend "off label" (outside of the licensed indications) use of products, if the UK licensed product can meet the clinical need, even "off-label", it should be used in preference to an unlicensed product. Licensed products available in the UK have been assessed for quality safety and efficacy. If used "off-label" some of this assessment may not apply, but much will still be valid. This is a better risk position than is the use of an unassessed, unlicensed product. The fact that the intended use is outside of the licensed indications is therefore not a reason to use an unlicensed product. It should be understood that the prescriber's responsibility and potential liability are increased when prescribing off-label.
- If the UK product cannot meet the special need, then another (imported) medicinal product should be considered, which is licensed in the country of origin.
- If none of these options will suffice, then a completely unlicensed product may have to be used, for example, UK manufactured "specials", which are made in GMP inspected facilities, but which are otherwise unassessed (GMP inspection of specials manufacturers is not product specific). There may also be other products available which are unlicensed in the country of origin.
  The least acceptable products are those that are unlicensed in the country of origin, and which are not classed as medicines in the country of origin (but are in the UK). Hence, for example, the use of melatonin products from the USA, where melatonin products are classed as supplements, not pharmaceuticals and may not be made to expected standards of pharmaceutical GMP should be avoided whenever possible.

Application Process

The following process must be followed prior to prescribing for all unlicensed medicines within NHFT

Applications can be made for either general approval or patient specific approval. (See appendix 1.)

General approval should be used for unlicensed medicines generally accepted as used in a specific condition and required for use in multiple patients.

Details of unlicensed medicines given general approval will be added to the Trust formulary including area of use.

Patient specific approval should be used were the use of the unlicensed medicine is for a specified patient only

The Medicines Management Committee will consider any applications at its next planned meeting and will maintain a list of approved unlicensed medicines within the formulary. In considering each application, the Committee will need the following information (outlined in the application form): -

- Which drug is required and in what form.
- What condition the drug is being used to treat.
- Rationale for prescribing
- Duration of use
- For products that require continuation post discharge: who will prescribe, is a shared care document needed etc.
- The cost of the product (based on current hospital purchase price) and estimated annual cost impact on the Trust

Approval will be granted if the Committee is satisfied that the drug requested is necessary for patient care and there is evidence for use. It is expected that expenditure on unlicensed medicines will be managed within the constraints of the existing drug budget.

By its nature drug treatment does often need to be commenced at short notice and gaining the appropriate approval from the Medicines Management Committee prior to treatment may not be possible. At such times, an application for patient specific approval can be considered by the Chief pharmacist/senior pharmacist for the specialty, in discussion with the Medical Director if required, and a decision taken. The submission will be presented to the Committee at its next meeting for consideration of general approval or noting for patient specific requests.

Prescribing of an Unlicensed Medicine

Any prescriber wishing to use a drug without marketing authorisation must:

- Check whether a licensed alternative is available
- Check whether a previous application has been submitted and accepted for general approval by MMC
- Ensure that the intended use is in line with this general approval

Where this is the case MMC need to be informed of the prescriber's intention but no further application needs to be made (Appendix 2).

Where the intended use is not in line with the general approval or a general approval does not exist a full submission should be made.

Patient Information

No additional measures beyond those taken when prescribing licensed medicines are required to obtain the consent of patients for the use of unlicensed medicines. Healthcare professionals must however respect the rights of patients and carers to participate in discussions regarding the health of the patient and to seek to ensure that these decisions are properly informed.

Patients must be given, sufficient information about the proposed course of treatment including any known serious or common side effects or adverse reactions. This is to enable them to make an informed decision. A record must be made in the patient's notes of the discussion and what information has been given.

Patients should receive a patient information leaflet (PIL), which explains why it is necessary to prescribe unlicensed medicines.

Falsified Medicines Directive (FMD)

Unlicensed medicines and "Specials" are exempt from the requirements of the Falsified Medicines Directive.

Training requirements associated with this Policy

Mandatory Training

Training required to fulfil this policy will be provided in accordance with the Trust's Training Needs Analysis. Management of training will be in accordance with the Trust's Statutory and Mandatory Training Policy'.

Specific Training not covered by Mandatory Training

Ad hoc training sessions based on an individual's training needs as defined within their annual appraisal or job description.

How this Policy will be monitored for compliance and effectiveness

The table below outlines the Trusts' monitoring arrangements for this document. The Trust reserves the right to commission additional work or change the monitoring arrangements to meet organisational needs.

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Aspect of compliance or effectiveness being monitored	Method of monitoring	Individual responsible for the monitoring	Monitoring frequency	Group or committee who receive the findings or report	Group or committee or individual responsible for completing any actions
Duties	To be addressed by the monitoring activities below.				
Request to prescribe unlicensed medicines	MMC minutes /annual report	Chief Pharmacist	Annually	MMC	MMC
Staff have completed training associated with this policy (as part of Medicines Management training) in line with Training Needs Analysis	Training will be monitored in line with the Statutory and Mandatory Training Policy.				
Where a lack of compliance is found, the identified group, committee or individual will identify required actions, allocate responsible leads, target completion dates and ensure an assurance report is represented showing how any gaps have been addressed.					

Equality considerations

The Trust has a duty under the Equality Act and the Public Sector Equality Duty to assess the impact of Policy changes for different groups within the community. In particular, the Trust is required to assess the impact (both positive and negative) for a number of 'protected characteristics' including:

- Age;
- Disability;
- Gender reassignment;
- Marriage and civil partnership;
- Race;
- Religion or belief;
- Sexual orientation;
- Pregnancy and maternity; and
- Other excluded groups and/or those with multiple and social deprivation (for example carers, transient communities, ex-offenders, asylum seekers, sex-workers and homeless people).

The author has considered the impact on these groups of the adoption of this Policy and does not believe that there are any specific equality considerations that need to be taken into account.

Reference Guide

Medicines Act 1968. London: HMSO

General Medical Council Ethical Guidance: Good practice in prescribing and managing medicines and devices (2013). Available online at: https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/prescribing-and-managing-medicines-and-devices

https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/prescribing-and-managing-medicines-and-devices

MHRA (2014) Guidance Note 14: The supply of unlicensed medicinal products ("specials"). London: HMSO

MHRA (2011) Summary report for importation of unlicensed medicines. 1 April -30 June 2011. London: HMSO

Falsified Medicines Directive (FMD) – Questions and Answers (SPS website)

https://www.sps.nhs.uk/wp-content/uploads/2018/07/FMD-Safety-Features-Mailbox-Common-QAs-v.4.pdf

Document control details

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Version No.	Date Ratified/ Amended	Date of Implementation	Next Review Date	Reason for Change (e.g. full rewrite, amendment to reflect new legislation, updated flowchart, minor amendments, etc.)
1.0	06.07.16	06.07.16	31.07.19	Review
2.0	25.06.19	26.06.19	25.06.22	Review; updated to include FMD

Appendix 1 - REQUEST FORM FOR UNLICENSED MEDICINES

This form should be completed by the Prescriber each time a new unlicensed medicine is required. The completed form is to be submitted to the Medicines Management Committee (MMC) for approval. In the case of urgent clinical need the Chief Pharmacist/ Senior Pharmacist for the speciality (Band 8a or above) may authorise the use of a new unlicensed medicine. This will be subject to formal ratification at the next MMC meeting.

Before completing this form you must have read the Unlicensed Medicines Policy and you must be aware of your responsibilities under this policy.

Parts 1- 5 to be completed by Prescriber

Part 1: Unlicensed Medicine Details

Approved Name: ……

Proprietary Name (if known): ……

Dose Form: ……

Strength: ……

Manufacturer (if known):……

Part 2: Patient Details

Is this to be used for a single patient only? YES/NO

Single Patient Only

Unit Number: …… Ward/Clinic: ……

Multiple Patients

Approximate number patients per year: ……

Part 3: Clinical Details

Indication: ……

Dose: ……. Frequency: ……

Route: …… Duration: ……

Why is an unlicensed medicine being considered?

1. Pharmaceutically equivalent licensed product temporarily unavailable*

……

2. Equivalent UK licensed product unavailable/unsuitable* (explain)

……

3. Other* (give details)

……

***** delete as appropriate.

Part 4: Clinical Evidence for Unlicensed Medicine

Is there any evidence to support its use for the proposed indication?	YES/NO
If not, is there any evidence to support its use for other indications?	YES/NO
Is there any evidence to support its proposed administration schedule?	YES/NO
Is the active drug currently in a licensed product for use via the same route?	YES/NO
Is the product licensed for the specific indication in an EU member state?	YES/NO/NOT KNOWN
Is the product licensed for the specific indication in a non-EU state? If Yes, please state which	YES/NO/NOT KNOWN If yes, name:
Are other centres using this medicine?	YES/NO/NOT KNOWN If yes, name:

Please summarise below any published evidence to support the use of the unlicensed medicine and any previous clinical experience with the medicine:

References (attach copies where these are available):

Authors:

Title:

Journal/Issue No/Volume/Year

Authors:

Title:

Journal/Issue No/Volume/Year

Authors:

Title:

Journal/Issue No/Volume/Year

Authors:

Title:

Journal/Issue No/Volume/Year

What are the risks to the patient of NOT using this medicine:

List any side-effects or toxic effects that have been reported:

List any significant interactions:

List any contraindications and any other risks to the patient:

List any precautions, including precautions in use and pharmaceutical precautions:

Is there a Patient Information Leaflet appropriate for intended use?

Yes*/No/Not Known (*Please attach) and any special instructions

How will patient obtain further supplies?

Is there a need for a shared care protocol? Yes/No

Cost of product (based on current hospital purchase price)?

Estimated Annual cost impact to Trust

(annual cost of product x number of patients)

Part 5: Details of person completing form

Prescriber Name: ……

Directorate/Speciality: …….

Contact Number: ……..

Email address: …….

I have read the NHFT Unlicensed Medicine Policy and accept full responsibility for use of this medicine.

Prescriber name: …….

Prescriber signature: ……..

Date: ……

Part 6: Outcome of Application

MMC approved? YES/NO

Date approved……

Reasons if not approved: …….

…….

Restrictions on prescribing YES/NO

If yes please state: ……

……

Date of review (max 5 years)……

Name: ……

Signed: …….. Date:

(MMC member)

Appendix 2 – Notification to MMC of intention to prescribe an unlicensed medicine from the general approved list

Prescriber Name: ……

Directorate/Speciality: ……

Contact Number: ……..

Email address: …….

I intend to prescribe …… (insert name of medicine) which is included in the general approved list of unlicensed medicines for patients within my care. I confirm the intended use also meets that covered by the general approval

I have read the NHFT Unlicensed Medicine Policy and accept full responsibility for use of this medicine.

Prescriber signature: ……..

Print name:……

Date:……