1 Introduction

In the UK medicinal products can only be placed on the market after a Marketing Authorisation (MA), commonly known as a product licence (PL) in the UK, has been granted by the Medicines and Healthcare Products Regulatory Agency (MHRA) or the European Medicines Agency (EMA). However in order to meet the needs of some patients it is sometimes necessary that they receive treatment with a product that has not been authorised for use in the UK (i.e. an unlicensed medicine) or to receive treatment with a medicinal product that is being used outside the terms of the product licence.

The regulatory bodies when assigning a MA consider safety, efficacy and pharmaceutical quality issues. This assessment has not been made for unlicensed medicines and therefore a governance process examining safety, efficacy and pharmaceutical quality must take place as part of the request and approval for use process.

2 Scope of the policy

This policy covers all processes involved in the approval, procurement and use of unlicensed medicines.

Unlicensed medicines are medicinal products that are not authorised for marketing in the UK.

The scope of this policy includes products that are:

a) Supplied from holders of a Manufacturing Authorisation (full manufacturing licence) either in the UK or abroad.

b) Manufactured by companies holding a ‘specials’ manufacturing licence to the specification of the doctor or pharmacist ordering them.

c) Manufactured in NHS units holding a specials manufacturing licence.

d) Use of a licensed medicine by a route other than the route (s) included in the MA.

e) Repackaged Medicines
These are licensed medicines that have become de-licensed as a result of being repackaged e.g. from manufacturer’s original containers. Although these are technically unlicensed medicines the associated risks are low and will not be considered further in the scope of this policy.

f) Compassionate Use Medication i.e. products required for compassionate use either where a patient is exiting a completed clinical trial or where the consultant has a medicines management approved agreement with the pharmaceutical company supplying the medication for treatment of an individual patient or group of patients (see paragraph c below).

Excluded from this policy:

a) Medicines which are classified as “prepared”. (commonly known as ‘Extemps’) Although these are not technically licensed products they are prepared in accordance with a Standard Operating Procedure (SOP) for a specific patient under the supervision of a pharmacist (section 10 exemption from the Medicines Act 1968) and are outside the scope of this policy. An example of this type of product would be preparation of a liquid formulation using a solid dosage form for a patient who cannot swallow.

b) Products required within a clinical trial which must be manufactured under a full Manufacturing and Importation Authorisation (MIA) - Investigational Medicinal Products - licence issued by the MHRA.

c) Governance and supply processes of compassionate use medication (procurement and quality assessment is included in the scope of this policy)

d) Use of a licensed medicine for an indication other than the indications(s) included in the MA but administered via a route which is included in the MA i.e. “off-label” use.

e) Borderline Substances, food supplements and medical devices.

3 Aims

To establish all the processes involved in the approval, procurement and use of unlicensed medicines.

4 Classification of Unlicensed Medicines

MHRA guidance (MHRA Guidance Note 14) requires that unlicensed medicines are subject to a detailed level of record keeping. The usage of unlicensed medicines within Newcastle Upon Tyne Hospitals NHS Foundation Trust is extensive. A pragmatic approach has been developed to categorise unlicensed medicines which allows resources to be directed to those unlicensed medicines that are considered to pose a higher risk to the organisation and ensure patient safety. For that purpose the policy recognises two risk categories of unlicensed medicines.

The use of all unlicensed medicines must be approved according to the Access to Drugs Policy. In practice this means that approval has been granted either for use
by an individual patient by the Medicines Management Committee chair, or has been granted full formulary approval by the North of Tyne Area Prescribing Committee. These approval processes include assessment of clinical suitability. As such the categories assigned below relate to pharmaceutical issues such safety in use, pharmaceutical quality and procurement risk.

4.1 Lower Risk Category

This group of unlicensed medicines consists of a range of medicines that meet all of the following criteria:

a) Medicines licensed for the same indication and the same route in a country with mutual recognition from the MHRA\(^1\) or licensed in the USA (with the availability of Transmissible Spongiform Encephalopathy Statement) and are either provided in English language or purchased pre-labelled in English language according to national Quality Assurance Standards\(^2\).

Or

Batch produced medicines procured from NHS units holding a Specials manufacturing licence, or other UK Specials licence holders.

b) Are considered to be of a suitable pharmaceutical quality.

c) Have a good clinical safety record, for example drugs that are included in the current British National Formulary (BNF) or BNF for children excluding medicines that are subsequently withdrawn on the grounds of safety.

4.2 Higher Risk Category

Unlicensed medicines that are not classified as lower risk would automatically default to the higher risk category. This category will include the following:

a) Medicines licensed in the UK or in a mutually recognised country\(^1\) and the USA where the intended route of administration is different from that included in the licence.

b) Medicines imported from countries without mutual recognition.

c) Medicines labelled in a foreign language.

d) “One-off” medicines procured from NHS units holding a Specials Manufacturing licence or other UK Specials licence holder i.e. not batch produced.

5 Responsibilities and Governance

Unlicensed medicines should only be used where their use is clearly justified and their clinical/pharmaceutical benefits are considered to outweigh the risks involved.

New unlicensed medicines must be subject to the same level of control and processes as that for licensed medicinal products, with particular attention being paid to any additional risks associated with their use.
Whenever an unlicensed medicine is prescribed, the prescriber is professionally accountable for his judgement in so doing, and may be called upon to justify their actions. As part of the request process for a new unlicensed medicine pharmacy must confirm that the prescriber has undertaken a suitable risk benefit assessment which must be documented.

It must be ensured that before a new unlicensed medicine is introduced into use:

- There is no suitable licensed alternative or that the patient may have either failed to respond or reacted adversely to the licensed alternative (unless approved by Medicines Management Committee).
- That the use is approved by the chair of the Trust’s Medicines Management Committee or the North Tyne Area Prescribing Committee, as appropriate.
- The prescriber is aware that the medicine he/she has requested is an unlicensed medicine.

The Director of Pharmacy is responsible for ensuring that suitable processes are in place within pharmacy for the safe procurement and supply of unlicensed medicines. Prescribers requesting the purchase of a new unlicensed medicine will be requested to document the patient details, indication for use, justification for use, acknowledgement of the unlicensed status of the medicine and their responsibilities in terms of communications with patients and other prescribers before the product can be sourced.

Additionally subsequent to receipt in the Trust, a favourable pharmaceutical quality assessment is required before the product can be released for use in the treatment of a patient.

Inevitably, the procurement process for unlicensed medicines will take longer than that for licensed medicines and in some cases may be quite protracted. For example, where a non English language medicine is received which therefore requires the provision of an English overlabel and translation of information leaflets. Prescribers should be aware of this when making their clinical decisions.

For unlicensed medicines only, any healthcare professional involved in the prescribing, supply, administration and monitoring should be:

- Made aware of its unlicensed status.
- Informed of any problems/risks involved and how to deal with them.
- Be given sufficient information to administer/use the product safely and correctly.

This information will be available on the web-BNF for unlicensed medicines classified as lower risk. In addition to this for higher risk unlicensed medicines consultants responsible for the patient’s care will be informed individually through the request and dispensing processes.

5.1 Specific Responsibilities

a) Referral to General Practitioners
It is the responsibility of the patient’s consultant to inform the patient’s General Practitioners (GP) that an unlicensed medicine has been initiated. GPs must not be asked to prescribe any unlicensed medicines containing drugs that are not licensed for any indication in the U.K. (unless they are included in the BNF, BNF for Children or North of Tyne Formulary). They may however be asked to prescribe other unlicensed products e.g. unlicensed oral liquid preparations for patients where licensed tablets cannot be given, or unlicensed preservative free eye drops where the patient is allergic to the preservative, but this should only be with the agreement of the GP.

If a GP agrees to prescribe an unlicensed medicine he/she must be given sufficient information about the product and its availability.

b) Communication with Patients /Carers

Patients have the right to participate in the making of properly informed decisions on their healthcare. Due to the greater risks and potential problems associated with the use of unlicensed medicines:

- Pharmacy will ensure that individual patients are given adequate information about any unlicensed medicines to ensure continuity of supply.
- Clinicians should consider obtaining informed consent to the use of a low risk unlicensed medicine. For high risk unlicensed medicines NuTH requires that either documented informed consent is obtained, or if it is decided that it is more appropriate not to seek informed consent, the reason why is recorded in the patient’s notes.
- Inadequate provision of information may increase the clinician’s or trust’s liability in the event of a mishap that results in a complaint and possible litigation.

A patient information leaflet explaining why it may be necessary to prescribe unlicensed medicines will be issued by pharmacy for each supply of a high risk medicine made directly to the patient.

c) Administration to Patients

Healthcare professionals administering medicines to patients should:

- Be aware of the unlicensed status of any medicines they are using.
- Notify pharmacy staff and/or the doctor looking after the patient, as appropriate:
  - If the labelling/any instructions supplied with the medicines are unclear.
  - They are unsure about any aspects involved in the use/administration of the medicine, its quality, likely side effects or patient monitoring required.
  - The patient experiences any serious or unexpected adverse reactions.
d) Records

Pharmacy staff must keep purchasing records of all unlicensed medicines for a period of at least 5 years.

In line with the pragmatic approach mentioned under Classification of Unlicensed Medicines (section 4) detailed patient specific supply records (including batch numbers issued) will be maintained by pharmacy for unlicensed medicines that come into the higher risk category and retained for a period of at least 5 years.

For the purpose of record keeping, lower risk category unlicensed medicines will be treated in the same way as licensed medicines and records will be kept for 2 years.

e) Monitoring

All staff involved in patient care have the responsibility to report any adverse reactions to the MHRA using the yellow card scheme. Additionally, any defects should be reported to the pharmacy department.

Pharmacy will:

- Monitor the usage of unlicensed medicines, confirming that continuing use remains as originally agreed. The more unlicensed medicines are used, the greater the risk that control of their use will be reduced.
- Notify clinicians of appropriate licensed alternative products becoming available
- Notify appropriate clinicians of any serious problems that they are alerted to with individual unlicensed medicines.
- Report any defects in unlicensed products to the regional quality assurance pharmacist.

f) Pharmaceutical Quality Assurance

During the procurement/supply process pharmacy staff should ensure that:

- The manufacturer’s licence status is clearly understood and their licence covers the appropriate types of product e.g. sterile products.
- The product must:
  - Comply with an agreed/adopted specification.
  - Be manufactured in an appropriate environment.
  - Have a validated shelf life.
  - Be quarantined on receipt until it has been formally checked and cleared for use by a pharmacy quality assurance/quality control staff.
  - Be labelled in English and where appropriate supplied with information in English to allow its use in a safe manner (Arrangements should be made for over-labelling and for translations to be prepared/obtained if necessary).
6 Policy

The use of unlicensed medicines within the Newcastle upon Tyne Hospitals NHS Foundation Trust (NuTH) is supported in accordance with the principles outlined below and any associated guidelines:

6.1 Unlicensed medicines should only be used when there are no licensed products available. Exception to this must be approved by Medicines Management Committee.

6.2 Unlicensed medicines should only be used if their use can be clearly justified clinically and pharmaceutically to meet the special needs of individual patients. An unlicensed product should not be used purely on the grounds of lower cost unless approved by Medicines Management Committee.

6.3 Those involved in the prescribing distribution or administration of an unlicensed medicine must be made aware of its unlicensed status the associated general risks with class of product and any known specific relevant risks associated with its use.

6.4 New unlicensed medicines must be subject to the same level of control and processes as that for licensed medicinal products, with particular attention being paid to any additional risks associated with their use. Access to Drugs Policy

6.5 Adequate records to an appropriate level must be kept with regard to the approval, purchase and the supply of unlicensed medicines. (see Section 5d Records).

6.6 Pharmacy staff issuing unlicensed medicines should ensure that they are labelled clearly in English and that the users have adequate information in English to use them properly.

6.7 Consultants and other clinicians must not ask others to prescribe unlicensed medicines without ensuring that they are adequately informed about the medicine, how it is used and any risks involved.

6.8 Individual patients (and/or their parents/carers) should be given adequate information about any unlicensed medicines they are prescribed. This should include information regarding the unlicensed status of the medicine and continuity of supply. It is recommended that informed consent to the use of an unlicensed medicine is obtained especially for those products that carry a significant clinical risk or have been categorised as higher risk under this policy. (see classification on unlicensed medicines and 5b Communication with Patient/Carers)

6.9 To minimise the risks to other patients, problems with the use of an unlicensed medicine (e.g. product defects, problems with labelling/instructions) must be reported promptly to the hospital pharmacy. Adverse drug reactions should be
reported to the MHRA using the yellow card scheme with a copy of the report being sent to the hospital pharmacy.

7 Training

Training for staff will be as outlined in the Mandatory Training Policy. Monitoring of staff training will be as detailed in the Mandatory Training Policy.

8 Equality and diversity

The Trust is committed to ensuring that, as far as is reasonably practicable, the way we provide services to the public and the way we treat our staff reflects their individual needs and does not discriminate against individuals or groups on any grounds. This document has been appropriately assessed.

9 Monitoring compliance

<table>
<thead>
<tr>
<th>Monitoring and audit</th>
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<tr>
<td><strong>Method</strong></td>
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<tr>
<td>Monitoring Trust approval for use prior to supply.</td>
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</table>

10 Consultation and review

Medicines Management Committee (April 2012)  
Senior Pharmacy Team

11 Implementation (including raising awareness)

Changes to Policy highlighted in Trust Policy Update newsletter  
Changes to Policy communicated to Pharmacy staff responsible for Policy implementation
For advice on answering the above questions please contact Helen Lamont, Director of Nursing, or, Christine Holland, Senior HR Manager. On completion this form must be forwarded electronically to Steven Stoker, Clinical Effectiveness Manager, (Ext. 24963) steven.stoker@nuth.nhs.uk togerther with the procedural document. If you have identified a potential discriminatory impact of this procedural document, please ensure that you arrange for a full consultation, with relevant stakeholders, to complete a Full Impact Assessment (Form B) and to develop an Action Plan to avoid/reduce this impact; both Form B and the Action Plan should also be sent electronically to Steven Stoker within six weeks of the completion of this form.

This form must be completed and attached to any procedural document when submitted to the appropriate committee for consideration and approval.

<table>
<thead>
<tr>
<th>Policy Title: Unlicensed Medicines Policy Document</th>
<th>Policy Author: Steve Brice, Asst. Director, Pharmacy</th>
<th>Yes/No?</th>
<th>You must provide evidence to support your response:</th>
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<tbody>
<tr>
<td>1. Does the policy/guidance affect one group less or more favourably than another on the basis of:</td>
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<tr>
<td>• Race</td>
<td>No</td>
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<td>• Ethnic origins (including gypsies and travellers)</td>
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<td>• Nationality</td>
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<td>• Culture</td>
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<td>• Religion or belief</td>
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<td>• Sexual orientation including lesbian, gay and bisexual people</td>
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<td>• Age</td>
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<tr>
<td>• Disability – learning difficulties, physical disability, sensory impairment and mental health problems.</td>
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<td>2. Is there any evidence that some groups are affected differently?</td>
<td>No</td>
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<td>3. If you have identified potential discrimination, are any exceptions valid, legal and/or justifiable?</td>
<td>n/a</td>
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<td>4(a). Is the impact of the policy/guidance likely to be negative?</td>
<td>No</td>
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<td>(If &quot;yes&quot;, please answer sections 4(b) to 4(d)).</td>
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<td>4(b). If so can the impact be avoided?</td>
<td>n/a</td>
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<td>4(c). What alternatives are there to achieving the policy/guidance without the impact?</td>
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<td>4(d). Can we reduce the impact by taking different action?</td>
<td>n/a</td>
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Comments: | Action Plan due (or Not Applicable): |
|---------------------------------------------------|--------------------------------------------------|

Name and Designation of Person responsible for completion of this form: Steve Brice, Assistant Director of Pharmacy Date: 11/07/2012
Names & Designations of those involved in the impact assessment screening process: As above
(If any reader of this procedural document identifies a potential discriminatory impact that has not been identified on this form, please refer to the Policy Author identified above, together with any suggestions for the actions required to avoid/reduce this impact.)