

## **Unlicensed Medicines Policy**

**February 2013**

<b>Policy Title</b>	<b>Regional Unlicensed medicines Policy</b>
<b>Policy Reference Number</b>	<b>Med13/012</b>
<b>Implementation Date</b>	<b>April 2013</b>
<b>Review Date</b>	<b>April 2015</b>
<b>Responsible Officer</b>	<b>Brian McBride</b>

## **1.0 INTRODUCTION / PURPOSE OF POLICY**

This policy supports the aim of ensuring that all medicinal products are safe, effective and of appropriate quality for use in patients. At the same time recognising that certain exemptions in legislation exist to enable a prescriber to, under their direct personal responsibility, prescribe unlicensed medicines to meet the specific needs of patients under their care.

### **1.1 Summary**

#### **1.1.1 Purpose**

This policy outlines the management of the prescribing, procurement, storage, supply and administration of Unlicensed Medicines within Northern Ireland HSC Trusts.

#### **1.1.2 Objectives**

This document ensures that the responsibilities and actions required of healthcare workers in relation to the prescribing, procurement, storage, supply and administration of unlicensed medicinal products are clear. This will help to minimise the risks to patients, to healthcare staff and to the organisation when the use of an unlicensed medicine is necessary.

### **1.2 Policy of Statements**

The use of unlicensed medicines within the HSC Trusts is supported in accordance with the principles outlined below:

**1.2.1** Where possible, licensed products will be used to treat patients.

**1.2.2** The use of an unlicensed medicine should only be considered when there is no equivalent licensed alternative available and if its use can be clearly justified clinically and pharmaceutically. The use of an unlicensed medicine should not be justified purely on the grounds of lower costs.

**1.2.3** It is recognised that the use of an unlicensed medicine is sometimes necessary in order to provide the optimum treatment for a patient. Any liability associated with the use of Trust approved unlicensed medicines will be accepted by the employing authority provided that best practice, as outlined in this policy is followed.

**1.2.4** Where a prescriber prescribes an unlicensed medicine, they are professionally accountable for their judgement in so doing, and may be called upon to justify their actions. Prescribers should satisfy themselves that they would obtain a professional body of support for their practice in relation to the use of the unlicensed medicine.

**1.2.5** Adverse drug reactions and medication incidents involving unlicensed medicines should be reported in the same manner as for licensed medicines.

**1.2.6** All healthcare professionals involved in the prescribing, procurement, supply and administration of medicinal products must be aware of a product's unlicensed status and any known relevant risks associated with its use.

**1.2.7** New unlicensed medicines should only be introduced following appropriate risk assessment and product categorisation. Approval of use should be reviewed and verified by Trust Drugs and Therapeutics Committee, if appropriate, according to risk category.

**1.2.8** Adequate records must be kept with regard to the purchase and supply of unlicensed medicines in accordance with the actions associated with the product risk category. These records may include details of the product

## **2.0 Background and Policy Description**

Medicines legislation requires that medicinal products are licensed before they are marketed in the UK or the EU. Accordingly no medicinal product may be placed on the market unless it holds a UK or an EU Marketing Authorisation (MA), also referred to as a Product Licence (PL) in the UK. An MA is assigned by the Medicines and Healthcare products Regulatory Agency (MHRA) or the EMA (European Medicines Agency).

The Marketing Authorisation provides assurance of the safety and efficacy of the medicine in relation to a specified use, which has been reviewed and accepted by an official expert body. It also defines the legal status of the product and ensures its quality. A Marketing Authorisation specifies the clinical condition(s), dose(s), route(s) of administration and packaging for the particular preparation, all of which are detailed in the Summary of Product Characteristics (SmPC). A pharmaceutical company cannot promote an unlicensed medicine or a licensed medicine for an unlicensed indication.

Types of unlicensed medicinal products are described in [Appendix 1](#).

Some patients may have specific clinical needs that cannot be met by licensed medicines. So that these specific needs may be met, the law allows the manufacture and supply of unlicensed medicines subject to certain conditions. The conditions are that there is a

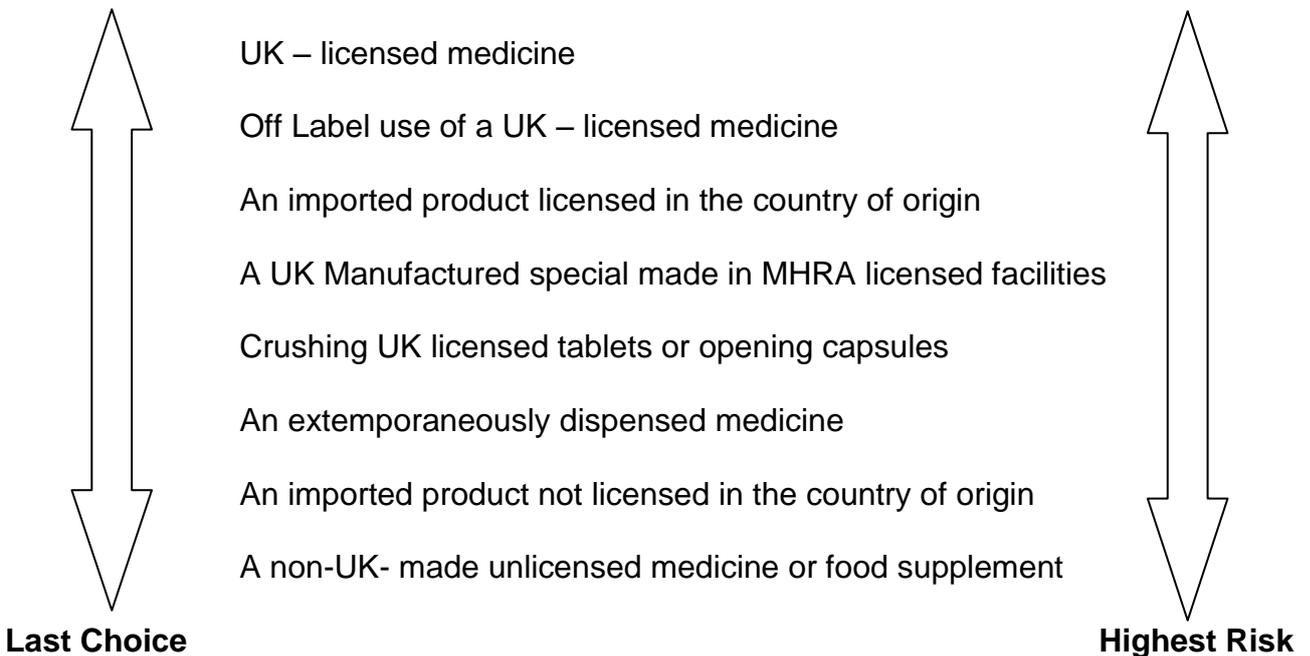
bona fide unsolicited order, the product is formulated in accordance with the requirement of a UK registered prescriber, and the product is for use by their individual patients under their direct personal responsibility.

It may be appropriate to select an option other than an unlicensed medicine when trying to provide medicines to facilitate the needs of the patient. Diagram 1 below, indicating the hierarchy of risk of medicines may be used as a useful guide to help decide on the most suitable option for a given clinical need and patient. Guidance is also available from the MHRA Guidance Notes (for example GN 14). These may be used as an aid in the decision making process as to which unlicensed medicine option is appropriate.

### Hierarchy of risk on basis of product origin (updated from MHRA guidance)

**Preferred Choice**

**Lowest Risk**



**Hierarchy may differ in particular patient groups such as neonates**

#### **Diagram 1** Hierarchy of risk produced by RPSGB (Pharmacy Professional 2010)

Unlicensed medicines can be prescribed by doctors, dentists and non-medical prescribers (examples are Independent Pharmacist and Nurse Prescribers and supplementary prescribers – see section 5.2)

To assist in managing the risk from unlicensed medicine use in Trusts in NI, a process of proposal for use, risk assessment and categorisation has been developed and is reflected in the steps indicated in the flowchart (appendix 2). The risk assessment and categorisation process takes account of clinical and procurement characteristics. Proposals to use a new unlicensed medicinal product must be submitted using appendix 3. The pharmacy department will also provide information on the medicine using an Unlicensed Medicines Evaluation form, UME (appendix 4). This will then enable a risk assessment of the medicine to be performed, usually by a QA pharmacist, or other competently trained staff member, using risk assessment form appendix 5. The unlicensed medicine will then be assigned to one of three categories: low, medium and high, and will have associated actions to be taken when the product is in use (Appendix 6). Appendix 6 is provided as guidance. These actions may be modified, for example to reduce the risk category or to make the medicine accessible in urgent situations while retaining the original category of risk assessment. any alterations should improve the safety of the medicine in use, not reduce the safety. Any modifications should be noted on the QA risk assessment form (Appendix 5). It is for each individual Trust to consider if such modifications are permissible for the individual product and the intended area of use.

When the request has been received and the risk assessment process to assign a category of risk completed, the requesting consultant may be required to sign a 'Declaration of Use Form' ([appendix 7](#)). This signature will indicate acknowledgement, by the consultant, of the unlicensed status of the medicine and the relevant actions that are to be adhered to when the product is being used.

The submission will be considered by the Drugs and Therapeutics Committee and approved as appropriate. Site designated pharmacists may agree to supply an unlicensed medicine prior to this process in exceptional circumstances. (See section 6)

The financial impact of a new unlicensed medicine should be evaluated and approved in accordance with the local Trust procedure for the introduction of new medicinal products.

### **3.0 THE PURPOSE**

The policy outlines the responsibilities and actions required of healthcare workers in relation to the prescribing, procurement, storage, supply and administration of unlicensed medicinal products in the HSC Trusts.

### **4.0 THE SCOPE**

This policy covers the prescribing, procurement, storage, supply and administration of medicinal products which do not hold a UK or EU marketing authorisation (product licence). The different types of unlicensed medicines are described in [Appendix 1](#).

The use of an unlicensed medicinal product, which may be in clinical development, but which is supplied outside a recognised clinical trial research protocol, for example as part of a compassionate-use or named-patient supply programme, is encompassed within this policy.

#### **4.1 The policy does not cover:**

**4.1.1** The use of licensed medicinal products for unlicensed indications (off-label use).  
Refer to [Appendix 9](#).

**4.1.2** Products prepared under Section 10 exemption to the Medicines Act.  
This includes aseptically prepared and extemporaneous preparations prepared, by the Trust in response to a prescription/order from a doctor or dentist for an individual patient.

**4.1.3** Investigational medicinal products as part of a recognised clinical trial research programme. These are covered by the policies of the Research Ethics Committees and Trust Research Governance approval processes.

**4.1.4** Over-labelled or repackaged licensed medicinal products.

**4.1.5** Homeopathic or unlicensed herbal remedies.

**4.1.6** Mixing of medicines prior to administration.

## 5.0 **ROLES AND RESPONSIBILITIES**

The specific roles and responsibilities of healthcare professionals involved with unlicensed medicinal products are described below.

### 5.1 **Introduction**

5.1.1 The introduction of new unlicensed medicinal products into hospital practice is subject to the same process as for new licensed medicines. A formal review of the request must occur through the Trust Drugs and Therapeutics Committee structures.

5.1.2 The introduction of an unlicensed medicine into practice in a HSC Trust may **only** be at the request of a consultant. When it is clear that an unlicensed medicine is being introduced into the Trust for a new indication, then this request should be processed as if it were a first introduction. A separate risk assessment should be performed for the drug and indication as a matter of good practice.

5.1.3 The introduction of an unlicensed medicine in a situation where the use of an unlicensed medicine is required to ensure availability of a therapy due to problems with procuring or supplying the licensed medicine, Pharmacy should assess the alternative preparation to be used and process it in accordance with the category of risk assigned (i.e. low, medium or high). Consultants with patients under their care requiring such a medicine should be informed of this change.

### 5.2 **Prescribers**

5.2.1 Where a prescriber prescribes an unlicensed medicine, they are professionally accountable for this judgement. In so doing, prescribers should satisfy themselves that they would obtain a professional body of support for their practice in relation to the unlicensed product.

5.2.2 Prescribers of unlicensed products carry their own responsibility for use and prescribing of unlicensed medicines. Prescribers are responsible for the patient's welfare and in the case of adverse events they may be called upon to justify their actions.

5.2.3 The prescriber must be aware that the medicine being used is unlicensed. It is common practice to have a signature from the prescriber confirming their awareness of the unlicensed status of the medicine. A signed form or statement (i.e. [Appendix 7](#)) indicating this awareness should be completed when a consultant first wants to commence the use of an unlicensed medicine. There may be a need to complete this form for each request thereafter depending on the risk category assigned to the unlicensed medicine.

5.2.4 [Appendix 6](#) may act as a guide, giving an indication of the prescribing controls that should be operated for an unlicensed medicine, in accordance with the risk category of the product.

5.2.5 If there is to be a change to the prescribing controls, then the grade of prescriber permitted to prescribe the unlicensed medicine must be indicated and recorded during the risk assessment process. This must be indicated on the declaration of use form. ([Appendix 7](#))

- 5.2.6** In certain circumstances the declaration of use form should also indicate the grades of prescriber permitted to initiate the medicine in a new patient, and also authorise a repeat prescription for the medicine. These alterations to prescribing authority must be supported by robust clinical treatment protocols for the use of the relevant unlicensed medicine.
- 5.2.7** These decisions should be made by each individual Trust on a case by case basis as part of the risk assessment of the use of the unlicensed medicine in practice. This approach is intended to provide better access to medicines that may be of a higher risk due to specific concerns, i.e. products in a foreign language. However robust evidence of safe therapeutic use and an agreed protocol may allow for acceptance of reduced restrictions on staff who may prescribe the unlicensed medicines, to improve access to the medicines for the benefit of the patient. It would not be appropriate to reduce prescribing restrictions for medicines that may present a higher clinical/therapeutic risk to patients due to limited evidence of safety of the medicine in use.
- 5.2.8** Non-medical prescribers may ONLY prescribe an unlicensed medicine in accordance with their Trust Non-medical prescribing policy.
- 5.2.9** Non-medical prescribers (NMP) include, amongst others, pharmacists and nurses who have undertaken and achieved a qualification allowing them to become independent and/or supplementary prescribers.
- 5.2.10** Nurse and pharmacist independent prescribers are allowed to prescribe unlicensed medicine that is listed in an agreed Clinical Management Plan (CMP). (Ref National Prescribing Centre, NPC).
- 5.2.11** The status in relation to a NMP's authority to prescribe an unlicensed medicine is in accordance with the prescribing status detailed in [Appendix 6](#), or as modified by an individual Trust and thus indicated on the Declaration of use form for the particular unlicensed medicine.
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- 5.2.12** Unlicensed medicines may not be prescribed, supplied or administered under a Patient Group Direction (PGD).
- 5.2.13** The prescriber should ensure that the use of the unlicensed medicinal product is justified by the clinical condition of the patient and that the benefits outweigh the risks.
- 5.2.14** The prescriber should be aware that clinical responsibility for prescribing lies with the prescriber who signs the prescription.
- 5.2.15** The prescriber should ensure that when a new unlicensed medicinal product is requested the prescriber follows the Trust's policies and relevant procedures.
- 5.2.16** The prescribers should ensure that they are familiar with the status of the medicinal product and know the protocols that control its use (where applicable).

**5.2.17** The prescriber should ensure that adverse drug reactions and medication incidents involving unlicensed medicines are reported in the same manner as for licensed medicines.

**5.2.18** Where a patient is prescribed an unlicensed medicine in the medium or high categories and where responsibility for ongoing care is to be transferred to the patient's General Practitioner (GP), the prescriber should ensure that the GP is informed of the licensed status of the medicinal product and that he or she is willing to accept clinical and legal responsibility for prescribing. The hospital doctor is responsible for continuing treatment if the GP will not accept responsibility for continuing care.

**5.2.19** The prescriber should ensure compliance with the Trust policy relating to informed patient consent. The prescriber should ensure that the patient is informed of the licensed status of the medicinal product that will be used or has been prescribed as ongoing treatment and the implications of using the unlicensed medicinal product. (It is recognised that there are circumstances where involving the patient in decisions is inappropriate and impractical, e.g. an unlicensed medicinal product routinely used in theatres or paediatrics. A record should be made as appropriate in the patient's notes.)

### **5.3 Staff administering medicines**

**5.3.1** Healthcare staff involved in the administration of unlicensed medicinal products should be satisfied that they have sufficient information to administer an unlicensed medicine safely. Where possible there should be acceptable published evidence for the use of the product for the intended indication. Liability for prescribing an off-label product sits with the prescriber and the dispenser or supplier of the unlicensed medicine.

**5.3.2** A registered nurse or midwife may administer an unlicensed medicinal product with the patient's informed consent against a patient-specific direction but not against a Patient Group Direction.

Where it is essential that a 'high risk' unlicensed medicine is held as stock on a ward or department, the ward/departmental manager is responsible for keeping a record of its use. Storing 'high risk' unlicensed medicines on wards as stock, should be an exception.

**5.3.3** Pharmacy will inform ward/departmental managers in writing of their responsibility to report patient details when it is initially agreed that 'high risk' unlicensed medicines can be kept as stock in the interests of patient care.

**5.3.4** In such cases as described above, the ward manager must ensure that the following information is recorded and forwarded to the Pharmacy Department:

- Date of supply
- Patient Name and Hospital Number
- Drug, strength and quantity supplied
- Batch Number issued

### **5.4 Pharmacists and pharmacy personnel**

Pharmacists' responsibilities:

- 5.4.1** As the purchaser of the product, particularly where this involves specifying the product to be purchased;
- 5.4.2** If his/her actions or omissions have contributed to harm.
- 5.4.3** All pharmacy personnel are responsible for ensuring that the Unlicensed Medicines Policy and standard operating procedures relating to the prescribing, purchase, receipt, storage and supply of unlicensed medicinal products are followed.
- 5.4.4** Pharmacy staff must ensure processes are in place to keep purchasing and issue records of all unlicensed medicinal products for the required storage period.
- 5.4.5** The Trust Head of Pharmacy has overall responsibility for ensuring implementation of the Unlicensed Medicines Policy in the Trust. Other pharmacists may be designated specific responsibilities to ensure the safe and effective operation of the policy (i.e. procurement, receipt, storage, supply etc). The designation of specific roles should be made clear to staff.
- 5.4.6** Clinical pharmacists must work alongside designated pharmacists across Trust Hospital sites to support the implementation of this policy.
- 5.4.7** The Trust Pharmacy department must designate a member or members of staff to perform duties as outlined below:
- 5.4.8 The designated pharmacist (s) is required to:**
- 5.4.8.1** Ensure completion of the relevant sections of the UME ([Appendix 4](#)), and the Risk Assessment Form for an Unlicensed Medicine ([Appendix 5](#)) before forwarding these to the Trust Drugs and Therapeutics Committee.
- 5.4.8.2** Ensure adherence to guidance relating to the risk assessment and categorisation of unlicensed medicines and the appropriate actions required for the receipt, storage and supply of unlicensed medicines.
- 5.4.8.3** Authorise for use new products that are needed for urgent clinical use before they can be formally assessed and approved by the Drugs and Therapeutics Committee.
- 5.4.8.4** Ensure written procedures to cover all aspects of the procurement, receipt, storage and issue of unlicensed medicinal products are produced, authorised, and reviewed.
- 5.4.8.5** Monitor the range and quantities of unlicensed medicinal products purchased, keeping a list of unlicensed medicines currently approved by the Trust. A register must be maintained within pharmacy.
- 5.4.8.6** Monitor and audit the handling of unlicensed medicinal products in the Trust.
- 5.4.8.7** Ensure there are satisfactory arrangements for patients to have continuing supplies of treatment. A generic leaflet for patients to obtain further supplies of unlicensed medicines is provided at [Appendix 8](#).

#### **5.4.9 Pharmacists involved in the initial review of requests for unlicensed medicines:**

- 5.4.9.1 Verify a definite clinical need for the medication, and that an alternative licensed preparation is not available.
- 5.4.9.2 Advise the prescriber that the product is unlicensed.
- 5.4.9.3 Verify if the unlicensed medicine is currently approved/not-approved for use in the Trust for the indication and follow the Trust policy as required.
- 5.4.9.4 If it is a new product, request from the prescriber relevant evidence, guidelines and protocols to support the safe and effective use of the product, including information on hazards associated with taking the medicine.
- 5.4.9.5 Obtain information from the prescriber/medicines information relating to country of origin, licence status in that country and supplier if known.
- 5.4.9.6 Establish the urgency of need, and discuss the consequence for the patient of a delay in supply.
- 5.4.9.7 Assist medical staff in completing appendix 3, 'Proposal for new unlicensed medicine form'.
- 5.4.9.8 Assist with the completion of the 'Risk Assessment form for an unlicensed Medicine', appendix 5.
- 5.4.9.9 Ensure the appropriate translations of PIL's and labelling are provided for the patient and that a SmPC is provided to ward staff.
- 5.4.9.10 Ensure a 'Declaration of Use' form, appendix 7, is completed as required.
- 5.4.9.11 Ensure if required, the patient is provided with a 'How to obtain a further supply of your unlicensed medicine' leaflet, appendix 8. Discussing any concerns they may have.
- 5.4.9.12 If appropriate, make arrangements for patients to have continuing supplies of treatment.

#### **5.4.10 Pharmacy staff involved in the procurement of unlicensed medicinal products must:**

- 5.4.10.1 Ensure that the person making the request is authorised to do so.
- 5.4.10.2 Ensure that purchases of unlicensed products are in accordance with written procedures.
- 5.4.10.3 Ensure the risk assessment is completed and appropriate action is taken according to the outcome of the risk assessment.
- 5.4.10.4 Liaise with the supplier as appropriate to obtain additional information or translations.

**5.4.10.5** Ensure any special requirements of suppliers are met.

**5.4.10.6** Receipt, quarantine and process deliveries in accordance with procedures.

**5.4.10.7** Ensure correct storage arrangements.

**5.4.11** A process of quarantine and formal checking and release for use or rejection must be employed. The Trust should utilise a QA pharmacist or suitable designated deputy. The grade/level of experience required of a pharmacist approved to perform this task may be dependent on the risk category assigned to the unlicensed medicine.

**5.4.12 Pharmacy staff involved in the dispensing/issuing of unlicensed medicinal products must:**

**5.4.12.1** Ensure that requests for unlicensed medicinal products are processed in accordance with Trust policy and local SOPs.

**5.4.12.2** In accordance with the risk category, ensure the prescriber is authorised to prescribe the unlicensed medicine.

**5.4.12.3** If appropriate, make arrangements for patients to have continuing supplies of treatment. A generic Patient Information Leaflet for Unlicensed Medicines is provided in [Appendix 8](#).

**5.4.12.4** Where practical (i.e. Medium and High risk medicines), label unlicensed medicines intended for in-patient use to indicate that they are an unlicensed product.

**5.4.12.5** Ensure the appropriate records of supply are made and retained. These records should include the product description, batch number and the quantity supplied, patient name, hospital number, prescriber's name, the ward/department supplied and the date of supply in accordance with the risk category of the unlicensed medicine.

**5.4.12.6** Ensure appropriate translations of PIL's and labelling are provided for the patient, and that a SmPC is provided to the ward staff.

## **5.5 Drugs and Therapeutics Committee**

**5.5.1** The Trust Drug and Therapeutics (D&T) Committee is responsible for approving the Local Trust policy, and reviewing and approving the use of new unlicensed medicinal products in the Trust. However, in the case of an urgent clinical need, the Medical or Clinical Director and Trust Designated Pharmacist (Senior Pharmacy Manager) may authorise the use subject to formal ratification at the next D&T Committee meeting.

**5.5.2** The Proposal for a New Unlicensed Medicine Form ([Appendix 3](#)) should be completed and submitted to the D&T Committee as part of the submission for approval to use the product. The D&T Committee will also receive the completed UME form ([Appendix 4](#)) and the QA Risk Assessment Form for an Unlicensed Medicine ([Appendix 5](#)) from the site designated pharmacist. The introduction of an unlicensed medicine into a Trust should also be considered for potential impact in conjunction with local Trust policy for the introduction of new treatments.

**5.5.3** The D&T Committee has a monitoring role and reappraises all unlicensed medicines used within the Trust on a rolling programme in conjunction with pharmacy. However a review of high risk unlicensed medicines should be performed annually. This process should be operated utilising the Trust Governance arrangements for medicines management ensuring a system of audit is introduced.

## **6.0 PROCEDURES**

Procedures should be developed in local trust hospitals to support the implementation and safe and effective operation of this policy. Examples of procedures that may need to be written at local trust level will include activities such as:

- Prescribing/requesting
- Risk assessment/completion of relevant appendices
- Procurement
- Receipt
- Quarantine
- Over-labelling
- Release for use
- Ward ordering
- Dispensing/issuing
- Record keeping
- Reporting of ADR's
- Audit/review

## **7.0 REFERENCES (INCLUDING RELEVANT EXTERNAL GUIDELINES)**

- 7.1** EEC Directive 65/65
- 7.2** Medicines Act Leaflet 81 (MAL 81). The Medicines for Human Use (Marketing Authorisations Regulations 1994) S.I. 1994/3144
- 7.3** MHRA Guidance Note No. 14, The Supply of Unlicensed Relevant Medicinal Products for Individual Patients, Revised May 2005
- 7.4** Controls Assurance Medicines Management (Safe and Secure Handling) Standards 2004
- 7.5** Guidance for the Purchase and Supply of Unlicensed Medicinal Products Notes for Prescribers and Pharmacists, NHS Pharmaceutical Quality Control Subcommittee, June 2002 (updated June 2004)
- 7.6** GMC Guidance on Good Practice-Prescribing Medicines – Frequently asked Question. [http://www.gmcuk.org/guidance/current/library/prescriptions\\_faqs.asp#p23](http://www.gmcuk.org/guidance/current/library/prescriptions_faqs.asp#p23)
- 7.7** BHSCT Unlicensed Medicine Policy, Version 2 October 2008
- 7.8** WHSCT Policy for the purchase and supply of unlicensed medicines pharmacy [1] March 2007
- 7.9** Medicines Act 1968
- 7.10** FAQ's National Prescribing Centre, [www.npc.co.uk/prescribers/faq](http://www.npc.co.uk/prescribers/faq)(accessed 9/11/2010)

## 8.0 EQUALITY STATEMENT

In line with duties under the equality legislation (Section 75 of the Northern Ireland Act 1998), Targeting Social Need Initiative, Disability discrimination and the Human Rights Act 1998, an initial screening exercise to ascertain if this policy should be subject to a full impact assessment has been carried out.

The outcome of the Equality screening for this policy is:

Major impact

Minor impact

No impact.

### SIGNATORIES

(Policy – Guidance should be signed off by the author of the policy and the identified responsible director).

\_\_\_\_\_  
Name  
Title

Date: \_\_\_\_\_

## **APPENDIX 1      Types of unlicensed medicinal products**

Unlicensed medicines are medicines, or substances used as medicines without a UK marketing authorisation and include:

Medicinal products prepared by a manufacturer but not on sale in this country and may include medicines awaiting a EU or UK marketing authorisation, medicines withdrawn from the UK market, or medicines manufactured for export.

Medicines prepared outside the UK with a marketing authorisation from the country of origin. Such medicines are imported into the UK.

Extemporaneously dispensed medicines prepared for a specific patient under the supervision of a pharmacist in accordance with a practitioners prescription, including PN compounding, IV additive and cytotoxic reconstitutions.

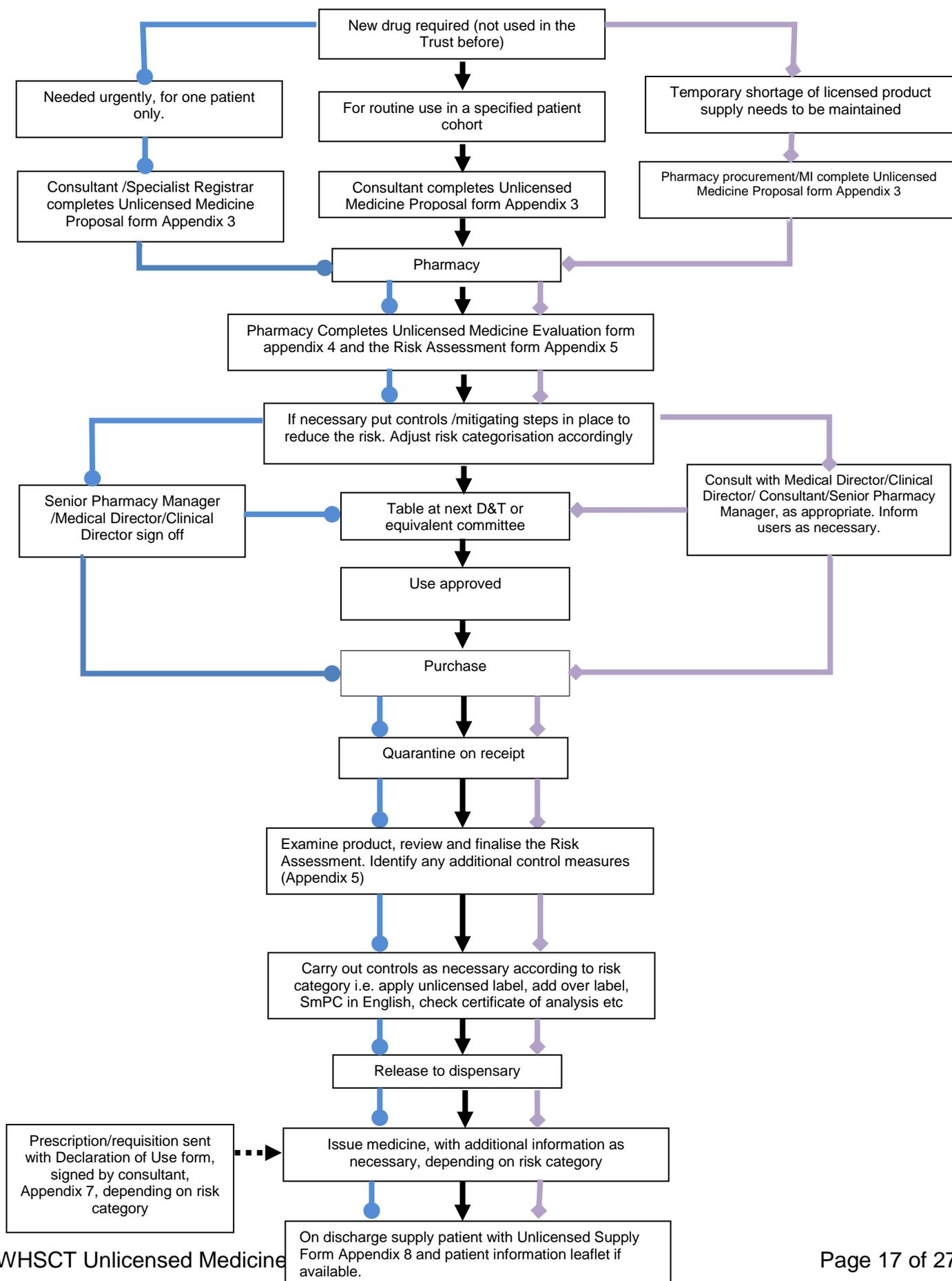
Unlicensed medicinal products obtained from a Hospital or commercial supplier with a manufacturers 'specials' licence.

Re-packed medicines. These are medicines which are removed from their original containers and re-packed during dispensing.

Medicines mixed prior to administration. Mixing is defined as “the combination of two or more medicinal products together for the purposes of administering them to meet the needs of a particular patient”.

## Appendix 2

### New unlicensed medicine request flowchart



### Appendix 3 Proposal for New Unlicensed Medicine Form Page 1 of 2

This form is to be used in conjunction with the Trust Policy for Unlicensed Medicines. Before completing this form, you must have read the Trust Unlicensed Medicines Policy which identifies your responsibilities under the policy.

Requester details					
Consultant name:		Hospital site:			
Speciality:		Ward/dept:			
Contact details:		Date requested:			
		Date required:			
Patient details					
Anticipated usage (please tick)		Apply addressograph if individual patient request			
Single patient/one-off	<input type="checkbox"/>			For your patients only	<input type="checkbox"/>
Fewer than 6 patients per year	<input type="checkbox"/>			For patients within your speciality on a single site	<input type="checkbox"/>
If more than 6 patients per year, please provide estimated numbers _____	<input type="checkbox"/>			For patients within your speciality on all sites	<input type="checkbox"/>
		Any patient within the Trust	<input type="checkbox"/>		
Unlicensed Medicine Details					
Product name: (International Non Proprietary Name) _____					
Proprietary Name (if known): _____					
Strength and Pharmaceutical Form: _____					
Manufacturer (if known): _____					
Indication: _____					
Dose / frequency / route: _____					
Duration of Treatment: _____					
Why is an unlicensed Medicine being considered? (Delete as appropriate) Pharmaceutically equivalent licensed product temporarily unobtainable. Therapeutically equivalent UK licensed product available/suitable (provide details): Other (provide details);					
Clinical Evidence					
Is there any evidence to support its use for the proposed indication?			Yes / No		
Is there evidence to support its proposed administration schedule? ( dose, duration, concentration for parenteral products and route)			Yes / No		
Is the active drug currently in a licensed product for use via the same route of administration e.g. tablet, suspension			Yes / No		

Is the product licensed for the specified indication in another EU member state?	Yes / No / Not known
Are other Trusts using this medicine? If so, name;	Yes / No / Not known
Summarise below the supporting evidence, list references and attach copies of references were available.	
What are the risks to the patient of not using this drug?	
What side effects <u>and</u> significant interactions have been reported? Is any monitoring required? Describe;	
Give details of contraindications and any other risks to the patient. Include precautions in use.	
Will there be any primary care implications? (e.g. need for a shared care protocol) If so, describe;	

Prescriber (Consultant or SpR – Circle one)			
Print name:		Speciality/ Directorate:	
Signature:		Date:	
If SpR, state name of patient's consultant:			

Forward completed form to Pharmacy Quality Assurance pharmacist or Pharmacy Services Manager

Documents for Drugs & Therapeutics (D&T) Committee	<i>Tick</i>
Proposal for New Unlicensed Medicine Form	
Unlicensed Medicine Evaluation (UME) Form	
Risk Assessment form for an Unlicensed Medicine (Quality Assurance)	

Outcome of D&T Evaluation	
Approval for use	Yes / No
If no, give reasons	
State restrictions on prescribing / use	
Signature of Chair of D&T:	Date:

## Appendix 4 Unlicensed Medicine Evaluation (UME) form

<b>Complete for all products:</b>	
Product Name and strength: (rINN, including salt and Brand name)	
Pack Size:	
Route of administration:	
Manufacturer (name & contact details):	
Supplier (name & contact details):	
Country of Origin:	
Storage Conditions:	
Shelf Life:	
Cost: ( include how long price is held)	
Delivery lead time: (with / without Certification)	
<b>Imported Product – contact supplier / manufacturer to obtain the following details:</b>	
<b>Supplier:</b> Attach written confirmation that importer has MHRA approval to import this product.	Attach confirmation
<b>Origin:</b> Is product licensed in country of origin? Yes / No (Circle as appropriate) If yes, record licence number:	
Is product licensed in: EU / USA / Canada / NZ / Australia / Japan Yes / No (Circle as appropriate). State country:	
Was product licence in UK withdrawn? Yes / No (Circle as appropriate) If yes, contact manufacturer to find out reasons for withdrawal. UK Product Licence applied for? Yes / No / Not known. If yes, record date of application for licence:	
<b>Certification:</b> Is certificate of analysis / conformity available? Yes / No (Circle as appropriate).	
<b>Packaging &amp; labelling:</b> Is product package English labelled? Yes / No (Circle as appropriate)	
Is English SmPC & PIL available? If yes, obtain copy of English SmPC & PIL and attach	Attach SmPC & PIL
Is SmPC translation guaranteed by supplier? If yes, obtain written statement from supplier. Is there an additional cost of translation of SmPC? If yes, state cost:	Attach statement from supplier
<b>Therapeutics:</b> Is product/ manufacturer listed in Martindale ( ) / AHFS ( ) / Therapeutic drugs ( ) tick box(es)	
<b>Product sourced from NHS / Non-NHS Specials Licensed Manufacturer in UK:</b>	
Manufacturer's Licence No:	
Is Stability data available Yes / No If yes, obtain specification and attach	Attach specification
Is product specification available Yes / No If yes, obtain specification and attach	Attach specification
Is product analysed using Physical / Chemical / Microbiological tests before release. If yes, obtain written confirmation stating the types of tests applied and attach.	Attach confirmation
Is certificate of analysis/conformity available? Yes / No State type of certificate: If yes, obtain written confirmation stating the product analysis applied and attach.	
Completed by:	Date:

Attach completed form to papers for D&T submission

## Appendix 5 Risk Assessment Form for an Unlicensed Medicine (Quality Assurance)

Name		Form		Strength	
Manufacturer		Brand Name		Pack Size	
Licence no.		Country of origin		Supplier	
<b>Supplier</b>					
MHRA licensed importer with full pharmacovigilance in QMS				1	
NHS Specials Unit				2	
Commercial Specials Manufacturer (UK) – Rosemount/Martindale				2	
Supplier not Manufacturer (e.g. Wholesaler)				3	
Registered Pharmacist – extemporaneous preparation				4	
<b>Origin</b>					
UK Manufacturers with Specials Licence				1	
EU / USA / Canada / NZ / Australia / Japan and licensed in country of origin				1	
Elsewhere – Licensed in country of origin				HIGH	
EU / USA / Canada / NZ / Australia / Japan and unlicensed in country of origin				HIGH	
UK – no specials licence ( Section 10)				HIGH	
<b>Certification</b>					
Fully licensed product with EMEA / Licence number (imports)				1	
Certificate of Analysis and GMP compliance available (Specials)				1	
Certificate of Conformity available - product analysis (Specials)				2	
Certificate of Conformity - no product analysis (Specials)				3	
No Certificate available / no analysis carried out (Specials / Section 10)				4	
<b>Documentation</b>					
Product TSE compliance certification				0	
Product has no TSE compliance certification				HIGH	
<b>Packaging &amp; Labelling</b>					
English				0	
Foreign language: purchased already over labelled in English, with translated SPC				3	
Foreign language				HIGH	
<b>Specification</b>					
Imported medicine: EU / USA / Canada / NZ / Australia / Japan licence in country of origin				0	
Manufacturer's specification available (special)				2	
No external specification available				HIGH	
<b>Route of Administration</b>					
Topical to intact skin (non-sterile)				0	
Mucous membranes, broken skin, oral (non-sterile)				1	
Sterile all routes except intrathecal / intravitreal				2	
Sterile intrathecal and intravitreal				3	
<b>Therapeutic Agent (Clinical input)</b>					
Established therapeutic agent – no special problems				0	
Recognised therapeutic agent – minor problems or little experience of use				2	
Novel therapeutic agent of unusual use				4	
Unrecognised therapeutic agent with some supporting information for use				6	
Unrecognised therapeutic agent with no information available				HIGH	
Recognised therapeutic agent with known problems				HIGH	
Product containing material of animal or human origin				HIGH	
<b>Risk category</b>					
			<b>Additional Local controls:</b>		<b>Final Risk Category</b>
LOW	1 to 7				
MEDIUM	8 to 14				
HIGH	15 to 21				

Risk Category Signed Off by:		Date	
Regional QA Verification:		Date	
Entered onto database		Date	

## **Appendix 5**

### **Guidance notes:**

The function of the risk assessment is to take a consistent approach across Trusts to assigning a risk category to the unlicensed medicine. How the medicine is handled is determined by the risk category so it is important that the category is accurate. Initially all current ULMs will be assigned using this and then new ones will be added. This guidance should remove any subjectivity from different people performing this.

### **Who should carry out the risk assessment?**

A member of staff who has been trained in the issues around the manufacture and procurement of unlicensed medicines should perform the risk assessment.

### **Supplier**

As for the procurement of the medicinal product, the purchaser should be satisfied with the supplier. This means ensuring the supplier has the appropriate authorisation to make or supply the medicine. This can be checked on the MHRA website. The NHS QA committee also carries out audits of some medicines manufacturers and suppliers.

It is becoming more common for special manufacturers to use wholesalers for distribution of their products.

It is also common for special manufacturers to sell products that have been prepared under Section 10 exemption under the supervision of a pharmacist. This can be done for small one off batches but shouldn't be done as routine to speed up turnaround time of orders or because testing cannot be carried out.

### **Origin**

Certain other countries are subject to reciprocal agreement with the MHRA that manufacture and licensing process takes place to a similar standard as the UK. E.g. Europe, Australia, USA  
In terms of risk it is always preferable to supply from a country with this agreement.

### **Certification**

This gives an indication of the level of testing an unlicensed medicine will have undergone. A product licensed in an approved country will have undergone clinical trials and testing as part of the process for gaining its authorisation for that country.

This is desirable, as countries with a reciprocal agreement will have testing similar to the UK. Special manufacturers in the UK are not obliged to include this level of testing and it is up to the purchaser to specify it is reported in Certificate of Analysis at the time of purchase. In some cases the manufacturer will only supply a Certificate of Conformity, which is saying the product has been made to conform to a standard but they may not have undertaken finished product testing to provide information to prove it does.

## **Appendix 5**

### **Guidance notes continued**

#### **Documentation**

Manufacturers and importers of unlicensed medicinal products operating under any type of MHRA licence should be able to give an assurance that their products are TSE free. This will not necessarily be the case with raw materials such as gelatine based capsules.

When notifications are received of the intended importation of unlicensed medicines, the MHR does not routinely request evidence of compliance with these Regulations. The Regulations state that no person shall import or market an unlicensed product unless that product has been manufactured in accordance with the TSE Guideline; therefore the importer is expected to maintain records demonstrating compliance. These records may be requested during an MHRA inspection.

#### **Packaging and labelling**

Foreign-labelled medicines are high risk when there is difficulty knowing details of direction and warnings, etc. Most importers now offer translation services. The risk is lowered if a reliable up to date detailed translation is available. There needs to be robust procedures in place to ensure translations are current and available where needed.

#### **Specification**

A specification is not required if the product is licensed in its country of origin as it will have been made according to the submission for authorisation.

For a special it is desirable that the manufacturer can make the product to the specification required of the purchaser. If not the manufacturer should make the specification available for the purchaser to ensure the product meets their requirements.

#### **Route of administration and therapeutic agent**

There is risk associated with how the medicine is to be administered together with its mode of action and side effects. Parenteral administration is the highest risk because of the speed of onset, the fact this route is by passing the bodies natural defence mechanisms, etc.

Predicting the medicinal product's effect and side effects will be based on the evidence available on its therapeutic use. Prescribers need to be aware of the responsibilities they have around the risks associated with using therapeutic agents when there is limited knowledge of the hazardous side effects.

## Appendix 6

### Categorisation of Unlicensed Medicines and Recommended Associated Actions

Category	Potential Risk	Prescribing status	Pharmacy Action
<b>Low</b>	None – no obvious harm. No obvious contraindications for use	Unrestricted General Use (i.e. initiation and repeat prescribing for any patient by all grades of prescriber)	<ul style="list-style-type: none"> <li>• Add JAC special consideration: 'Unlicensed Medicine – Low risk'</li> <li>• Quarantine and check against CofA/CofC. Formal release process.</li> <li>• Permitted on ward top-up</li> <li>• Receipt and issue recorded through computer stock control system</li> <li>• Review use at least every 5 years</li> </ul>
<b>Medium</b>	Non-permanent harm to include side effects which are transient and/or readily manageable Some contra –indications for use	General Use with Restrictions (i.e. may only be initiated by a consultant, but repeat prescribing permitted by any grade of prescriber)	<ul style="list-style-type: none"> <li>• Add JAC special consideration: 'Unlicensed Medicine – Medium risk'</li> <li>• Quarantine and check against CofA/CofC. Formal release process.</li> <li>• Not permitted on ward top-up</li> <li>• Provide English SmPC/PIL. Must over-label in English</li> <li>• Request CofA, CofC, TSE certificate as appropriate</li> <li>• Receipt and issue recorded through computer stock control system</li> <li>• Declaration of use form completed once by an individual consultant, valid for two years</li> </ul> <p>Review use at least every 2 years</p>
<b>High</b>	Non-permanent harm to include significant side effects. Significant contraindications for use. Packaging and information leaflet unlikely to be in English or complex manipulation required to administer. Harm due to permanent or long-lasting side effects.	Consultant prescribing only	<ul style="list-style-type: none"> <li>• Add JAC special consideration 'Unlicensed Medicine – High risk'.</li> <li>• Enter batch number when receipting onto JAC</li> <li>• Quarantine and check against CofA/CofC. Formal release process.</li> <li>• Not permitted on ward top-up.</li> <li>• Consider QA / QC testing if required</li> <li>• Provide English SmPC/PIL. Must over-label in English</li> <li>• Enter patient name, H&amp;C Number &amp; consultant name when dispensing.</li> <li>• Declaration of use form completed for every request for each patient</li> <li>• Review use every year</li> </ul>



## Appendix 8

### How to obtain a further supply of your unlicensed medicine

You have been given a supply of:

(Affix copy of dispensing label or complete below)

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Currently, this medicine does not have a full U.K. or EU Marketing Authorisation. Medicines are often used without this authorisation. This can be for many reasons, for example:

- It is awaiting the granting of a U.K. or EU authorisation
- It is undergoing a clinical trial
- Usage of the product is low and therefore it is not economic for the makers to send the product for approval or it would be difficult to get enough patients to do a clinical trial
- It has been withdrawn from the U.K. market
- There is no suitable commercial formulation available

However, please be reassured that your doctor and pharmacist have thought very carefully about what is the best medicine for you. If you have any concerns regarding this medicine please contact your doctor.

### How to Obtain a Further Supply

If you require a further supply of this medicinal product please:

- *Go to your GP to obtain a prescription and take it to your local pharmacy (chemist) along with this leaflet.* You will probably need to give the pharmacist one or two weeks notice to obtain the supply for you, so it is important that you do not let your supply run out before going to the GP.
- Arrangements will be made for ongoing supplies by a hospital pharmacy.

## Appendix 9

### For Information only

#### **The use of licensed medicinal products for unlicensed indications (Off-label use).**

The use of licensed medicinal products for unlicensed indications (off-label use) is not covered by this policy. However in circumstances where this practice is known, medicinal products should be risked assessed in a similar manner to unlicensed medicinal products and subject to similar controls based on the outcome of that risk assessment.

'Off-label' medicines are medicines with a UK or EU marketing authorisation, which are prescribed for an unlicensed indication or via a different route, etc (i.e. out with the terms of the marketing authorisation).

It is recognised that the use of an off-label medicine is sometimes necessary in order to provide the optimum treatment for a patient. The use of medicines 'off-label' is often necessary and is common in many areas of medicine, for example palliative care, paediatrics, intensive care and psychiatry. The following information provides evidence of accepted practice within these specialties.

If a patient is harmed by such use of a medicine then the manufacturer is unlikely to be found liable, unless the harm is directly attributable to a defect in the medicine, rather than the way it was prescribed.

**Recommendations from bodies such as the General Medical Council and the Medical Defence Organisations place a duty on doctors to act responsibly, and to provide information to patients on the nature and associated risk of any treatment, including 'off-label' and unlicensed medicines.**

**'Off-label' use of medicines must be informed and guided by a respectable and responsible body of expert opinion. In relevant clinical areas guidance should be taken from expert guideline groups or reference material**

**Examples may be: (this is not exhaustive)**

**BNF for Children**

**Royal College of Paediatrics and Child Health (RCPCH) policy statement**

**Association for Palliative Medicines and The Pain Society, 2001 position statement**

**Palliative Care Formulary (PCF3)**

**Royal College of Psychiatrists consensus statement (CR142) on 'Use of licensed medicines for un-licensed applications in psychiatric practice (Jan 2007) ([www.rcpsych.ac.uk](http://www.rcpsych.ac.uk))**

**It is the responsibility of each HSC Trust to decide if they would advocate 'off-label' medicine use in accordance with recognised expert guidance and evidence based practice.**