Unlicensed and Off-label Medicines Policy

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2	November 2012		Approved	No change
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4	July 2021	Fatima Hafesji (Lead Pharmacist Tower Hamlets Community Health Service)	Approved via Chairs Action (Paul Gilluley); July 2021	Policy rewritten and renamed **'Unlicensed and off-label medicines policy'**. Policy restructured and reformatted into designated trust template. **Paragraph 1** Paragraph summarised. Removal of reference to central European legislation (mainly Directive 2001/83/EC).Emphasis on MHRA as sole medicine and appliance regulator in the UK. Addition of hyperlink to MHRA website. **Paragraph 2** Scope edited to include all staff involved in prescribing and administration of unlicensed and off-label medicines. **Paragraph 4** Changed to Definitions**.** Definitions updated to include definition of unlicensed medication **Paragraph 5** Changed to Unlicensed Medicines. Section updated to include extemporaneous preparation and imports. Addition of paragraph summarising unlicensed use of medicines in palliative care with reference link to Medusa Injectable guide.

				Paragraph 6 Title changed to off-label medicines. Section updated with examples of off-label prescribing and administration of these including those in the CHS setting. Reference to Appendix 3 for a list of commonly prescribed off-label medicines in ELFT. **Paragraph 7** Changed to 'Prescribing of Unlicensed and Off-Label medicines' **Paragraph 7.1** General Principles reworded and summarised. Addition of Figure 1 summarising factors affecting unlicensed and off-label prescribing decision making. Addition of Appendix 1 (Bolam & Bolitho test). **Paragraph 7.2** changed to 'Prescribing and unlicensed medicine'. Paragraph updated with opening statement to include relevance to other settings including CHS, prescribing in children. Change of reference of 'MH pharmacist' to 'designated service/ward pharmacist'. Removal of reference to ELFT Medicines Information Service. **Paragraph 7.3** Addition of new paragraph. Requesting an addition to the 'ELFT Approved Unlicensed Medicines List'. Reference to Appendix 4 - Request to use an Unlicensed Medicine Form **Paragraph 7.4** Addition of new paragraph summarising prescribing of off-label medicines. Reference to Appendix 3 - ELFT List of approved off-label medicines **Paragraph 7.5** Addition of New paragraph 'Non-medical prescribing of Unlicensed and off-label medicines' **Paragraph 8** Liabilities and Responsibilities – paragraph updated to include all prescribers i.e. including NMPs **Paragraph 8.1** updated to include statement on NMP prescribers and responsibility of prescribers to provide adequate information to nursing staff to facilitate safe administration of the unlicensed or off-label medicine. **Paragraph 8.2** Responsibilities of Pharmacy staff. Addition of referral to senior pharmacy team/medicines committee for further advice. Addition of providing sufficient reliable information to support safe administration of

				unlicensed medicines by nurses. Addition of requirement to record Batch numbers and expiry date of Unlicensed medicines prior to supply. **Paragraph 8.3** New addition. Responsibilities of nursing staff when administering Unlicensed or off-label medicines. **Paragraph 9** Addition of new paragraph. Continuation in primary care. **Paragraph 10** Addition of new paragraph. Recommendations for consent & documentation including reference to T2/T3 forms. **Paragraph 11** Addition of new paragraph detailing best practice for patient information. **Paragraph 12** Reporting of adverse drug reactions – Yellow card scheme. Paragraph 3.7 from previous policy renamed and moved to Paragraph 12. Subheading changed from *'3.7 availability of yellow cards'* to *'12. Reporting of adverse drug reactions – yellow card scheme'* Paragraphs 4.1 & 4.2 from previous policy deleted, moved & merged into paragraph 12. Addition of Yellow card reporting by HCPs and patients via Yellow card website. Addition **of** *'Coronavirus yellow card reporting'* **Paragraph 13** Existing references updated, addition of new references utilised to update this version of policy. **Appendix 1** New appendix. Addition of Bolam & Bolitho test. **Appendix 2** Update of PIL. Addition of title 'Patient Information Leaflet Unlicensed and "Off-label" medicine'. Addition of subsection on how to obtain further supplies of medication. Update of pharmacy contact details for queries or further information. **Appendix 3** List of approved off-label medicines, reviewed & updated. **Appendix 4** Title changed from' request to use a medicine without a UK marketing authorisation' to 'request to use an unlicensed medication form'

Contents

1. Introduction

The Medicines and Healthcare Products Regulatory Agency (MHRA) is the UK's standalone medicines and medical devices regulator. The manufacture, sale or supply of medicinal products is controlled by national legislation (Human Medicines Regulations 2012 [SI 2012/1916) [1].This ensures that the medicinal product is safe, effective and of appropriate quality. All medicinal products on the market must have a marketing authorisation. In the UK there are exemptions[1] from the regulations to allow for the supply of unlicensed medicinal products for individual patients:

- In response to an unsolicited order
- Manufactured and assembled according to specification of a person who is a doctor, dentist, nurse / pharmacist independent prescriber or a supplementary prescriber
- For use by individual patient to meet their special needs

A Marketing Authorisation (MA) is granted when the regulatory authority is satisfied that the drug in question has proven efficacy in the treatment of a specified condition, along with an acceptable side-effect profile, relative to the severity of the condition being treated and other available treatments.

The use of unlicensed and off label medicines is an area of potentially increased risk, since it means that the MHRA has not examined the risks or benefits of using these drugs for that particular indication. However, the use of unlicensed or off-label medicines is often necessary in many areas of healthcare, for example but not limited to psychiatry, palliative care and paediatrics.

2. Scope

This policy aims to describe the Trusts policy for the use of unlicensed medicines and also for "off-label" prescribing. It applies to all clinical staff involved in the prescribing and administration of these. The policy does not apply to clinical trial medicines.

3. Policy Statements

3.1. Where a licensed medicine is available, it should be considered before an unlicensed alternative to treat patients.

3.2. It is recognised that the use of an unlicensed or 'off-label' medicine is sometimes necessary in order to provide the optimum treatment for a patient.

3.3. In most cases, unlicensed medicines will only be authorised when no licensed medicine product is available. This is in the interests of public health.

3.4. The Trust will accept vicarious liability associated with the use of unlicensed medicines (or medicines used outside their licensed indications) provided there is evidence of compliance with this policy and associated procedures for the use of such medicines. The Trust Medicines Committee has the responsibility to manage the use of unlicensed medicines within the Trust.

3.5. Adverse drug reactions and medication incidents involving unlicensed and 'off-label' medicines should be reported in the same manner as for licensed medicines.

3.6 If a patient experiences an adverse drug reaction to a medicine, it should be documented in their notes and on their medicines chart. The doctor, pharmacist or nurse should complete a yellow card via the Yellow Card website.

4. Definitions

Licensed medicines are medicines with a UK marketing authorisation. When prescribed within the terms of the marketing authorisation the manufacturer is likely to be found liable for any harm caused by that medicine.

Off-label medicines are medicines with a UK marketing authorisation, which are prescribed outside the parameters of the relevant Summary of Product Characteristics (SmPC), in terms of indication, dosage, route, method of administration, or patient factors e.g. age, pregnancy, lactation. If a patient is harmed by the use of such 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 in the way in which it was prescribed.

Unlicensed medicines are normally referred to those medicines which do not have a Marketing Authorisation (MA) issued by the MHRA.

5. Unlicensed Medicines

Unlicensed medicines may include:

- Medicines prepared by a UK manufacturer but not for sale in the UK
- 'Specials' [2] i.e. a category of unlicensed medicines that are manufactured or procured under a 'specials' license specifically to meet the clinical needs of an individual patient
- Extemporaneous preparations where licensed medicines are mixed together forming an unlicensed preparation before being administered [18]
- Medicines undergoing clinical trial (note: this policy does not apply to clinical trials)
- Medicines awaiting a UK Marketing Authorisation
- Medicines withdrawn from the UK market, including those where marketing authorisation is suspended
- Medicines manufactured for export
- Medicines imported from another country e.g. Parallel imports Pirenzepine, Melperone.

For good clinical reasons, the use of such medicines is widespread in hospitals and were this practice curtailed, the treatment of many patients would be impeded. It is therefore important that all prescribers and pharmacists should be aware of the associated medico-legal implications.

An unlicensed medicinal product may only be supplied to meet the special needs of the individual patient. It should not be supplied where there is an equivalent licensed medicinal product which can adequately meet the needs of the patient.

Responsibility for deciding whether an individual patient has "special needs" which a licensed product cannot meet should be a matter for the prescriber responsible for the patient's care. Examples of "special needs" include an intolerance or allergy to a particular ingredient, or an inability to ingest solid oral dosage forms[1].

The term "special needs" is in reference to special clinical needs of the individual patient. It does not include cost, convenience or operational need. Where an unlicensed medicine is supplied, where an equivalent licensed product is available, the prescriber must be convinced of the need for the unlicensed medicinal product.

It is also important to consider the administration of unlicensed medicines particularly in settings such as palliative care where it is usual to mix two or more licensed medicines in a syringe driver before administration [3]. The MHRA states that mixing drugs together, where one is not a vehicle for the administration of the other, creates an unlicensed medicine [4]. In such circumstances nurses should refer to the Medusa Injectable Medicines Guide to determine compatibility of mixing licensed medicines for administration.

6. Off-Label Medicines

Off-label prescribing is where licensed medicines are prescribed outside of their marketing authorisation [6].

Although the MHRA does not recommend off label use of products, if the UK licensed product can meet the clinical need, even off-label, it should be used instead of an unlicensed product [1]. Licensed products available in the UK have been assessed for quality safety and efficacy.

The prescribing and administration of off-label medicines may be routine practice and widespread in certain specialities e.g. psychiatry [5], palliative care [3] paediatrics etc. but may not be so frequent in others.

Some common examples of off-label use of medicines include [1, 6]:

- Disorder: When a medicine is prescribed for an unlicensed indication e.g. Hyoscine hydrobromide tablets prescribed for Clozapine associated hypersalivation
- Demographic: When medicines are prescribed for a different patient group outside the terms of the marketing authorisation e.g. in children, pregnant or breastfeeding women
- Dosage: If prescribed at a higher dose than stated in the marketing authorisation e.g. Olanzapine prescribed in excess of the maximum licensed dose of 20 mg per day
- Route: If administered via a different route to that stated in the marketing authorisation
- Altered Formulation: When the formulation of a medicine has been altered, for example when crushing tablets or opening capsules for use via alternative routes e.g. enteral feeding tubes or where the form of a preparation has changed to add a medication to food/drink for covert administration[13] (Refer to the ELFT Covert Medicines policy [7] for further information)

The risks associated with some off-label medicine use may be due to poor evidence base or to the risk of adverse effects associated with the off-label treatment. Medications

whose off-label use is supported by evidence-based texts (e.g. BNF, BNF for Children, SIGN, NICE or BAP Guidelines etc.) are generally considered lower risk provided the prescribing information in that text is followed.

It would be impractical to highlight all cases of 'off-label' use particularly when it is simply the matter of route or dose being different from those in the manufacturer's Summary of Product Characteristics, however a list of some commonly prescribed 'off-label' medicines at ELFT can be found in **Appendix 3**.

7. Prescribing Unlicensed and 'Off-label' Medicines

7.1 General Principles

Prescribing a medicine within its marketing authorisation does not guarantee that the patient will come to no harm. Likewise, prescribing outside a marketing authorisation does not mean that the risk-benefit ratio is automatically adverse. Prescribing both Unlicensed and off label medicines confer extra responsibilities on prescribers [1] who will be expected to be able to show that they acted in accordance with a respected body of medical opinion (the Bolam test) and that their action was capable of withstanding logical analysis (the Bolitho test) [8] (**see Appendix 1**).

Figure 1[3] summarises the factors influencing rationality of prescribing decisions with regard to Unlicensed and 'Off-Label' medicines.

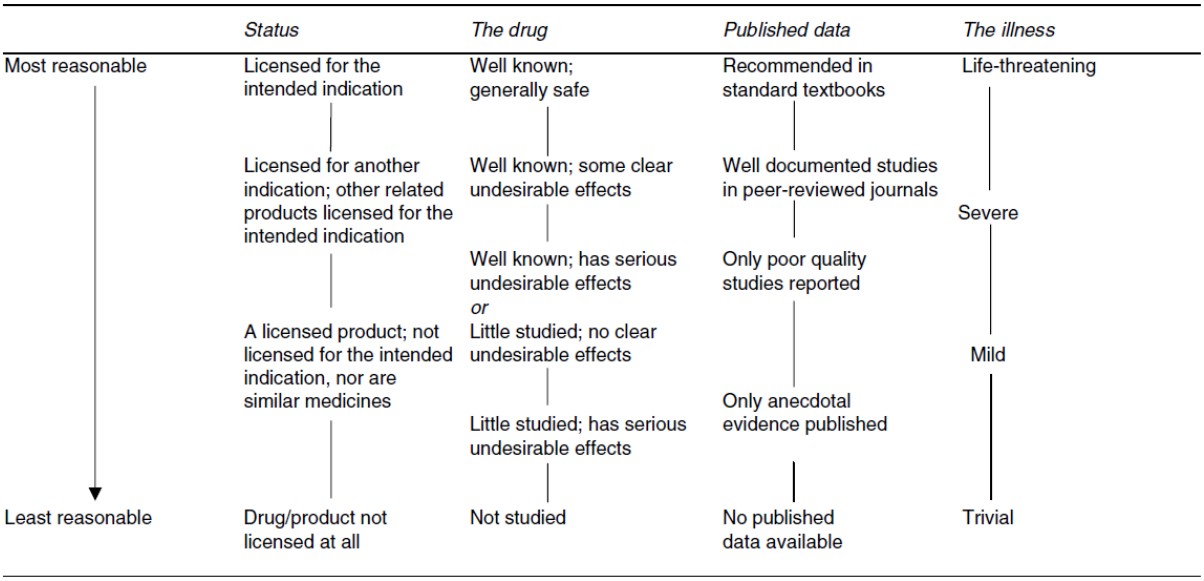

Figure 1 Factors influencing the reasonableness of prescribing decisions.

The responsibility that falls on healthcare professionals when prescribing an unlicensed medicine or a medicine "off-label" may be greater than when prescribing a licensed medicine within the terms of its licence. Prescribers should pay particular attention to the risks associated with using unlicensed medicines or using a licensed medicine "off-label". The recommendations from professional bodies summarised below should be considered by prescribers before prescribing Unlicensed or "off-Label" medicines [2, 5, 9, 10, 14]

Before prescribing an Unlicensed or 'Off-label' medicine

- Exclude licensed alternatives (ineffective or not tolerated).
- Ensure familiarity with the evidence base for the intended unlicensed use.
- If unsure, seek advice.
- Consider documenting the potential risks and benefits of the proposed treatment giving particular thought to vulnerable groups such as children and adolescents, women and girls of child-bearing potential, elderly patients, physically ill patients and patients with impaired insight and judgement. Share fully the anticipated benefits and potential risks of the proposed medication with the patient, and carers if applicable. Document the discussion and the patient's consent or lack of capacity to consent.
- If prescribing responsibility is to be shared with primary care, ensure that the risk assessment and consent issues are shared with the GP in writing.
- Discuss individual cases with the multidisciplinary team and document decisions made.
- Monitor for efficacy and side-effects.

Guidance on prescribing Unlicensed or 'Off-Label' medicines

- Although the MHRA does not recommend 'off-Label' (outside the licensed indications) use of products, if a UK licensed product can meet the clinical need, even off-label, it should be used instead of an unlicensed product[1]
- The rationale for prescribing an Unlicensed or 'off-label' medicine should be clearly documented in the patient records.
- Prescribe the medicine at a low dose and monitor effects carefully. If well tolerated but ineffective consider cautiously increasing the dose whilst carefully monitoring its effects
- The patient should be informed about the decision to prescribe an Unlicensed or off-label medicine. A patient information leaflet explaining the unlicensed use of medicines can be found in **Appendix 2**
- If the medicine has no beneficial effect or there are emerging risks and hazards which outweigh the benefits, withdraw it (best gradually) and document the reasons why it is being withdrawn. If there is a persistent need for further treatment with unlicensed medicines consider a wash-out period prior to introducing the next medicine.

7.2 Prescribing an Unlicensed medicine

It is accepted that the informed use of some unlicensed medicines or licensed medicines for unlicensed applications is sometimes necessary. Absence of a marketing authorisation does not necessarily indicate an absence of evidence for the proposed intervention.

A high percentage of medicines are not licensed for use in psychiatry however, it is accepted practice that unlicensed products are used when appropriate in this group of service users [5]. Similarly, unlicensed medicines are also prescribed for the treatment of physical health conditions but will normally be prescribed or authorised by a consultant or prescribing specialist who has the competence, specialist knowledge and expertise to do so in the relevant area.

The ELFT Approved Unlicensed Medicines List can be found below. This is not a comprehensive list of all unlicensed medicines prescribed but serves to summarise some of the commonly prescribed medicines used in the trust.

ELFT APPROVED UNLICENSED MEDICINES LIST		
Medicine	**Established Use**	**Further Information**
Pirenzepine	Clozapine-induced hypersalivation	Established Practice
Melperone	Treatment refractory schizophrenia	See Guidelines for The Use of Melperone.
Chloral Hydrate 500mg/5ml liquid	Insomnia (short term use)	Limited evidence. If indicated, consider chloral betaine which is both licensed and also available as tablets and liquid.
Diazepam 10mg/5ml liquid	Anxiety, rapid tranquillisation, alcohol withdrawal	Other licensed preparations should be used first line (2mg/5ml and 5mg/5ml). This preparation should only be used in the event of a supply problem.
Clozapine 100mg/5ml Suspension	Resistant Schizophrenia or patients unresponsive to conventional antipsychotics who are unable to take clozapine tablets	Established practice
Fluphenazine 1mg tablets	Schizophrenia and other psychoses	
Streptomycin 1g injection	Treatment of TB. Under microbiology recommendation.	
Mepacrine 100mg tablets	Rheumatoid Arthritis, other autoimmune disorders.	
Isoniazid 50mg/5ml liquid	Treatment or prophylaxis of TB in patients with swallowing problems	Established practice RMOC have issued recommendations[15] of standardised strengths to be used
Midazolam & Lidocaine intranasal	Procedural sedation used by dental services where IV Midazolam is unsuitable	Established practice
Procaine penicillin injection	Treatment of Syphillis	Benzathine penicillin used first line.
Sucralfate 1g tablets	Treatment of Benign gastric ulceration, Benign duodenal ulceration, Chronic Gastritis (see BNF)	Established practice

7.3 Requesting an addition to the 'ELFT Approved Unlicensed Medicines List'

If an ELFT consultant or prescriber requests an addition to the "ELFT Approved Unlicensed Medicines List" (See **Appendix 4** for the request form), this request should be supported by

a thorough review of the literature and a summary of the current evidence base for the request. The consultant may request the support of the ELFT pharmacist designated to the service/ward to prepare the review.

The Chief Pharmacist will be responsible for reviewing costs and determining whether the approval of an unlicensed indication for a licensed medicine represents a financial risk to the Trust.

The review will then be presented at the Medicines Committee for discussion. The Committee will then:

Recommend that the medicine be added to the "Approved Unlicensed Medicines list", thereby endorsing use across the Trust.

OR

Recommend that the medicine be added to the "Unlicensed Medicines" list, subject to compliance with a protocol or guideline approved by the Medicines Committee.

OR

Non-approval where the new medicine is not recommended to be used within the Trust.

7.4 Prescribing 'Off Label' Medicines

Medicines are frequently used "off label" in the mental health specialties [5] and there are a number of 'off-label' medicines in common usage within the Community Health Services particularly in palliative care [3]. The dosage, side-effects, monitoring etc. of these drugs for each indication will be well known to the prescriber and pharmacist and be documented in the patient's notes.

In the context of prescribing "off label" medicines in mental health, the psychopharmacology special interest group at the Royal College of Psychiatrists has published a consensus statement[5] on the use of licensed medicines for unlicensed uses. They note that unlicensed use is common in general adult psychiatry with cross sectional studies showing that up to 50% of patients are prescribed at least one drug outside the terms of its licence. They also note that the prevalence of this type of prescribing is likely to be higher in patients under the age of 18 or over 65, in those with a learning disability, in women who are pregnant or lactating and those in patients who are cared for in forensic psychiatry settings.

Examples of acceptable "off-label" prescribing of medicines outside their product licences can be found in **Appendix 3**.

7.5 Non-Medical Prescribing of Unlicensed and "Off Label" Medicines

Non-medical independent prescribers are permitted to prescribe unlicensed and "off-label" medicines within their competence and field of expertise where it is accepted clinical practice and has been agreed by the Trust Medicines Committee[11]. Supplementary prescribers may only prescribe an unlicensed medicine as part of a Clinical Management Plan. [11, 14]

All healthcare professionals who can prescribe as outlined above are subject to: their individual clinical competence; the professional codes and ethics of their statutory bodies; and ELFT prescribing policies. Refer to the ELFT Non-Medical Prescribing Policy [11] for further information and guidance.

8. Liabilities and Responsibilities

- A doctor may prescribe medication for any purpose for the treatment of their patients, however they may be called upon to justify their actions.
- All prescribers are professionally accountable [14] for this judgement and should satisfy themselves that they could obtain a professional body of support for their practice in relation to the unlicensed product.
- If a patient is harmed by a licensed medicine as a result of it being used for an unlicensed indication and not because of any defect in the product itself, then the prescriber is liable for the harm.
- If a patient is harmed by a defective medicine, whether licensed or unlicensed, then the supplier of that medicine is liable for the harm. If the supplier can identify the manufacturer of the medicine, then liability passes to the manufacturer. If the medicine has been prepared by or under the supervision of a pharmacist, then that pharmacist is liable for the harm, as the manufacturer of the medicine. If the medicine has been procured from a 'specials' manufacturer then the pharmacist who placed the order is considered in law to be the manufacturer and as such is liable.
- The Trust carries a liability for the actions of its employees and will accept liability for the use of unlicensed medicines or unlicensed uses of medicines provided, Trust procedures are adhered to.

8.1 Responsibilities of Prescribers

- A consultant must initiate all prescribing of unlicensed medicines.
- A NMP may only initiate an unlicensed or "off-label" medicine if this is within their professional and clinical scope of practice. [2,11]
- The prescriber is professionally accountable for this judgement.[14]
- The prescriber should advise the patient/ parent/carer that they are being treated with an unlicensed medicine. This should then be recorded in the patient's medical notes.
- The prescriber should advise nursing staff or administering staff of the unlicensed nature of the medication and provide appropriate information to allow safe administration.
- All other clinical staff involved in the treatment of the patient with the unlicensed /off- label medication should be:
    - Made aware of its status
    - Given information to administer and use the product safely
    - Informed of any potential problems and how to deal with them

8.2 Responsibilities of Pharmacy Staff

- The pharmacist must be satisfied that the need for the unlicensed medication is justified. If they feel that it is not then it is their professional responsibility not to supply and the matter escalated to senior management for further advice.

- Pharmacy staff will ensure that the supply of the unlicensed medication conforms to standard operating procedures for procurement, receiving and supplying of unlicensed medications.
- The pharmacist will ensure that sufficient information to support the safe and informed administration of the unlicensed medicine is provided to both nursing and medical teams. This may be by means of a summary of product characteristics/ medicine information leaflet or reputable literature where this is unavailable (translated where not written in English).
- Pharmacy staff will retain all documentation regarding the unlicensed medication for at least 5 years which includes expiry dates and batch numbers when booking in or dispensing.
- Pharmacy Staff should:

    - Inform the prescriber of licensed alternatives as they become available
    - Inform the prescriber of any serious problems with the unlicensed medicines as they occur
    - Report any defects in the product to the relevant lead pharmacist, purchasing lead or medicines management pharmacist.

8.3 Responsibilities of nursing staff

- To question the prescriber or pharmacist if an instruction to administer a medicine is thought to be outside the terms of a product licence with regard to its dose, route of administration or other aspect and this has not been previously clarified.
- To request further information from the pharmacist or prescriber to support the safe administration of the unlicensed or “off-label” medicine where required.
- To satisfy themselves that the medicine may be administered safely and wherever possible there is acceptable evidence for the intended use of the unlicensed medicine.

9. Continuation in Primary Care [2]

General practitioners (GPs) are typically involved in the continuing care of outpatient service users who have been discharged to primary care.

Where it is intended that either unlicensed or “off label” treatment will be continued after patient discharge, the GP should be made aware of the unlicensed or “off-label” use of the medicine and informed of the risks and benefits of treatment. The full agreement of the GP should be sought before transfer of clinical responsibility.

The primary care team may not be familiar with the use of the agent at all, or not in the setting for which it is being used. Unless adequate information is supplied to the primary care team, errors in dosing, response, assessment etc. can be made, particularly where medicines are used “off label” as, although information will be readily available from sources such as the BNF it may not be applicable to the current setting.

Where initiation of treatment with an unlicensed or “off label” medicine occurs in an ELFT setting, the consultant/prescriber recommending the medicine is responsible for ensuring that clear arrangements have been agreed between primary and secondary care regarding clinical, prescribing and dispensing responsibilities prior to discharge of the service user.

GPs may refuse to prescribe within primary care if they have not been given sufficient information to prescribe safely or that this is outside their level of expertise.

Overall the prescriber should take responsibility for prescribing the medicine, informing the service user (or carers), overseeing treatment, monitoring and any follow up treatment, or liaising with GPs as appropriate.

The responsible clinician/prescriber who has initiated treatment with the unlicensed or "off label" medicine is responsible for ensuring that the relevant GP is given sufficient information about the medicine. The following information should be provided:

- Name of Drug
- Dose and formulation
- Licensed status of drug
- Reason for prescribing
- Monitoring requirements if any
- Duration of treatment
- Common side effects

10. Consent and Documentation

Good record-keeping and documentation is fundamental to all prescribing practice. When prescribing is off-label or unlicensed, it is even more important to document the rationale for treatment, the evidence-base where appropriate, record the key elements of discussion with the patient and/or carer and consider ongoing review of the treatment.

Unlicensed medicines can be included in a treatment plan when a patient lacks capacity and is sectioned under the Mental Health Act 1983. Consent to Treatment forms T2, T3 and Section 62 must be completed in the normal way. The indication should be recorded on the form in accordance with best practice [16].

11. Patient Information

Individual patients should be given information **(Appendix 2)** that meets their needs about relevant unlicensed medicines. This should be documented in patient notes.

Best practice for communication includes [10]:

- To give patients, or those authorising treatment on their behalf, sufficient information about the proposed treatment, including known serious or common adverse reactions, to enable them to make an informed decision
- Where current practice supports the use of a medicine outside the terms of its license, it may not be necessary to draw attention to the license when seeking consent. However, it is good practice to give as much information as patients or carers require or which they may see as relevant
- To explain the reasons for prescribing a medicine off-label or prescribing an unlicensed medicine where there is little evidence to support its use, or where the use of a medicine is innovative

12. Reporting of Adverse drug reactions – Yellow Card Scheme

The Yellow Card Scheme is the UK system for collecting and monitoring information on suspected safety concerns or incidents involving medicines and medical devices [17]. The Scheme is run by the MHRA and currently relies on voluntary reporting of suspected ADRs by health professionals and patients. The purpose of the Scheme is to provide an early warning that the safety of a product may require further investigation. Reports can be made for all medicines & appliances including unlicensed medicines.

Healthcare professionals and patients are encouraged to report adverse reactions relating to the use of unlicensed medicines via the Yellow Card website. This remains the same process for both healthcare professionals and patients.

Coronavirus Yellow Card Reporting

Adverse drug reactions relating to the use of unlicensed medication to treat or due to Coronavirus should be reported via the Coronavirus Yellow Card Reporting Site

13. References

1) MHRA Guidance Note 14: The supply of unlicensed medicinal products ("specials) Medicines and Healthcare Products Regulatory Agency, 2014. (Accessed September 2020)

2) Prescribing Specials: Guidance for the prescribers of Specials. Professional Standards. April 2016 Royal Pharmaceutical Society of Great Britain (Accessed March 2021)

3) Palliative Care Guidelines – Off label Drug Use (Accessed April 2021)

4) MHRA Drug Safety Update. Medical and non-medical prescribing: mixing medicines in clinical practice. Gov.uk. (Accessed March 2021)

5) The use of licensed medicines for unlicensed applications in psychiatric practice (CR210) – Royal College of Psychiatrists, Psychopharmacology Committee 2nd Edition Dec 2017 (Accessed February 2021)

6) Evidence summaries: unlicensed and off-label medicines – Integrated process statement. Process and Methods. Published May 2013. (Accessed March 2021)

7) East London Foundation Trust. Covert Administration of Medicines Policy. September 2018. (Accessed March 2021)

8) Bolam and Bolitho Tests: How The Bolitho Test Changed the Understanding of Medical Negligence (Accessed February 2021)

9) Good practice in prescribing and managing medicines and devices (2013) General Medical Council (Accessed September 2020)

10) MHRA Off-label or unlicensed use of medicines: prescribers' responsibilities – Drug Safety Update. Gov.uk. December 2014. (Accessed March 2021)

11) East London Foundation Trust, Non-Medical Prescribing Policy. Version 7. March 2020. (Accessed February 2021)

12) Non-Medical Prescribing; BNF Online (Accessed February 2021)

13) What legal and pharmaceutical issues should be considered when administering medicines covertly? Specialist Pharmacy Service Q&A: 23/02/2017

14) A Competency Framework for all Prescribers. Royal Pharmaceutical Society of Great Britain. July 2016. (Accessed March 2021)

15) NHS England Regional Medicines Optimisation Committee (RMOC) statement on TB standardisation of TB products, February 2018. (Accessed February 2021)

16) ELFT Mental Health Law Office via email (March 2021)

17) MHRA Yellow Card Scheme website. (Accessed September 2020)

18) The use of Unlicensed and Off-label Medicines Policy. Solent NHS trust. (Accessed February 2021)

Appendix 1

Bolam & Bolitho test [7]

The Bolam test establishes whether a medical professional has breached their duty of care which could lead to a clinical negligence claim. By **law**, any doctor, nurse, anaesthetist or other medical professional must provide a reasonable standard of care while going about their duties. This is known as a duty of care.

In 1957, The Bolam Test had stipulated that no doctor can be found guilty of negligence if they are deemed to have acted "in accordance with a responsible body of medical opinion."

The Bolitho Test, which resulted from the 1996 court case of *Bolitho v City and Hackney HA*, is an amendment to the Bolam Test, one of the most important rulings with regard to medical negligence. The Bolitho Test helped to clarify what was meant by "a responsible body," in the Bolitho test, defining it as one whose opinion had a "logical basis."

Combined together, the Bolam Test and the Bolitho Test make up the twin pillars of all assessments of medical negligence. They state that a doctor is not negligent if he or she acts in accordance with a responsible body of medical opinion, *provided that the Court finds such an opinion to be logical*.

Appendix 2

Patient Information Leaflet
Unlicensed and "Off-label" medicines

This leaflet is about the information you get with your medicines

Please read it carefully

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

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

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

Why have I been given this leaflet?
It is often necessary for doctors or clinicians to prescribe medicines for use that is not in the license. This is true for a lot of medicines used for children or in special circumstances, or as part of a clinical trial.

If you are given this leaflet it is because you have been prescribed medicine for use outside of its license.

Is it safe?
All medicines prescribed by a doctor or clinician in East London NHS Foundation Trust whether licensed or not, have been approved by the Medicines Committee. Also, your doctor or clinician will have carefully thought about the best care for you. Even if the medicine is used outside the license, we make sure there is good evidence of the benefits and you can be sure that any other similar doctor would also prescribe it.

How do I obtain more supplies of this unlicensed medicine?
If you need to continue with this medicine after your first few prescriptions, your hospital doctor or clinician may ask your GP to prescribe it for you. Your GP may then give you a prescription which you will need to take to your community pharmacist or chemist to get your medicine. If your GP is unable to do this for any reason, or if the pharmacist is unable to get hold of the unlicensed medicine, please contact your doctor or clinician who initiated the medicine to obtain further supplies.

What if I have more Questions?

If you have any worries or concerns about any

- Medicine, or
- Information you have been given with the medicine
- Are confused or not sure about any information or directions you have been given
- Just want more information

Your doctor, clinician or pharmacist will be happy to help and will be pleased to answer your questions.

Contact details for the Pharmacy teams in each area are:

City and Hackney centre for mental health: elft.pharmacycityandhackney@nhs.net
Newham centre for mental health: elft.pharmacynewham@nhs.net
Tower Hamlets centre for mental health & Tower Hamlets Community Health Service: elft.pharmacytowerhamlets@nhs.net
Luton and Bedford centres for mental health: elft.pharmacyluton@nhs.net
Community Health Bedford: elft.pharmacybchs@nhs.net
Community Health Newham: elft.pharmacychs@nhs.net

Appendix 3

ELFT List of approved off-label medicines

The table below provides examples of common unlicensed uses of drugs within the Trust. These examples would all fulfil the Bolam and Bolitho criteria in principle. An exhaustive list of unlicensed uses is impossible to prepare as:

- The evidence base is constantly changing.
- The expertise and experience of prescribers varies.

A strategy may be justified in the hands of a specialist in psychopharmacology based in a tertiary referral centre but be much more difficult to justify if initiated by someone with a special interest in psychotherapy who rarely prescribes.

ELFT Approved Off-Label Medicines		
Drug / Drug Group	**Established Unlicensed or 'Off Label' Use(s)**	**Further Information**
Second generation antipsychotics	Psychotic illness other than schizophrenia	Licences vary. All are licensed
Clonidine	ADHD in children	Limited evidence
Cyproheptadine	Akathisia	Some evidence
Methylphenidate	ADHD in children under 6 years	Established practice
Naltrexone	Self-injurious behaviour in people with learning disabilities	Limited evidence
Sodium valproate	Treatment and prophylaxis of bipolar disorder	Established practice
First and Second Generation Antipsychotics	Use in those less than 18 years of age	Limited evidence.
Mood stabilisers	Use in those less than 18 years of age	Limited evidence.
Clonazepam 0.5mg/5ml and 2mg/5ml liquid	Anxiety and rapid tranquillisation in psychiatry	Established practice
Clonazepam 0.5mg and 2mg tablets	Anxiety and rapid tranquillisation in psychiatry	Established practice
Midazolam 2.5mg/ml liquid	Anxiety, rapid tranquillisation where other benzodiazepines not appropriate or available	Established practice
Probenecid 500mg tablets	Treatment of Gonococcal infections	Used by Sexual Health and BBV team.
Atropine 1% minims/eye drops	Used as an adjunct, administered sublingually for clozapine related hyper salivation	Some evidence

Appendix 4

Request to Use an Unlicensed Medicine Form

This form must be completed by a consultant wishing to use an unlicensed product without UK marketing authorisation or an unlicensed indication for an existing product. Supporting literature is required to be attached to support the request. Failure to supply references may delay processing of the request whilst references are being obtained.

Patient Name:	
DOB	
Hospital Number:	
Ward/Unit	
Directorate	
Diagnosis	
Medicine Details **Drug and preparation requested (including strength, and formulation)** **Clinical indication for use** **Dosage (including strength and frequency)** **Intended Duration**	
What treatment would have previously been used for this condition?	
What is the reason for preferred use of the named product? **If discharged how will the patient obtain further supplies?**	

The manufacturer is only likely to be found liable if harm results from a defect in the product. The manufacturer carries no legal liability for use of medicines without a UK license. This puts greater responsibility on individual prescribers and the Trust. The ultimate responsibility for prescribing any drug lies with the doctor who signs the prescription and is professionally accountable for his/her judgement. Doctors have a duty in common law to take reasonable care and to act in a way consistent with practice of a responsible body of their peers of similar professional standing. If use of this product is deemed to have significant risks, the request will be referred to the Medical Director.

The purpose of this policy is to provide an internal means of assessing the use of these products, thereby safeguarding patients against the risk of injury as well as minimising the likelihood of claims against the Trust.

Declaration by Consultant

1. I have read the above and understand that the product which will be supplied will be used as a medicine without a UK license.

2. I am registering my wish to use this product for the reasons detailed above and will await confirmation from the Pharmacy Department prior to prescribing it.

3. I accept responsibility for fully informing the patient/carers of the fact the prescribed medicine is currently unlicensed in the UK. If deemed to have significant risks, the request will be referred to the Medical Director.

4. I will initiate each prescription for a patient and obtain their consent.

5. Providing the above has been undertaken, I understand that this prescription and its consequence will be covered for vicarious liability under terms of my contract with the Trust.

6. The use of an unlicensed medicine has been discussed with the patient/carer and information has been provided regarding this e.g. Trust Unlicensed and Off Label PIL.

Consultant Name:	
Email address	
Signature:	
Date:	
Directorate:	

The completed form must be sent to the Senior or Lead Pharmacist at the respective locality.