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Guidance on Unlicensed and Off-Label Use of Medicines

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Overarching policy: Medicines Overarching Framework

Contents

1 Introduction

The Medicines and Healthcare Products Regulatory Agency (MHRA) grant marketing authorisations ("product licences") for medicines in the UK. To be granted a marketing authorisation (MA), medicines must meet minimum standards of safety, quality and efficacy. The authorisation covers all the main activities associated with the marketing of a medicinal product. No medicinal product may be marketed and promoted within the UK unless it has a marketing authorisation.

Manufacturers of medicines may limit the parameters of their marketing authorisation for commercial reasons, where the costs of the necessary testing (clinical trials), licensing or production are likely to exceed the financial return. It is possible that the MA of equivalent products, containing the same medicine but from different manufacturers will differ due to commercial decisions made by an individual manufacturer.

The use of unlicensed medicines, or off-label use of licensed medicines, is often necessary in many areas of healthcare, for example paediatrics, palliative care and psychiatry. This practice is legally covered through the provision of exemptions which allow practitioners to prescribe, and pharmacists to order, dispense, manufacture and assemble such medicines when needed. However, should any untoward incident occur, legal liability will rest with the practitioner or the organisation that employs them.

The vast majority of medicines used within Tees, Esk and Wear Valleys NHS Foundation Trust have an appropriate marketing authorisation, and they are usually used within the parameters of that authorisation. However there are occasions when the treatment of a patient requires:

- Use of a medicine that does not have a marketing authorisation (**unlicensed medicine)**
- Use of a medicine that has a marketing authorisation but for an indication (condition), at a dose, via a route or for a patient category (e.g. age) that is not listed in the Summary of Product Characteristics for that medicine (**off-label use**)
- A change to the formulation of a licensed medicine to allow administration by a method that is not described in the Summary of Patient Characteristic, e.g. crushing tablets and/or dissolving them in water to enable administration via an enteral tube or mixing with food / drink to facilitate covert administration (**off-label use**)
- Use of a medicine that has been temporarily exposed to temperatures above the maximum storage temperature advised in the product information, which could be considered by the manufacturer as outside their MA (**off-label use)**

This guidance applies to any of the above circumstances.

Recommendations from bodies such as the General Medical Council and medical defence organisations place a duty on doctors and other prescribers to act responsibly, and to choose treatment in partnership with patients/carers. To support decision-making they must provide information to patients or carers on the nature of and risk associated with any treatment, including information about unlicensed and off-label medicines when their use is deemed necessary. Informed consent for any treatment should be obtained whenever possible. The provision of information and patient/carer consent should be recorded in the patient record.

2 Why we need this guidance

The Trust recognises that there will be occasions when the prescribing and/or administration of a medicine without a marketing authorisation (unlicensed) or outside the parameters of its marketing authorisation (off-label) is necessary. This document sets out guidelines to be followed to minimise the risks associated with such practice, whilst optimising the availability of potentially effective treatments to patients.

2.1 Purpose

This guidance provides a framework for the prescribing and/or administration of medicines which do not have a marketing authorisation or are being used outside the terms of the marketing authorisation.

2.2 Objectives

The objectives of this guidance are:

- To ensure good practice in decision-making around treatment choice in conjunction with parents and carers;
- To allow use of unlicensed or off-label medicines in line with recognised clinical practice and/or published evidence;
- To minimise risk associated with unlicensed and off-label use of medicines.
- To define the unlicensed medicines and off-label use of medicines that are approved by the Trust;
- To describe the procedure to seek approval for use of an unlicensed medicine or off-label use of a medicine, for general or patient-specific purposes, when such approval is not already in place.

3 Scope

This guidance applies to the prescribing and/or administration of medicines which do not have a marketing authorisation (unlicensed) or are being used outside the terms of the marketing authorisation (off-label).

3.1 Who this guidance applies to

All clinical staff who are involved in the prescribing, supply and administration of medicines within the Trust

3.2 Roles and responsibilities

Role	Responsibility
Chief Pharmacist / Deputy Chief Pharmacist	• To publish the guidance on InTouch and raise awareness via pharmacy communications • To update the specialty registers in line with approved applications
Associate Medical Directors / Group Medical Directors	• To raise awareness of this guidance within their area of responsibility
Medical & Non-medical Prescribers	• To follow best practice as set out by the relevant professional body when prescribing unlicensed or off-label medicines • To prescribe unlicensed / off-label medicines in line with this guidance whenever possible • To inform patients when an unlicensed or off-label medicine is required for their needs and to seek and record their consent
Clinical Pharmacy Team	• To identify unlicensed / off-label prescribing in inpatient settings and annotate prescription charts accordingly • To support prescribers and nursing staff in following this guidance
Nursing staff	• To administer unlicensed / off-label medicines with the patient's informed consent against a patient-specific prescription (NMC Standard 22)

4 Guidance

4.1 Professional body guidance

The Trust endorses the following guidance from professional bodies in relation to prescribing and administration of unlicensed medicines, or medicines off-label:

Guidance from the General Medical Council (2013) - prescribing unlicensed medicines

When prescribing an unlicensed medicine, or prescribing a medicine outside the terms of its UK licence, prescribers must:

a) be satisfied that there is sufficient evidence or experience of using the medicine to demonstrate its safety and efficacy

b) take responsibility for prescribing the medicine and for overseeing the patient's care, monitoring, and any follow up treatment, or ensure that arrangements are made for another suitable doctor to do so

c) make a clear, accurate and legible record of all medicines prescribed and, where you are not following common practice, your reasons for prescribing an unlicensed medicine.

Royal College of Psychiatrists (2017) - Use of licensed medicines for unlicensed applications in psychiatric practice (2nd Edition, CR210)

1. First check that medicines with a product licence (marketing authorisation) for the particular indication have either had an adequate therapeutic trial or have been considered carefully, but excluded on clinical grounds (such as treatment contraindications and risk of drug-drug interactions).
2. Become familiar and be satisfied with the evidence base for the proposed pharmacological intervention, including its probable effectiveness, treatment-emergent adverse effects, and drug interactions
3. Get the advice of another prescribing clinician (and possibly a specialist pharmacist) with greater experience or expertise if the medicine to be used does not have an extensive evidence base to support its use for the proposed indication, or if you have particular concerns, or if you feel insufficiently expert in this field.
4. Consider the anticipated risks and benefits of treatment, giving particular thought to vulnerable groups such as children and adolescents, women of child-bearing age, elderly patients, physically ill patients and patients with impaired insight and judgement; and document your thoughts on the likely balance of risk and benefit.
5. Explain fully the anticipated benefits and potential risks of the proposed medication to the patient (and if possible their relative or partner) stating that the medicine will be used outside the restricted terms of its product licence and make a record of this explanation.
6. In a situation where prescribing an unlicensed medicine is supported by authoritative guidance, describe in general terms why the medicine is not licensed for the proposed indication, but if you intend to prescribe an unlicensed medicine where that is not routine, provide the patient with a more detailed explanation.
7. Record the agreement of the patient to the proposed intervention. If the patient is unable to provide consent to a necessary treatment, document that it has not been possible to obtain formal consent.
8. Start the medicine at a low dose and monitor its effects carefully. If it is well tolerated but not effective, give thought to cautiously increasing the dose, with further careful monitoring of its effects.

9. Tell other health professionals involved in the care of the patient that the medicine is being prescribed outside the terms of its licence and encourage them to discuss their observations of its beneficial and untoward effects.
10. If the medicine has no beneficial effects or the emergent risks and hazards outweigh the benefits, withdraw it (generally, best done gradually) and document the reasons why it is being withdrawn. If there is a persistent need for further treatment, consider possible alternatives (using the process described above) and after a suitable 'wash out' cautiously introduce the next medicine.

Nursing & Midwifery Council – standards of proficiency for nurse and midwife prescribers

Practice standard 18 – Prescribing medicines for use outside the terms of their licence (off-label)

1. Off-label prescribing is where licensed medications are prescribed outside of their licence. There are a number of circumstances in which nurses may prescribe licensed medicines for the purposes for which they are not licensed (this is most likely to be the case when prescribing for children, see the Guidance below). It is possible under current legislation for nurse or midwife independent/supplementary prescribers to prescribe off-label as independent prescribers. However in order to do so you must ensure the following conditions are met:

   a) You are satisfied that it would better serve the patient/client's needs than an appropriately licensed alternative

   b) You are satisfied that there is a sufficient evidence base and/or experience of using the medicine to demonstrate its safety and efficacy. Where the manufacturer's information is of limited help, the necessary information must be sought from another source

   c) You should explain to the patient/client, or parent/carer, in broad terms, the reasons why medicines are not licensed for their proposed use (see the Guidance below)

   d) You make a clear, accurate, and legible record of all medicines prescribed and the reasons for prescribing an 'off-label' medicine

2. You may also, as a supplementary prescriber, prescribe a medicine for use outside the terms of its licence providing:

   a) There is a clinical management plan in place, written in conjunction with the doctor/dentist and in voluntary partnership with the patient/client or parent/carer

   b) A doctor/dentist takes responsibility for prescribing the medicine and you jointly oversee the patient/clients care, monitor and ensure any follow-up treatment is given as required

4.2 Approved medicines

The Trust supports the use of unlicensed or off-label medicines provided:

- The use is in accordance with a responsible body of professional opinion in the appropriate specialty. This includes recommendations made by the National Institute for Health & Care Excellence (NICE) and in the BNF or BNF for Children.
- The use is in accordance with evidence-based practice where available
- The use is necessary for the specific clinical needs of the individual patient, e.g. the administration of licensed liquid/dispersible medicines considered suitable for administration via NG, NJ or PEG tubes; or covert administration.

The Trust also approves the use of medicines that have been temporarily exposed to temperatures above the maximum storage temperature advised in the manufacturer's product information (SPC), where a risk: benefit assessment and an appropriate adjustment of the expiry date of the medicine has been completed by the Trust pharmacy team.

The Trust Pharmacy team, in conjunction with the Drug and Therapeutics Committee, will maintain a register of unlicensed medicines or off-label uses of medicines which have been approved in each patient group (see appendix 2). This register will be updated as and when applications are approved by the D&T committee and approvals for each specialty will be fully reviewed by specialty leads as part of the overall review of this guidance.

4.3 Applications for a new unlicensed or off-label medicine

Applications for specific individual patients

Any prescriber who wishes to use an unlicensed medicine or a medicine off-label which does not appear on the approved register, must apply for approval to do so from their Associate Medical Director / Group Medical Director using the Trust single application form. Prescribing must not commence for that patient until approval has been granted. . The Pharmacy team will maintain a log of applications (approved or rejected) and report this to the Drug & Therapeutics Committee intermittently (at least every 6 months).

Applications for general approval

Any Consultant, Associate Specialist or Consultant Non-Medical Prescriber may, at any time, apply to the Drug & Therapeutics Committee for an unlicensed medicine or off-label use of a medicine to be approved and added to the approved register for "general" use, i.e. removing the need for AMD / GMD approval for each individual patient. Applications must be submitted on the single application form (with patient-specific information and responses left blank)

In considering applications, the D&T committee will need the following information (outlined in the application form):

- The name of the medicine (and the form if this is the unlicensed element)
- The unlicensed indication/condition the medicine be prescribed for
- A summary of clinical evidence and/or expert opinion to support its use for this indication
- The benefits offered by the medicine over licensed alternatives (where they exist)
- Any additional costs associated with using the unlicensed medicine

Approval will be granted if the Committee is satisfied that the medicine is effective and necessary for patient care, and that every reasonable precaution will be taken to safeguard patients. If approved the medicine will be added to the register for the appropriate specialties and the applicant and all other prescribers in the relevant specialties will be notified. The medicine may then be prescribed for any patient in whom it is considered appropriate by any competent prescriber (without the need for any further approval).

Exemptions

- Clinical Trials - a marketing authorisation is not required for the sale, supply, manufacture or assembly of a medicinal product for the purpose of a clinical trial. Therefore, providing the clinical trial has been approved by the Ethical Committee, approval to prescribe is not required.
- "Specials" which do not have a marketing authorisation but have been recommended by a specialist for a specific patient need, e.g. compound topical preparations recommended by a dermatologist.

4.4 Patient Consent and Information

A patient must be informed if an unlicensed medicine or off-label use of a medicine is being considered for their treatment. They must provide consent to such treatment before it is prescribed and their consent must be recorded in the electronic patient record using the template in appendix 3.

An appropriate Patient Information Leaflet (PIL) must be supplied to the patient with their dispensed medication. The manufacturer's PIL only contains information relating to the marketing authorisation, and therefore licensed use, of the medicine. This may cause misunderstanding and poor concordance with treatment if the medicine is being used off-label. Therefore, patients should be counselled on the difference between their treatment and the information contained in the manufacturer's leaflet, and should be provided with a leaflet specific to the off-label use of the medicine, such as those on the Choice & Medication website. Choice & Medication also provides "handy fact sheets" on unlicensed medicines and unlicensed uses of licensed medicines to support discussions with patients and carers.

4.5 Procurement

All medicines without a marketing authorisation approved as above, will be purchased by the Pharmacy from manufacturers who either: -

- Hold a UK manufacturers licence, or
- Manufacture the products according to EU Council Directive 65/65/EEC and SI 1994 No. 3144.

To provide some guarantee of the quality of the product, a certificate of analysis will be requested for all such products, and this will be monitored and retained by the Pharmacy.

4.6 Liability

The Trust recognises that there will be occasions when the prescribing of a medicine without a marketing authorisation is necessary for the treatment of patients. Providing this policy has been followed, the Trust accepts liability for any untoward incident that might occur as a result of the prescribing, supply or administration of a medicine without a marketing authorisation or outside the parameters of its marketing authorisation.

4.7 Transfer of prescribing

- Medicines highlighted in RED in the appendices are considered unsuitable for transfer of prescribing and requests should not be made to GPs to take on prescribing of these medicines. Prescribing (and monitoring) responsibility should remain with the Trust prescriber
- If a medicine is considered suitable for transfer, GP's should be informed within the request that the medicine is unlicensed or being used outside its marketing authorisation, using the following wording:

  Please be aware that (insert name) is prescribed an unlicensed / off label medicine. This has been discussed with the patient (and/or carer). If you are not happy to accept prescribing responsibility, please contact the consultant's secretary within (insert response time) working days, to enable this prescribing to be retained by the Trust, and arrangements to be made with the patient/carer regarding further supplies.
- The transfer request should provide a clear rationale for using the unlicensed or off-label medicine, including reference to relevant clinical evidence or guidelines (e.g. NICE).The reasons for excluding licensed alternatives should be explained.
- Transfer of prescribing should only be requested once patients have shown a response to and are stabilised on the medicine.
- There may be situations when the GP may not wish to accept prescribing responsibility for an unlicensed or off-label use of a medicine, in which case the patient should continue to be seen by specialist services and continuity of prescribing will be retained in secondary care.

5 Definitions

Term	Definition
Marketing authorisation (MA)	By law, before a medicine can be placed on the market, it must be given a marketing authorisation (product licence) by a medicines regulator. The UK regulator is the Medicines and Healthcare products Regulatory Agency (MHRA)
Unlicensed medicine	A medicine that does not have a marketing authorisation
Off-label	Use of a medicine outside the parameters of the relevant Summary of Product Characteristics, in terms of indication, dosage, route or method of administration, or patient factors (e.g. age)
Summary of Product Characteristics (SPC)	A specific document required before any medicinal product is authorised for marketing. It defines the indications, dosage, cautions, contra-indications, side effects and storage requirements under which the medicine is marketed.
Patient Information Leaflet (PIL)	A leaflet which provides information to a patient about the medicine they are taking. This could be the leaflet provided with the medicine by the manufacturer, and/or a leaflet from the Trust-approved source of PILs.
Choice and Medication	The Trust-approved source of patient information leaflets for psychotropic medication. Leaflets are available in different formats and many languages, and where relevant, cover the off-label use of medicines.
Covert administration	Covert administration involves the administration of a medicine disguised in food or drink to a patient without their knowledge or consent. It should only be considered, within a legal framework, for patients who are deemed to lack capacity, consistently refuse medication and it is deemed in their best interests to receive the medicine.

6 Related documents

- Medicines Overarching Framework
- Safe Transfer of Prescribing Guidance
- Covert administration of medicines SPD
- Nasogastric tube feeding procedure
- Single application form

7 How this guidance will be implemented

- This guidance will be published on the Trust's intranet and external website.
- Publication of this guidance will be notified to Trust staff in the Pharmacy Newsletter
- Line managers will disseminate this guidance to all Trust employees through a line management briefing.

7.1 Training needs analysis

Staff/Professional Group	Type of Training	Duration	Frequency of Training
All Trust staff	Communication of updated guidance via Pharmacy communications		Once only

8 How the implementation of this guidance will be monitored

Auditable Standard/Key Performance Indicators		Frequency/Method/Person Responsible	Where results and any Associate Action Plan will be reported to, implemented and monitored; (this will usually be via the relevant Governance Group).
1	This will be added to the Pharmacy topic list for potential audit and will be considered for addition to future pharmacy audit programmes		

9 References

- Electronic Medicines Compendium - https://www.medicines.org.uk/emc/
- General Medical Council (2013) – guidance on prescribing unlicensed medicines
- Royal College of Psychiatrists (2017) - Use of licensed medicines for unlicensed applications in psychiatric practice (2nd Edition, CR210))
- Nursing & Midwifery Council – standards of proficiency for nurse and midwife prescribers
  Practice standard 18 – Prescribing medicines for use outside the terms of their licence (off-label)

10 Document control (external)

To be recorded on the policy register by Policy Coordinator

Date of approval:	24th March 2022	
Next review date:	31 December 2024	
This document replaces:	V8.1	
This document was approved by:	Name of committee/group	Date
	Drug and Therapeutics Committee	24th March 2022
This document was ratified by:	Name of committee/group	Date
	n/a	
An equality analysis was completed on this document on:	yes – 28 May 2021	
Document type	Public	

Change record

Version	Date	Amendment details	Status
7	23rd March 17	Complete review and update. New specialty registers incorporated	Superseded
7.1	28th September 17	Clonazepam added to AMH approved list (appendix 2)	Superseded
7.2	8th August 18	Added statements re. use of medicines exposed to temperatures above SPC storage requirements; amended criteria for off-label use of clonazepam in AMH register (appendix 2)	Superseded
7.3	23rd May 19	Ketamine added to AMH approved list (app 2)	Superseded
7.4	26th September 2019	Appendix 2 – added: Only following effective use as part of the PAXBD trial: pramipexole for treatment-resistant bipolar depression Where there are supply / availability issues associated with prazosin: Doxazosin for PTSD	Superseded
8	28th May 2020	Full review and update Specialty registers of approved treatments combined into single register.	Superseded.
8.1	22nd July 2021	Addition of aripiprazole for weight gain with clozapine/olanzapine to appendix 2 Aripiprazole for raised prolactin approved in MHSOP services	Superseded
8.2	24th March 2022	Amendments to appendix 2 relating to off-label use of medicines in CYPS: <u>Removed</u>: • Amitriptyline for ADHD <u>Added:</u>	Published

		• CNS stimulants + guanfacine combination for ADHD • Mirtazapine for depression <u>Changed:</u> • Fluoxetine approved up to 40 mg daily for anxiety and depression • Tics added to approved indication for clonidine Hyperlink to new single application form updated "Clinical Director" changed to "Associate Medical Director / Group Medical Director" to reflect new Trust structure	
8.2	Feb 2023	Review date extended to 01 Sept 2023	Published
8.2	July 2023	Review date extended to 31 Dec 2023	Published
8.2	March 2024	Review date extended to 30 June 2024	Published
8.2	Aug 2024	Review date extended from 30/06/2024 to 31/12/2024	Published

11 Appendices

11.1 Appendix 1 - Equality Analysis Screening Form

Please note; The Equality Analysis Policy and Equality Analysis Guidance can be found on InTouch on the policies page

Name of Service area, Directorate/Department i.e. substance misuse, corporate, finance etc.	Pharmacy					
Name of responsible person and job title	Richard Morris, Deputy Chief Pharmacist					
Name of working party, to include any other individuals, agencies or groups involved in this analysis	Drug & Therapeutics Committee					
Policy (document/service) name	Guidance on Unlicensed and Off-label Use of Medicines					
Is the area being assessed a;	Policy/Strategy		Service/Business plan		Project	
	Procedure/Guidance			X	Code of practice	
	Other – Please state					
Geographical area	Trustwide					
Aims and objectives	This guidance provides a framework for the prescribing of medicines which do not have a marketing authorisation or are being used outside the terms of the marketing authorisation. The objectives of this guidance are: • To ensure good practice in decision-making around treatment choice in conjunction with parents and carers; • To allow use of unlicensed or off-label medicines in line with recognised clinical practice and/or published evidence;					

	• To minimise risk associated with unlicensed and off-label use of medicines. • To define the unlicensed medicines and off-label use of medicines that are approved by the Trust; • To describe the procedure to seek approval for use of an unlicensed medicine or off-label use of a medicine, for general or patient-specific purposes, when such approval is not already in place.
Start date of Equality Analysis Screening (This is the date you are asked to write or review the document/service etc.)	26th January 2020
End date of Equality Analysis Screening (This is when you have completed the analysis and it is ready to go to EMT to be approved)	28th May 2020

You must contact the EDHR team as soon as possible where you identify a negative impact. Please contact the E&D team.

1. Who does the Policy, Service, Function, Strategy, Code of practice, Guidance, Project or Business plan benefit?					
All prescribers in the Trust All patients and carers					
2. Will the Policy, Service, Function, Strategy, Code of practice, Guidance, Project or Business plan impact negatively on any of the protected characteristic groups below?					
Race (including Gypsy and Traveller)	No	**Disability** (includes physical, learning, mental health, sensory and medical disabilities)	No	**Gender** (Men, women and gender neutral etc.)	No
Gender reassignment (Transgender and gender identity)	No	**Sexual Orientation** (Lesbian, Gay, Bisexual and Heterosexual etc.)	No	**Age** (includes, young people, older people – people of all ages)	No

Religion or Belief (includes faith groups, atheism and philosophical belief's)	No	**Pregnancy and Maternity** (includes pregnancy, women who are breastfeeding and women on maternity leave)	No	**Marriage and Civil Partnership** (includes opposite and same sex couples who are married or civil partners)	No

Yes – Please describe anticipated negative impact/s

No – Please describe positive impacts/s

The guidance provides a framework for prescribing of unlicensed or off-label medicines based on the needs of the patient and their condition, regardless of any of the above characteristics.

An overarching policy to cover the particular needs of protected characteristic groups in relation to all Trust policies, procedures and guidelines on prescribing or administration of medication is in development and will be published by 30 June 2017.

3. Have you considered other sources of information such as; legislation, codes of practice, best practice, nice guidelines, CQC reports or feedback etc.? **If 'No', why not?**	**Yes**	**X**	~~**No**~~	

Sources of Information: • NICE guidelines • BNF / BNF for Children • Guidance from professional bodies		

4. Have you engaged or consulted with service users, carers, staff and other stakeholders including people from the following protected groups?: Race, Disability, Gender, Gender reassignment (Trans), Sexual Orientation (LGB), Religion or Belief, Age, Pregnancy and Maternity or Marriage and Civil Partnership

Yes – Please describe the engagement and involvement that has taken place

Patient and carer representatives were members of Drug & Therapeutics Committee when this guidance was considered and approved

No – Please describe future plans that you may have to engage and involve people from different groups

5. As part of this equality analysis have any training needs/service needs been identified?					
No	Please describe the identified training needs/service needs below				
A training need has been identified for;					
Trust staff	Yes/No	Service users	Yes/No	Contractors or other outside agencies	Yes/No
If you need further advice or information on equality analysis, the EDHR team host surgeries to support you in this process, to book on and find out more please call E&D Team..					

11.2 Appendix 2 – Register of approved unlicensed and off-label use of medicines

It is the prescriber's responsibility to be aware of this list. Please consult the latest BNF for marketing authorisation of drugs.

- Please note that any medication that is crushed or mixed with food or drink prior to administration (with or without the patients knowledge) is rendered unlicensed, unless the manufacturer states that it can be crushed, capsules opened or mixed with food in the BNF. Please see the Trust Guidance on the covert administration of medication for further information.
- Medicines highlighted **red** are considered not suitable for transfer of prescribing

Prescribing in Children and Young Peoples services:

- Many of the medicines that are prescribed for children by the Children and Young Peoples Service do not have a marketing authorisation for use in children or are used outside the terms of their marketing authorisation (i.e. off-label use)
- This is an area of concern as the risks and benefits of using these drugs have not been examined by the licensing authority and robust clinical trials are a rarity; however, without such prescribing, effective treatment would be denied to many children
- The Medicines Act 1968 and European legislation make provision for doctors to use medicines in an off-label capacity or to use unlicensed medicines. Individual prescribers are always responsible for ensuring that there is adequate information to support the quality, efficacy, safety and intended use of a drug before prescribing it. However prescribing a drug outside the recommendations of the product licence alters and increases the doctor's professional responsibility
- The Trust has agreed that it will accept liability where a prescribed drug is listed in the BNF for Children as long as:
  - It is prescribed for an indication specified in BNF for Children even if the drug is not licensed for this indication
  - It is prescribed within the dosage limits specified in BNF for Children
  - The patient is within the age range specified in BNF for Children
- To support prescribers the Trust has also approved the following additional list of off-label / unlicensed use of medicines for which it will take liability, as long as prescribing is for the specified indications and within the specified dosage and age range
- If a prescriber wishes to prescribe a drug which is not listed either in BNF for Children or in the following list, or if they wish to prescribe for an unlisted indication, or at a dose or for an age outside that listed below they must follow the Trust procedure for approval to do so, i.e. apply to the Drug & Therapeutics Committee for either general approval or patient-specific approval.
- The responsibility for assessing the suitability of a medication for a particular patient before prescribing remains solely with the prescribing clinician
- The patient information leaflet provided with the drugs will not reflect usage of medicines in these circumstances, and parents and patients may be concerned and confused if they read that "the medicine is not indicated in children"; to avoid misunderstanding or complaints, patients and carers should always be informed

when a medicine is unlicensed or being used off-label, including provision of the relevant Trust-approved leaflet:
  - Handy Fact Sheet - Unlicensed medicines
  - Handy Fact Sheet - Unlicensed uses of licensed medicines
- The prescriber decision and patient/carer consent to use an unlicensed medicine or a medicine "off-label" must be clearly documented in the patient's clinical record

Treatment goals

- Resolution of symptoms
- Prevention of relapse
- Resumption of - normal development; academic and vocational development; social skills and progressive independence
- Avoidance of - iatrogenic problems; EPS and tardive dyskinesia; obesity and diabetes; sedation and cognitive dulling

References:

1. The Maudsley Prescribing Guidelines 13th edition, 2018
2. National Institute of Health and Clinical Excellence; NICE guideline 97; June 2018
3. O'Brien JT at al. Clinical practice with anti-dementia drugs: a revised (third) consensus statement from the British Association for psychopharmacology. J Psychopharmacol 2017 Feb;31(2):147-168
4. National Institute of Health and Clinical Excellence; Clinical guideline 103 - Delirium: prevention, diagnosis and management (July 2010)
5. BNF for Children – via Medicines Complete
6. NICE CG155: Psychosis and schizophrenia in children and young people: recognition and management (2013)
7. NICE Guideline 10: Violence and aggression - short-term management in mental health, health and community settings (2015)
8. Medicines for Children website - http://www.medicinesforchildren.org.uk/
9. Psychotropic Drug Directory (2018)
10. Department of Health (England) and the devolved administrations (2007). Drug Misuse and Dependence: UK Guidelines on Clinical Management. London: Department of Health (England), the Scottish Government, Welsh Assembly Government and Northern Ireland Executive
11. TEWV NHS Foundation Trust, Substance Misuse Directorate: Prescribing Guidelines Drug Misuse

Drug / Therapeutic Group	Unlicensed condition	AMH	Secure Services (Forensics)	LD	MHSOP	CYPS	Protocols/Limitations
Acetylcholinesterase inhibitors	Severe dementia	✓	✓	✓	✓		Dementia Care Pathway: Guidance for prescribing acetylcholinesterase inhibitors and memantine NICE NG97 Dementia: assessment, management and support for people living with dementia and their carers
Acetylcholinesterase inhibitors **with** Memantine (Combination)	Moderate to severe Alzheimer's disease	✓	✓	✓	✓		
Donepezil Rivastigmine Galantamine Memantine (if AChEi not tolerated or contraindicated)	Dementia with Parkinson's disease	✓	✓	✓	✓		
Donepezil Rivastigmine Galantamine (if donepezil & rivastigmine are not tolerated Memantine	Mild to moderate dementia with Lewy bodies	✓	✓	✓	✓		
Donepezil Rivastigmine Memantine (if donepezil & rivastigmine not tolerated)	Severe dementia with Lewy bodies	✓	✓	✓	✓		
Donepezil Rivastigmine Galantamine Memantine	Mixed dementia	✓	✓	✓	✓		

Drug / Therapeutic Group	Unlicensed condition	AMH	Secure Services (Forensics)	LD	MHSOP	CYPS	Protocols/Limitations
Amisulpride	Treatment of refractory bipolar & unipolar depression with prominent psychotic features	✓	✓	✓			
Anticholinergics	Akathisia	✓	✓	✓			May only be effective in patients who also have parkinsonian symptoms
Antidepressants: *Trazodone* *Sertraline* *Citalopram** *Mirtazapine* *Fluoxetine*	Management of behavioural & psychological symptoms of dementia Agitation	✓	✓	✓	✓		Trazodone widely used to reduce irritability & agitation, but sedative. Modest benefits seen with SSRIs *caution with citalopram; risk of dose dependent QTc prolongation; see Trust Guidance
Antiepileptics	Bipolar affective disorder	✓	✓	✓	✓		Bipolar disorder treatment algorithm In MHSOP, follow functional pathway – bipolar disorder
Antiepileptics	Doses above BNF maximum for the treatment of epilepsy	✓	✓	✓			All patients will have a comprehensive epilepsy treatment plan encompassing medical and social managements & will include where appropriate clear guidance as to the use of rescue medication. Treatment must be regularly reviewed & particular attention be given to enquiring about potential side effects.

Drug / Therapeutic Group	Unlicensed condition	AMH	Secure Services (Forensics)	LD	MHSOP	CYPS	Protocols/Limitations
							Capacity & consent, in relation to medication & the off license use thereof, should be assessed and documented in the case notes. In the case of an incapacitous adult, evidence of a best interest discussion with carers should be recorded. If no further improvement is gained, the drug dose is reduced to that at which most benefit is obtained
Antipsychotics	Acutely disturbed behaviour (inpatients)	✓	✓	✓	✓		Use as per rapid tranquilisation protocol
Antipsychotics	Doses above BNF maximum for age group (HDAT)	✓	✓	✓	✓		Follow High Dose Antipsychotic Treatment Guideline
Antipsychotics	Delirium				✓		Haloperidol 1st line choice but avoid in Parkinson's disease & Lewy Body dementia
2nd generation antipsychotic LAIs: Paliperidone Aripiprazole	Use in the elderly				✓		SPCs: safety and efficacy in the treatment of schizophrenia in patients 65 years of age or older has not been established
Antipsychotics (atypical)	Delusional disorders				✓		

Drug / Therapeutic Group	Unlicensed condition	AMH	Secure Services (Forensics)	LD	MHSOP	CYPS	Protocols/Limitations
Antipsychotics: Risperidone > 6 weeks Olanzapine **Alternatives:** Quetiapine Amisulpride Aripiprazole	Management of behavioural & psychological symptoms of dementia (BPSD)				✓		**Caution:** All antipsychotics are considered to have increased risk for all-cause mortality & cerebrovascular events **Only consider antipsychotics to treat severe symptoms of BPSD (psychosis &/or agitated behaviour causing significant distress) or where other specific interventions have been unsuccessful** Refer to summary of Pharmacological treatment options for BPSD
Antipsychotics (oral) & SSRIs	Learning disability & challenging behaviour	✓	✓	✓			Treatment of challenging behaviour with medication should be commenced only following a full psychiatric behavioural & psychosocial assessment, except where urgency of the situation dictates otherwise. Treatment with medication should be a part of a comprehensive behavioural & social treatment plan. Target behaviours should be clearly identified & expected outcomes should be explicit. The lowest effective dose should be used. Treatment must be regularly reviewed

Drug / Therapeutic Group	Unlicensed condition	AMH	Secure Services (Forensics)	LD	MHSOP	CYPS	Protocols/Limitations
							against expected outcomes, & particular attention be given to enquiring about potential side effects. Dose reduction and/or discontinuation of medication should be considered at each review. Capacity & consent in relation to medication & the unlicensed use thereof, should be assessed & documented in the case notes. In the case of an incapacitous adult evidence of a best interest discussion with carers should be recorded.
Aripiprazole	Raised prolactin levels	✓	✓	✓	✓		See hyperprolactinaemia guidance for monitoring requirements
	Antipsychotic-induced weight gain	✓	✓	✓	✓		With clozapine or olanzapine only
	Affective psychoses & other functional psychoses in children below 15 years of age.					✓	
	Managing challenging behaviour in children with learning disabilities					✓	
Aripiprazole + SSRI	Obsessive-compulsive disorder					✓	A 6-week trial of low dose antipsychotic augmentation should be enough to assess efficacy; discontinue if no

Drug / Therapeutic Group	Unlicensed condition	AMH	Secure Services (Forensics)	LD	MHSOP	CYPS	Protocols/Limitations
							response noted (Maudsley)
Atropine sulfate (eye drops)	Clozapine induced hypersalivation	✓	✓	✓			
Benperidol	Sexual disinhibition				✓		Refer to summary of Pharmacological treatment options for BPSD
Benzodiazepines (Including unlicensed lorazepam products when Ativan unavailable)	Acute phase of mania	✓	✓	✓			Use as per rapid tranquilisation protocol; If using doses above BNF maximum, monitor vital signs (especially respiration) regularly & seek advice from senior medical staff if in doubt
	Acutely disturbed behaviour (Inpatients only)	✓	✓	✓	✓	✓	
	Oxazepam for alcohol detoxification	✓	✓	✓			Chlordiazepoxide is licensed for this indication
Beta-blockers	Akathisia	✓	✓	✓			
Bupropion	Severe depression	✓	✓	✓	✓		No response to SSRI or SNRI or sexual side effects In MHSOP, follow functional pathway - depression
Buspirone	Augmentation of antidepressants in anxious or agitated patients				✓		See MHSOP functional pathway - depression
Carbamazepine	Aggressive & impulsive behaviour	✓	✓	✓			

Drug / Therapeutic Group	Unlicensed condition	AMH	Secure Services (Forensics)	LD	MHSOP	CYPS	Protocols/Limitations
	Bipolar disorder (lithium naïve & lithium responsive cases)	✓	✓	✓			Licensed for bipolar disorder unresponsive to lithium
	Management of behavioural & psychological symptoms of dementia				✓		May be beneficial but not recommended for routine use. Use may be justified where other treatments are contraindicated or ineffective. Refer to summary of Pharmacological treatment options for BPSD
	Mood stabilisation					✓	
	Severe, impulsive aggression in conduct disordered young people aged 12-18 years resistant to psychosocial interventions					✓	
Citalopram	Obsessive-compulsive disorder	✓	✓	✓		✓	See NICE guideline for Obsessive-compulsive disorder
	Anxiety					✓	
Clomipramine	Obsessive Compulsive Disorder					✓	

Drug / Therapeutic Group	Unlicensed condition	AMH	Secure Services (Forensics)	LD	MHSOP	CYPS	Protocols/Limitations
Clonazepam	Severe agitation / aggression	✓	✓	✓			For initiation by a consultant psychiatrist on PICUs only; patients transferred back to home ward must have a plan to reduce and stop before discharge
Clonazepam	REM myoclonic jerks / REM sleep disorder				✓		
Clonidine	Tics (monotherapy) Hyperkinetic disorder & ADHD used alone & in combination with methylphenidate					✓	Carry out cardiovascular examination & ECG prior to treatment
Clozapine	Treatment of refractory rapid cycling bipolar disorder	✓	✓	✓			
CNS stimulants (methylphenidate, lis/dexamfetamine & guanfacine)	Attention Deficit Hyperactivity Disorder (ADHD)	✓	✓	✓			Refer to safe transfer of prescribing guidance & follow shared care guidelines where they exist
CNS stimulants (methylphenidate, lis/dexamfetamine) **with** guanfacine	Attention Deficit Hyperactivity Disorder (ADHD)					✓	Any existing shared care for monotherapy would no longer apply – responsibility for combination therapy transfers back to specialist
Diazepam	Cover of withdrawal symptoms					✓	

Drug / Therapeutic Group	Unlicensed condition	AMH	Secure Services (Forensics)	LD	MHSOP	CYPS	Protocols/Limitations
Diazepam	Short Term Management of agitation					✓	
Doxazosin	Nightmares & sleep problems in PTSD/Trauma	✓	✓	✓			Where there are supply/ availability issues associated with prazosin. Once switched to doxazosin, patients can remain on this medication if effective
Drugs for dementia	Management of behavioural & psychological symptoms of dementia				✓		Refer to summary of Pharmacological treatment options for BPSD
Fluoxetine	Reduction of sexual drive in dementia				✓		Refer to summary of Pharmacological treatment options for BPSD
	Obsessive Compulsive Disorder					✓	
	Bulimia					✓	
	Aggression, repetitive or self-injurious behaviour in autistic spectrum disorder					✓	
	In line with Trust pathway for: Depression Social anxiety disorder/social phobia Panic disorder					✓	See CYPS depression and anxiety pathways Approved up to 40 mg daily (licensed up to 20 mg daily for depression)

Drug / Therapeutic Group	Unlicensed condition	AMH	Secure Services (Forensics)	LD	MHSOP	CYPS	Protocols/Limitations
	Phobic anxiety disorder Generalised anxiety disorder Separation anxiety						
Gabapentin	Generalised anxiety disorder	✓	✓	✓			See Trust anxiety medication pathway
Haloperidol	Agitation/challenging behaviour					✓	
	Rapid Tranquilisation					✓	
Hyoscine Hydrobromide	Clozapine-induced hypersalivation	✓	✓	✓	✓	✓	
Ketamine (IV)	Severe treatment resistant depression	✓	✓	✓			Ketamine protocol
Lamotrigine	Mood stabilisation					✓	Annual health check; no special monitoring required
Lorazepam	Aggression in psychosis					✓	
	Short Term Management of agitation					✓	
Melatonin **RED if not Circadin**	Sleep disorders, as listed in shared care guidelines	✓	✓	✓		✓	Melatonin shared care guidelines

Drug / Therapeutic Group	Unlicensed condition	AMH	Secure Services (Forensics)	LD	MHSOP	CYPS	Protocols/Limitations
Melatonin (Circadin)	Primary sleep disorders when exceeding short term use (>13 weeks) Sleep reversal and REM sleep disorder				✓		See MHSOP functional pathway
Metformin	Antipsychotic-induced weight gain	✓	✓	✓			
Midazolam (Buccal)	Status epilepticus	✓	✓	✓	✓		Licensed in patients under 18 years Buccolam® is preferred product (licensed)
Midazolam (IM)	Acutely disturbed behaviour (inpatients)	✓	✓	✓			Only during supply shortages of lorazepam injection. Flumazenil **must** be available
Mirtazapine	Depression					✓	Mirtazapine in the treatment of adolescents with major depression: an open-label, multicenter pilot study - PubMed (nih.gov)
Mood stabilisers	Emotionally Unstable Personality Disorder symptoms: • Affect dysregulation • Impulsivity • Cognitive-perceptual symptoms	✓	✓	✓			**Reasonable evidence base:** • Lamotrigine • Topiramate • Valproic Acid • Aripiprazole • Quetiapine • Clozapine

Drug / Therapeutic Group	Unlicensed condition	AMH	Secure Services (Forensics)	LD	MHSOP	CYPS	Protocols/Limitations
							Weaker evidence base: • Olanzapine • Haloperidol • Flupentixol decanoate
Naltrexone	Self-injurious behaviour in autism or learning disability	✓	✓	✓		✓	
Olanzapine	Anorexia nervosa second line to psychological approaches					✓	Physical monitoring dependent on weight, CMHT & GP informed of unlicensed use. Evidence of efficacy & safety reviewed annually
Pramipexole	Treatment-resistant bipolar depression	✓	✓	✓			Only following effective use as part of the PAXBD trial: Pramipexole for treatment-resistant bipolar depression
Prazosin	Nightmares & sleep problems in PTSD/Trauma	✓	✓	✓			See doxazosin if not available due to supply disruption
Promethazine (Oral)	Agitation / anxiety / disturbed behaviour	✓	✓	✓	✓	✓	
Promethazine (IM)	Acutely disturbed behaviour	✓	✓	✓	✓	✓	Use as per age-specific algorithms in rapid tranquilisation policy
Propranolol	Drug induced akathisia					✓	
	Anxiety with symptoms such as palpitations, tremor, sweating					✓	

Drug / Therapeutic Group	Unlicensed condition	AMH	Secure Services (Forensics)	LD	MHSOP	CYPS	Protocols/Limitations
Quetiapine	Monotherapy for unipolar depression & anxiety disorders	✓	✓	✓			
	Refractory depression (monotherapy & augmentation of antidepressant); Generalised anxiety				✓		See MHSOP functional pathway - depression
Quetiapine (including modified release)	Mania in children under 12					✓	
	Maintenance in bipolar affective disorder and acute and chronic treatment of other functional psychoses (e.g. delusional disorder)					✓	
Quetiapine (including modified release)	Augmentation of SSRIs in severe OCD resistant to psychological treatment & monotherapy with SSRIs/Clomipramine					✓	
	Treatment of distressing psychotic symptoms in those fulfilling the criteria for the “at risk mental state for psychosis” resistant to psychological approaches					✓	

Drug / Therapeutic Group	Unlicensed condition	AMH	Secure Services (Forensics)	LD	MHSOP	CYPS	Protocols/Limitations
	Anorexia nervosa second line to psychological approaches.					✓	Physical monitoring dependent on weight, CMHT & GP informed of unlicensed use. Evidence of efficacy & safety reviewed annually
Quetiapine (Standard-release preparations)	Adjunctive treatment of major depression	✓	✓	✓			
Risperidone	Hyperactivity, anxiety, agitation, managing challenging behaviour in children with learning disabilities					✓	
Sertraline	Aggression in autistic spectrum disorder					✓	
	Post-traumatic stress disorder					✓	
Sertraline	In line with Trust pathway for: Social anxiety disorder/social phobia Panic disorder Phobic anxiety disorder Generalised anxiety disorder Separation anxiety					✓	

Drug / Therapeutic Group	Unlicensed condition	AMH	Secure Services (Forensics)	LD	MHSOP	CYPS	Protocols/Limitations
Sodium valproate	Bipolar disorder / Mood Stabiliser	✓	✓	✓		✓	Hypomania
SSRI	Frontal lobe dementia symptoms				✓		
SSRIs & SNRIs	Anxiety	✓	✓	✓			Consider sertraline, escitalopram, venlafaxine & duloxetine which are licensed for this indication
Temazepam	Primary Insomnia					✓	
Topiramate	Antipsychotic-induced weight gain	✓	✓	✓			
Tricyclic Antidepressants	Doses above BNF maximum	✓	✓	✓			ECG every 3 months & monitor QTc interval
Valproic acid (Semisodium valproate)	Mood stabiliser	✓	✓	✓			Licensed for manic episodes associated with bipolar disorder
Valproic acid (Semisodium valproate)	Severe, impulsive aggression in conduct disordered males aged 12-18 years NOT co-morbid with ADHD & resistant to at least 4 sessions of psychosocial intervention					✓	This indication applies only to the forensic adolescent Outpatient Team in the Controlling Anger & Learning to manage mood (CALMM) clinic
Zopiclone	Primary Insomnia					✓	

Drug / Therapeutic Group	Unlicensed condition	AMH	Secure Services (Forensics)	LD	MHSOP	CYPS	Protocols/Limitations
Zuclopenthixol (Oral)	Schizophrenia					✓	
Zuclopenthixol Acetate	Acute Psychosis					✓	

11.3 Appendix 3 – Template record of patient consent

To be copied, pasted and edited into the electronic patient record:

I have discussed treatment with *[insert drug, + formulation & strength if necessary]* at a dose of *[insert dose & frequency]* for the management of *[insert indication].* The rationale for this treatment is *[insert rationale, e.g. licensed options exhausted or not appropriate].*

S/he has been provided with verbal and/or written information about this treatment, and understands that:

- This is an unlicensed product / unlicensed use of this medication *[delete as appropriate]*
- There is a sufficient evidence base and/or experience to demonstrate that the benefits of this unlicensed product / unlicensed use of this medication *[delete as appropriate]* are considered to outweigh the potential risks

S/he has provided consent to this treatment.

I acknowledge and accept my clinical responsibilities for prescribing this treatment

[Inpatients only] Nursing staff are aware of potential side-effects and adverse reactions that may occur, and monitoring that is necessary.

11.4 Appendix 4 - Approval checklist

	Title of document being reviewed:	Yes/No/ Not applicable	Comments
1.	**Title**		
	Is the title clear and unambiguous?	Yes	
	Is it clear whether the document is a guideline, policy, protocol or standard?	Yes	
2.	**Rationale**		
	Are reasons for development of the document stated?	Yes	
3.	**Development Process**		
	Are people involved in the development identified?	Yes	
	Has relevant expertise has been sought/used?	Yes	
	Is there evidence of consultation with stakeholders and users?	Yes	
	Have any related documents or documents that are impacted by this change been identified and updated?	Yes	
4.	**Content**		
	Is the objective of the document clear?	Yes	
	Is the target population clear and unambiguous?	Yes	
	Are the intended outcomes described?	Yes	
	Are the statements clear and unambiguous?	Yes	
5.	**Evidence Base**		
	Is the type of evidence to support the document identified explicitly?	Yes	
	Are key references cited?	Yes	
	Are supporting documents referenced?		
6.	**Training**		
	Have training needs been considered?	Yes	
	Are training needs included in the document?	Yes	
7.	**Implementation and monitoring**		
	Does the document identify how it will be implemented and monitored?	Yes	

	Title of document being reviewed:	Yes/No/ Not applicable	Comments
8.	**Equality analysis**		
	Has an equality analysis been completed for the document?	Yes	Appendix 1
	Have Equality and Diversity reviewed and approved the equality analysis?	Yes	
9.	**Approval**		
	Does the document identify which committee/group will approve it?	Yes	Drug & Therapeutics committee
10.	**Publication**		
	Has the document been reviewed for harm?	Yes	
	Does the document identify whether it is private or public?	Yes	
	If private, does the document identify which clause of the Freedom of Information Act 2000 applies?	N/A	