

MEDICINES STANDARD C4: PRESCRIBING UNLICENSED AND OFF-LABEL MEDICINES

This guidance covers the use of the following within the CCG:

- **Unlicensed medicinal products:** products that have not received a Marketing Authorisation in the UK. These may be imported, or alternatively produced as “Specials” in the U.K. by large reputable companies, small independent companies or within hospital pharmacies.
- **Off-label prescribing:** Licensed products being used outside of the terms of the Marketing Authorisation. This includes prescribing for unlicensed indications, at higher than licensed doses, by routes and to age groups not included in the licence, etc. Also included are those situations where the form of a preparation is changed before administration (e.g. tablets need to be crushed, capsules opened, etc.).
- Products where the licence has been suspended, revoked or not renewed (usually for commercial reasons), but where the company continues to make product available for named individuals, e.g. co-proxamol.
- Products that are not a medicine but are being used to treat a rare condition (e.g. a metabolic disease).

DEFINITIONS

A licensed medicine meets acceptable standards of efficacy, safety, and quality. A licensed medicine has been assessed for efficacy, safety, and quality; has been manufactured to appropriate quality standards, and when placed on the market is accompanied by appropriate product information and labelling.

An unlicensed medicine is a medicine that does not have a UK marketing authorisation (or product licence).

An off-licence (or off-label) medicine is a medicine with a product licence but being used outside the terms of that licence. This may include being used for an unlicensed indication or dose, or in a patient population which has not been studied in clinical trials.

Off-licence and unlicensed medicines can fall into many categories. These may include:

- products derived from licensed indications (e.g. low dose formulations for children, higher than normally recommended doses in psychiatry);
- product 'specials' (e.g. liquid products for patients unable to swallow, products free of sensitising agents);
- drugs used when the product licence has been suspended;
- compassionate use of newly developed drugs (e.g. to treat cancer).

A drug may be unlicensed for a variety of reasons for example:

- It is undergoing clinical trials;
- It has been imported from another country;
- It has been prepared extemporaneously;
- It has been prepared under a specials licence (e.g. liquid preparations, low dose products for children, or preservative free formulations).

Throughout this guidance, "ULMP" refers to an unlicensed medical product and "OLMP" refers to the use of a medicine off-licence.

PRINCIPLES OF PRESCRIBING UNLICENCED MEDICINAL PRODUCTS

There are clinical situations when the use of unlicensed medicines or use of medicines outside the terms of the licence (i.e., 'off-licence') may be judged by the prescriber to be in the best interest of the patient on the basis of available evidence. However, all healthcare professionals who can prescribe off-licence or unlicensed medicines must do so within:

- their individual clinical competence
- the professional codes and ethics of their statutory bodies
- the prescribing policies of their employers

The responsibility that falls on healthcare professionals when prescribing an unlicensed medicine or a medicine off-licence 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-licence. These risks may include: adverse reactions; product quality; or discrepant product information or labelling (e.g., absence of information for some unlicensed medicines, information in a foreign language for unlicensed imports, and potential confusion for patients or carers when the patient information leaflet is inconsistent with a medicine's off-licence use).

ADVICE FOR PRESCRIBERS

The MHRA guidance states that:

- Before prescribing an unlicensed medicine, be satisfied that an alternative, licensed medicine would not meet the patient's needs.
- Before prescribing a medicine off-license, be satisfied that such use would better serve the patient's needs than an appropriately licensed alternative
- Before prescribing an unlicensed medicine or using a medicine off-license:
 - Be satisfied that there is a sufficient evidence base and/or experience of using the medicine to show its safety and efficacy
 - Take responsibility for prescribing the medicine and for overseeing the patient's care, including monitoring and follow-up
 - Record the medicine prescribed and, where common practice is not being followed, the reasons for prescribing this medicine; you may wish to record that you have discussed the issue with the patient
 - You have given 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
- You explain the reasons for prescribing a medicine off-license or prescribing an unlicensed medicine where there is little evidence to support its use, or where the use of a medicine is innovative
- Report suspected adverse reactions to the MHRA and Commission on Human Medicines (CHM) via the Yellow Card Scheme (see www.yellowcard.gov.uk). Such reporting is equally important for unlicensed medicines or those used off-license as for those that are licensed.

REQUESTS TO PRESCRIBE UNLICENSED / OFF LABEL MEDICINES FROM SECONDARY CARE

Any specialist who asks a GP to prescribe a medicine that is unlicensed or off-license should clearly state the licence status of the medicine. The specialist initiating therapy must ensure that the GP is aware of their responsibilities in relation to prescribing the medicine on an unlicensed or off-license basis.

The specialist must present the case for using this medicine and justify its use in preference to licensed alternatives. The evidence base behind the recommendation must be given and

it should be made clear whether or not the treatment recommended is a peer-supported option.

The specialist initiating therapy must inform the patient of the unlicensed / off-licence use of the drug and obtain their informed consent for its use.

The specialist must ensure that the patient is aware of the known side-effects of the drug and that there may be other unknown side-effects.

It should not be assumed that GPs will take on responsibility for prescribing unlicensed or off-licence medication. Unless the GP volunteers to take over prescribing responsibility, this should continue to rest with the consultant initiating treatment.

The GP should reassure him/herself that a body of medical opinion supports the use of the drug in these circumstances e.g. check in an appropriate formulary for paediatric use.

The GP should keep detailed notes of the reasons for using an unlicensed or off-licence drug, a copy of the patient consent form and consultation notes. The GP must also satisfy him/herself that the patient has been informed about known side effects and is aware that there may be other unknown side-effects.

Prescribing responsibilities between the specialist and the GP must be clearly documented and state the specific responsibilities of each party. Shared-care protocols, where available, should be used to assist in this process.

It should be noted that a GP is under no obligation to continue to prescribe ULMPs or OLMPs. Each case, in agreement with the patient, must be discussed with the GP individually, to obtain their full agreement, and the following written information must also be provided:

- sources of supply if appropriate
- supporting evidence,
- monitoring requirements
- provision of appropriate information to support transfer of prescribing responsibility (e.g. relevant patient history, physical assessments etc)

In addition, the patient must be reviewed regularly to assess benefit and adverse effects. Outcomes of these reviews must be shared with the GP.

Secondary care clinicians should not recommend the use of medicines to GPs or patients that are categorised as “red” within the traffic light system, or medicines that have been reviewed by the Dorset Medicines Advisory group or its predecessors and classified as “not recommended”.

It is important that patients are not led to expect that their GP will follow a particular course of action. It is also important that there is appropriate dialogue between the consultant and GP to prevent conflicting messages being given to patients and carers.

If there is a financial concern in terms of the impact on primary care drug budgets then this needs to be clarified before treatment is initiated.

NON-MEDICAL PRESCRIBERS

Prescribing unlicensed medications (ULMPs)

Non-medical prescribers (NMPs), apart from nurses, optometrists and pharmacists, must not prescribe an unlicensed medication independently. However they may prescribe unlicensed medication as a supplementary prescriber as part of a clinical management plan providing:

- The doctor/dentist and NMP acting as a supplementary prescriber have agreed the plan with the patient/client in a voluntary relationship
- The NMP is satisfied an alternative, licensed medication would not meet the patient/client's need
- The NMP is satisfied there is a sufficient evidence base and/or experience to demonstrate the medications safety and efficacy for that particular patient/ client
- The doctor/dentist is prepared to take the responsibility for prescribing the unlicensed medicine and has agreed the patient/client's clinical management plan to that effect
- The patient/client agrees to a prescription in the knowledge that the drug is unlicensed and understands the implications of this
- The medication chosen and the reason for choosing it is documented in the clinical management plan

Prescribing medicines for use outside the terms of their licence (off-licence) (OLMPs)

There are a number of circumstances in which NMPs 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).

It is possible under current legislation for nurse, optometrist and pharmacist independent prescribers to prescribe unlicensed or off-licence medicines as independent prescribers. However in order to do so these NMP's must ensure the following conditions are met:

- The NMP is satisfied that it would better serve the patient/client's needs than an appropriately licensed alternative
- The NMP is satisfied that there is a sufficient evidence base and/or experience of using the medicine to demonstrate its safety and efficacy. Where information from the manufacturer is of limited help, the necessary information must be sought from another source (for example, a medicines information centre).

- The NMP should explain to the patient/client, or parent/carer, in broad terms, the reasons why medicines are not licensed for their proposed use.
- The NMP must make a clear, accurate, and legible record of all medicines prescribed and the reasons for prescribing an 'off-licence' or unlicensed medicine.

IMPLICATIONS OF USE OF UNLICENCED MEDICINAL PRODUCTS (ULMPS) OR OFF LABEL MEDICINAL PRODUCT (OLMPS)

Doctors are free to prescribe approved medicines as they deem appropriate. However, prescribers have a duty in common law to take reasonable care and to act in a way consistent with the practice of a responsible body of their peers of similar professional standing, and have evidence to support the use of medicines in an unlicensed or off-licence manner. This may include using the medication for purposes not investigated or in patient groups not studied as part of the licence application. However, since all healthcare professionals have a duty of care for the interests of their patients, the prescriber then accepts the liability normally assumed by the product licence holder.

The prescriber must have sufficient knowledge, information or experience to show they are acting reasonably and in the best interests of the service user.

Since ULMPS have not usually been subjected to the rigorous independent assessment of efficacy and safety applied to licensed products, their use may carry a higher level of risk for patients.

The ultimate responsibility for prescribing any drug lays with the prescriber who signs the prescription, who is professionally accountable for her/his judgment. Consequently, when prescribing an ULMP or OLMPS the prescriber is professionally accountable and personally responsible for any adverse consequences arising from its use.

The manufacturer is only likely to be found liable if harm results from a defect in the product, thus putting a greater responsibility on individual prescribers and where applicable their Trust.

Failure to follow this guidance and any policy from the employing organisation may mean that the prescriber is not indemnified for any liability arising out of the use of the unlicensed or off-licence medicinal product concerned.

Liability can include fault (or negligent liability) and strict liability. Strict liability is where the manufacturer is liable for a defective product under the Consumer Protection Act or Product Liability Directive (EEC/85/374). Fault liability is where a prescriber gives an unlicensed or off-licence drug and prescribes or administers it negligently, fails to inform the patient of side-effects or fails to obtain informed consent.

In using an unlicensed or off-licence medicine the prescriber must act responsibly, with reasonable care and skill. If they fail to do so they may be liable to claims of negligence liability.

OBTAINING SUPPLIES

It should be noted that unlicensed medicines may be 'specials' that community pharmacies may have difficulty in obtaining. Adequate time must be allowed for products to be obtained. Until a regular supply is established in primary care, secondary care should continue to obtain supplies for the patient.

OTHER INFORMATION

Where shared care guidelines exist, the principles within them must be adhered to. GMC guidance states:

“If you share responsibility for a patient’s care with a colleague, you must be competent to exercise your share of clinical responsibility. You should:

- keep yourself informed about the medicines that are prescribed for the patient
- be able to recognise serious and frequently occurring adverse side effects
- make sure appropriate clinical monitoring arrangements are in place and that the patient and healthcare professionals involved understand them
- keep up to date with relevant guidance on the use of the medicines and on the management of the patient’s condition.”

When GPs are requested to take over the prescribing of a drug under a shared care guideline, they will be expected to agree.

If you are uncertain about your competence to take responsibility for the patient’s continuing care, you should seek further information or advice from the clinician with whom the patient’s care is shared or from another experienced colleague. If you are still not satisfied, you should explain this to the other clinician and to the patient, and make appropriate arrangements for their continuing care. If there is disagreement, the medicines team will investigate the circumstances and try to resolve the issue.

It is important not to give patients an expectation that a prescriber will follow a particular course of action, which may not be taken (for example, specialists should not inform patients that GPs will take over prescribing of a drug until this has been confirmed).

PATIENT / RELATIVE SUPPORT & INFORMATION

Informed consent must be obtained and documented wherever possible. The patient (or his/her relative when relevant) must be given a full explanation, including the information that the drug will be used outside its MA. This explanation must be documented.

If a patient is unable to consent to a necessary treatment, document that it has not been possible to obtain consent. In such cases a clear rationale must always be documented.

In situations where the use of an ULMP or OLMP is uncommon, novel, or believed to carry a substantial hazard, the patient should be informed to this effect and a record of the consent and rationale for use must be made in writing in the patient's medical records.

Patients and/or carers should be given clear written information (or a form which is suitable to their needs) on the use of the unlicensed or off label drugs. It is noteworthy that the manufacturer's patient information leaflet may be inappropriate for OLMP use, and may be non-existent for ULMPs or "specials".

Conversations with relatives and carers/relatives regarding treatment options must be recorded in the medical records and/or care plan.

REFERENCES

Bolan versus Freeman Hospital Management Committee 1957 The supply of unlicensed medicinal products ("specials").

[MHRA Guidance Note 14](#). Medicines and Healthcare Products regulatory Agency. 6 May 2014.

[Off-label or unlicensed use of medicines: prescribers' responsibilities](#). Drug Safety Update. April 2009: 2(9): 6-7. Medicines and Health care products Regulatory Agency.

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[Nurse and midwife independent prescribing of unlicensed medicines](#). Nursing and Midwifery Council circular. 10 March 2010