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Pan Mersey
Area Prescribing Committee

Good Practice for Prescribing Unlicensed and “Off-Label” Medicines, including “Specials”

This document is a good practice guide to support prescribers with prescribing unlicensed and “off-label” medicines. It describes the differences between licensed medicines, unlicensed medicines and “off-label” medicines. It advises prescribers on a stepped approach when considering what to prescribe, and highlights the prescriber’s responsibilities and best practice around patient communication.

1. Licensed medicines

Before a medicine can be widely used in the UK, it must first be granted a product licence (also known as a marketing authorisation). In the UK, licences can be granted by the Medicines and Healthcare Products Regulatory Agency (MHRA) or by the European Medicines Agency (EMA).¹ The marketing authorisation or product licence defines a medicine’s terms of use.²

A medicine’s ‘summary of product characteristics’ (SPC) outlines, among other things, the indication(s), recommended dose(s), contraindications, special warnings and precautions for use on which the licence is based, and it is in line with such use that the benefits of the medicine have been judged to outweigh the potential risks. Furthermore, 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.²

Summaries of product characteristics for medicines can be found on the electronic Medicines Compendium (eMC) or MHRA website at: <http://www.medicines.org.uk/emc/> or <http://www.mhra.gov.uk/spc-pil/>

2. Unlicensed and “off-label” medicines

For the purposes of this document definitions of unlicensed and ‘off-label’ medicines are:

‘Off-label’ – the medicine has a product licence in the UK, but that product licence does not cover the indication/dose/route for which the medicine is being prescribed.

Unlicensed – a medicine with no product licence for any indication within the UK.

‘Off-Label’

Wherever possible, a **licensed** medicine, in a suitable formulation, should be used to meet the patient’s needs.^{3,4,5} However, there are clinical situations when the use of licensed medicines outside of the terms of the licence (**‘off-label’**) or an **unlicensed** medicine may be judged by the prescriber to be in the best interest of the patient on the basis of evidence available. Such practice is particularly common in certain areas of medicine e.g. in paediatrics where difficulties in the development of age-appropriate formulations means that many medicines used in children are used off-label or are unlicensed.² Although the MHRA does not recommend “off-label” use of products, if a UK licensed product can meet the clinical need (even if ‘off-label’) it should be used instead of an unlicensed product.³

Unlicensed

Healthcare professionals may regard it necessary to prescribe or advise on the use of an **unlicensed medicine**, e.g. as a so-called **‘special’** when no equivalent licensed product as a suitable alternative is

available.² An unlicensed medicinal product may only be supplied in order to meet the “**special needs**” of an individual patient. Responsibility for deciding whether an individual patient has “special needs” which a licensed product cannot meet should be a matter for the doctor, dentist, nurse independent prescriber, pharmacist independent prescriber or supplementary 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. It does not include reasons of cost, convenience or operational needs.³

‘Specials’ are unlicensed products and have not been assessed by the regulatory authority for safety, quality and efficacy in the same way as licensed products. This means that the quality, bioavailability and consistency can vary even where the same product is prescribed. They have no SPC outlining the dose, contra-indications, storage and side-effect profile. ‘Specials’ are often considerably more expensive than licensed medicines and may have a short shelf-life.

A review of the patients need for a ‘Special’ should regularly occur to ensure continued appropriateness; as the patient’s needs or condition may have changed or a new licensed treatment option may have become available.^{4,6}

Approximately £1.3 million per annum is spent on non-Drug-Tariff ‘Specials’ across the Pan Mersey health economy, with a further £0.6 million per annum spent on Drug-Tariff listed ‘Specials’. Spend on ‘Specials’ within Pan Mersey has not changed significantly over the last two years.

The Royal Pharmaceutical Society has published two documents. [Professional Guidance for the Procurement and Supply of Specials](#)⁴ (Dec 2015) and Prescribing Specials: [Guidance for the prescribers of Specials](#) (April 2016) that gives some practical advice and considerations for prescribers.⁸

3. Stepped approach to choosing a suitable medicines

When considering what to prescribe, a stepped approach to choosing a suitable medicine is suggested:^{3,4,5}

1. Wherever possible, use a **licensed** medicine in a suitable formulation to meet the patient’s needs (e.g. a dispersible tablet or licensed liquid medicine). Consider switching to a different agent in the same class, or to a different route of administration, to allow a licensed medicine to be used.
2. Consider using a UK licensed medicine in an unlicensed manner “**off label**” (e.g. use of a licensed liquid not licensed for administration via a feeding tube, crushing/dispersing tablets or opening capsules). Not all medicines are suitable for use in this manner and it is important to check beforehand. Prescribers should seek pharmaceutical advice from within their organisation regarding suitability to administer individual medicines in an unlicensed manner.
3. If a UK licensed product cannot meet the **special need**, then another (imported) **medicinal product which is licensed in the country of origin** should be considered
4. In situations where the patient’s needs cannot be met by licensed medicines, consider using a **UK batch-prepared unlicensed ‘Special’** that is listed in Part VIII B of the Drug Tariff.
5. If all options above are unable to meet the patient’s needs then an **unlicensed Special that is not listed in the Drug Tariff** may be considered.

Further information:

UKMI document: [What are the therapeutic options for patients unable to take solid oral dosage forms?](#) July 2013 provides further detail on the suggested step-wise approach to choosing a suitable formulation and suggestions options for some therapeutic areas.⁵

A specials service to supply unlicensed medicines to children under the joint care of Alder Hey and primary care is available. Further information is available from the Alder Hey Children’s NHS Foundation Trust Specials Team on 0151 282 4878.

4. Prescriber’s responsibilities

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'. These risks may include the following:

- adverse reactions
- product quality (e.g. differences in formulations between unlicensed specials - these may be particularly important from a paediatric perspective, differences in method of manufacture and testing, difference in excipients should be considered and if necessary seek advice from the local Medicines Information where possible to ensure they are safe and suitable for the patient);
- 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-label use).

When prescribing an unlicensed medicine or a medicine 'off-label', prescribers should:

- be satisfied that an alternative, licensed medicine would not meet the patient's special needs before prescribing an unlicensed medicine
- be satisfied that such use would better serve the patient's special needs than an appropriately licensed alternative before prescribing a medicine off-label.

Before prescribing an unlicensed medicine or using a medicine 'off-label' prescribers should:

- 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; prescribers should record that they have discussed the issue with the patient.^{2,7}

5. Patient communication

Best practice for patient communication regarding unlicensed and "off-label" medicines includes:

- giving 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 licence, it may not be necessary to draw attention to the licence 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
- explaining 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^{2,7}
- patient information leaflet for children about unlicensed medicines is available from the Medicines For Children website: http://www.medicinesforchildren.org.uk/sites/default/files/content-type/leaflet/pdf/MfC_Unlicensed_medicines.pdf

Note: In some cases it may also be appropriate to give information on formulation details (e.g. alcohol free, flavourings), how to use the medicine, how to store the medicine and expiry details.

6. Transfer of prescribing of unlicensed/ 'off label' medicines into primary care

Unlicensed medicines may carry a 'Red' or 'Amber' designation as shown in the Pan Mersey formulary. <http://www.panmerseyapc.nhs.uk/>, but others may be rarely used and therefore do not appear in the formulary.

Red drugs and non-formulary unlicensed medicines should normally continue to be prescribed by the Trust. However, in some circumstances non-formulary unlicensed medicines or "off label" prescribing which is outside recognised national/local prescribing pathways may be transferred to primary care by mutual **prior** agreement.

For unlicensed/"off label" medicines transferred to primary care, the GP should be provided with following documented information:

- Rationale for the use of the medicine
- For unlicensed medicines, detailed information about the medicines to be prescribed (including sourcing, manufacturing and formulation where appropriate). Note: Trust pharmacy personnel may need to contact the patient's community pharmacist to provide the relevant information on sourcing the unlicensed medicine.
- A record of discussions that have been had with the patient, including patient consent
- Arrangements for monitoring and review.

Information on unlicensed medicines may also be found in the BNF/BNFC.

7. References:

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8. Acknowledgements

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