Packaging and labelling for safety: Unlicensed imported medicines - Guidance for the overlabelling and provision of translated information

Edition 2

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Authors

Mark Jackson
Lesley McAvoy
Sharon Jackson

Contributions from

Mark Santillo
Tim Root
Andrew Lowey
Lynn Morrison
Kay Pollock
Rob Lowe
Anne Black
Linda Hardy
Lauren Stewart

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Edition 1	National Requirements for the Overlabelling of Foreign (non-English language) Imported Medicines Unlicensed in the UK Issued December 2011
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Edition 3	
Edition 4	

1. Purpose

This document provides best practice guidance for overlabelling of imported unlicensed medicines and provision of translated leaflets in the UK. Its primary aim is to reduce the risk of medication errors by ensuring essential information relating to the medicines is in English and comprehensible to the healthcare professional.
This guidance will be of use to anyone purchasing, overlabelling or supplying imported unlicensed medicines, and obtaining or providing translated leaflets (patient information and user instructions).

2. Background

Medication errors are a leading cause of avoidable patient harm in healthcare systems. Medicines frequently require complex calculations and manipulation prior to and during their administration. Confusing labelling and instructions for their use have been frequently identified as contributing towards medication errors. This has been further highlighted in the May 2017 publication *WHO Global Patient Safety Challenge: Medication Without Harm*[1]*.*
There have been a number of initiatives to drive the improvement of packaging and labelling of medicines licensed in the UK. The MHRA produced *detailed Best Practice Guidance on the Labelling and Packaging of Medicines*[2]; however this is not applicable to imported unlicensed medicines, which present a significantly greater risk of medication error as the critical packaging and labelling

- may not be in English
- may have not been designed for safety in accordance with MHRA best practice guidance

3. Scope

This document refers only to unlicensed imported medicines, with regard to

- overlabelling
- provision of translated information e.g. package leaflets, patient information leaflets and SPCs.

It does not include medicines licensed in the UK (including Parallel Imports), UK manufactured Specials, or dispensing to individual patients.
It is recommended that this document is read in conjunction with NHS Pharmaceutical Quality Assurance Committee (PQAC) Edition 1 (2016): *Quality Assessment of Unlicensed Medicines*[3] and the MHRA's Guidance Note 14[4].

4. Guidance

4.1. Identifying the need for overlabelling and provision of translated information

a) Overlabelling:

Unlicensed imported medicines may need to be overlabelled to ensure that essential information is available to the user in English and/or to address any confusing or ambiguous English labelling on the packaging e.g. use of negative labelling; trailing zeroes; confusing labelling of strength; use of 'non-standard' abbreviations. It is permissible to overlabel small quantities in a dispensary[5], but for large quantities this operation should be carried out under a Manufacturing Specials licence and Good Manufacturing Practice (GMP).

- For overlabelling small quantities in dispensaries, an assessment should be made locally to identify what information is required, depending on how, where and by whom the medicine will be used. The information identified in section 4.2 should be considered for inclusion, but as a minimum this should include the critical information (section 4.2 a)).

- For batch overlabelling in MS licensed facilities, all the information in section 4.2 (a, b and c) should be included, and the label specification agreed between all relevant parties e.g. the MS holder, the importer, and the requesting/purchasing pharmacist.

See 4.2 and 4.3 below for further guidance on labels.

b) Provision of translated information

Purchasers of unlicensed imported medicines should ensure that they are provided with sufficient and validated English language information to label, quality assess, clinically evaluate and safely administer the medicine. Translated patient information leaflets or user information (e.g. SPCs) may also be required, if clinically appropriate.
See 4.4 below for further guidance on translated information where this is provided as part of a commercial batch overlabelling service.

4.2. Label design and content

The label should include:

a) Critical information, as defined by the MHRA Guidance[2] and the BP General Monograph for Unlicensed Medicines[6]:

- *The common name of the product*.

  The generic name should generally be given prominence over the brand name, except where the medicine is more appropriately prescribed by brand (e.g. Fumaderm 120mg whose generic name is 120mg dimethyl fumarate, 87mg ethyl hydrogen fumarate calcium salt, 5mg ethyl hydrogen fumarate magnesium salt, 3mg ethyl hydrogen fumarate zinc salt). This should be agreed between the purchaser, prescriber and overlabeller.

- *A statement of the active ingredients expressed qualitatively and quantitatively per dosage unit or for a given volume or weight*

  This should be expressed as for MHRA best practice for licensed medicines e.g. for injections, the strength should be expressed both as total quantity per total volume and as amount per unit dose (e.g. milligrams per ml) where appropriate. Base and salt strengths should be clearly defined where appropriate.

  For oral liquids the dose should be expressed per 5ml if this is a normal dose volume. Leading and trailing zeros should not be used. Fractions of milligrams should be stated in micrograms (unless there is a regulatory requirement e.g. when the medicine is part of a range including products containing 1 milligram or greater). “Micrograms” should be spelt out in full rather than abbreviated.

- *Route of administration*, for all medicines including the oral route

- *Instructions for use, including any special warnings*

  This should include any information that is needed to allow the product to be administered e.g. a specific volume of diluent for reconstitution, “shake the bottle” for suspensions, cytotoxic etc. Negative warnings should not be used.

  N.B. literal translations of the warnings on some cartons may not be appropriate, especially where the warning is expressed as a negative.

b) Other information required, as defined in the BP General Monograph for Unlicensed Medicines[6]:

- *The pharmaceutical form*
- *The contents of the container by weight, volume or by number of doses*
- *Excipients of known effect*[7]. For injectable, topical (including inhalation products) and ophthalmic medicines, all excipients
- *'Keep out of reach and sight of children'* (statutory requirement)
- *The expiry date expressed in unambiguous terms* (mm/yy)

  This will already be stated on the carton, so it is not necessary to repeat it on the overlabel provided it is in a format that will be readily understood.

- *Storage conditions,* ideally expressed as temperature range in degrees Celsius

  For products requiring reconstitution, e.g. dry powders for syrups, the expiry after reconstitution should be clearly expressed. An area on the label for "Date of Reconstitution" is advisable if space allows.

- *Special storage precautions*
- *Statutory warnings* required by The Human Medicines Regulations 2012 for particular actives, e.g. paracetamol (Schedule 25, Part 4 of the 2012 Regulations)

c) Information about the overlabeller, for traceability (N.B. in BP General Monograph for Unlicensed Medicines[6] refers to "Manufacturer", but this is changed to "overlabeller" in this document for clarity of meaning.

- The overlabeller's MS number
- The overlabeller's name and address
- The batch number (or "job number") assigned by the overlabeller for the specific batch overlabelling activity

d) "This medicine is unlicensed in the UK"

NB: the previous recommended wording was "This medicine is *not licensed* in the UK". The use of "unlicensed" is preferred, as it is aligned with MHRA terminology and is not negative labelling. It is recognised that importers and

overlabellers will be using the original wording on their label templates, so use of the new preferred wording will need to be implemented over time.

4.3. Label positioning

Labels should be positioned on the original pack so that they

- can be read in one field of view, or with minimal turning of the carton. Flag labelling may be needed to achieve this, however care should be taken when labelling eye drop primary containers to avoid the risk of injury to the patient

- do not cover the manufacturer's batch number, expiry date or marketing authorisation number (product licence in country of origin).

- Do not break the seal on FMD compliant packs

4.4. Translated information

Validated translated information should be

- a full and accurate translation of the original document
- comprehensive and legible
- current

It should be provided by a professional medical translation service, with

- ISO 17100 (or equivalent) accreditation and/or membership of a recognised translation association
- appropriate Professional Indemnity Insurance

For packs without a tamper evident seal, the purchaser may request that the original PIL/SPC/Insert is be removed and replaced with the validated translated PIL/SPC/Insert as part of the over labelling process.

Where packs are tamper evident sealed the PIL/SPC/insert should either be neatly attached to each individual pack ensuring over label details are not obscured, or supplied separately (one per individual pack). If the leaflet is attached, it is recommended that the method of attachment should be free from natural latex rubber, so that the pack would be suitable for a patient with latex allergy.

References

1. WHO Global Patient Safety Challenge: Medication Without Harm (May 2017) http://www.who.int/patientsafety/medication-safety/medication-without-harm-brochure/en/

2. Best Practice Guidance on the Labelling and Packaging of Medicines (MHRA 2014) https://www.gov.uk/government/publications/best-practice-in-the-labelling-and-packaging-of-medicines

3. NHS Pharmaceutical Quality Assurance Committee (PhQAC) *Quality Assessment of Unlicensed Medicines* Edition 1 (2016) https://www.sps.nhs.uk/wp-content/uploads/2016/11/QA-of-ULM.pdf (registration required)

4. Supply of unlicensed medicinal products (specials). MHRA Guidance Note 14 https://www.gov.uk/government/publications/supply-unlicensed-medicinal-products-specials

5. NHS Pharmaceutical Quality Assurance Committee (PhQAC) *Guidance on the Licensing Requirements of Prepacking and Overlabelling Operations* Edition 1 (2013) https://www.sps.nhs.uk/wp-content/uploads/2013/07/Prepacking20and20Overlabelling20Guidance202013.pdf (registration required)

6. British Pharmacopoeia General Monograph for Unlicensed Medicines (subscription required) https://www.pharmacopoeia.com/bp-2018/formulated-general/unlicensed-medicines.html?date=2018-04-01&text=unlicensed

7. European Commission Guideline on Excipients in the labelling and package leaflet of medicinal products for human use (March 2018) http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_001683.jsp&mid=WC0b01ac05808c01f6