



**Statement on the use of
unlicensed medicines or
licensed medicines for
unlicensed uses in critically
ill patients**

Neither the Intensive Care Society nor the authors accept any responsibility for any loss of or damage arising from actions or decisions based on the information contained within this publication. Ultimate responsibility for the treatment of patients and interpretation of the published material lies with the medical practitioner. The opinions expressed are those of the authors and the inclusion in this publication of material relating to a particular product or method does not amount to an endorsement of its value, quality, or the claims made by its manufacturer.

Prepared on behalf of the Council of the Intensive Care Society by:

Dr G R Park Cambridge University Hospitals NHS Foundation Trust
Mr M Borthwick Oxford Radcliffe Hospitals NHS Trust

1 Introduction

The Intensive Care Society recognizes that both licensed medicines used outside the terms of their Marketing Authorisation and unlicensed medicines are needed for effective treatment of the critically ill. This statement aims to inform and guide health professionals who prescribe, dispense or administer medicines to critically ill patients (and health service managers) about the use of unlicensed medicines or licensed medicines for unlicensed uses in critically ill patients.

- 1.1 Those prescribing for the critically ill should choose products which offer the best prospect of clinical benefit, with the lowest administration risk profile and with due regard to cost. Licensed products should be the first choice where they are fit for purpose.
- 1.2 Licensed products are developed for specific markets and may not be suitable for use in the critically ill within the terms of their marketing authorization.
- 1.3 The informed use of unlicensed medicines or use of licensed medicines outside the terms of the marketing authority is therefore essential for good patient care.
- 1.4 Health professionals must have ready access to and use sound information on any medicine they prescribe, dispense or administer, including information on its availability.
- 1.5 NHS Trusts, Health Authorities and care providers in the private sector should support therapeutic practices that are advocated by a respectable, responsible body of professional opinion.

2 Use of Licensed Medicinal Products

- 2.1 For a medicinal product to be marketed in the United Kingdom it must have received a marketing authorisation (previously termed Product License). It is then said to be licensed.
- 2.2 The manufacturer may then market the product for the approved indications, using the approved formulation, etc. The Summary of Product Characteristics (formally Data Sheet) sets out the approved details.
- 2.3 Use of the product outside of the details specified in the Summary of Product Characteristics is use outside of the marketing authorisation.
- 2.4 The manufacturer is unlikely to be found liable for any harm caused by a medicine that has been used outside of the marketing authorization unless any harm arises out of a defect in the product itself.

3 Use of Licensed Medicinal Products outside the terms of the Marketing Authorisation ('Off-label')

- 3.1 Many licensed medicines used in the critically ill are used outside of the terms of the Marketing Authorisation (specified in the Summary of Product Characteristics) such as an unauthorised indication or method of administration.
- 3.2 Licensed medicinal products are used in this way when no pharmaceutically equivalent licensed product or suitable alternative product is available for use at the time the patient requires it.
- 3.3 The risk surrounding the use of these products is generally low because the manufacturer assures the quality, safety and efficacy of the product. However, specific risks may be presented by the way the product is used.
- 3.4 The off label use of medication must be within the scope of an established body of medical opinion.
- 3.5 New and emerging practice must be agreed by the wider multi-professional team before introduced into routine practice and a formal risk assessment may be carried out to support such practice.
- 3.6 The use of a medicinal product outside the terms of the marketing authorization remains the responsibility of the prescriber.
- 3.7 **The risk of using these products has generally been judged to be low. No patient consent, completion of an additional clinical/product risk assessment or pharmacy record of dispensing should normally be required when prescribing a drug to be used in this way. Additional controls may be required where specific risks are presented by the way the product is used for new and emerging practice.**

4 Use of Unlicensed Medicinal Products

- 4.1 Unlicensed medicinal products are normally only used when no pharmaceutically equivalent licensed product or suitable alternative licensed product is available for use at the time the patient requires it. They do not carry the same guarantee of safety, quality or efficacy of a licensed medicinal product.
- 4.2 Unlicensed use of such medicines is the responsibility of the prescriber.

- 4.3** The Hospital Drug and Therapeutics Committee is responsible for the governance of the prescribing and administration of unlicensed medicines (MHRA Guidance Note 14).
- 4.4** The Pharmacy is responsible for the procurement and quality of sourced unlicensed medicines.
- 4.5** A risk assessment should be performed before the product is prescribed

In the first instance the use of an alternative licensed product should be sought. Where this is not possible, a risk assessment should examine the following elements.

- The clinical pharmacology of the requested medicine including contraindications, side effects and the potential for harm.
- The demonstrable quality of the product to be procured.

Products are assigned a risk status using similar categories to those established by the National Patient Safety Agency (NPSA). The risk assessment of an unlicensed medicine is a two-stage process using the following grading systems;

Assessment of risk of harm from clinical pharmacology of unlicensed medicine

| Category of risk | Risk |
|---|-----------------|
| None. No obvious harm No obvious contra-indications for use | Low |
| Non-permanent harm to include side effects which are transient and/or readily manageable Some contra-indications for use | Minor |
| Non-permanent harm to include significant side effects. Significant contra-indications for use | Moderate |
| Harm due to permanent or long-lasting side effects. | Major |

Assessment of risk of harm from the pharmaceutical quality, the preparation and administration of the unlicensed medicine

| Characteristics | Risk |
|---|-----------------|
| Product from within an ICH* country. Quality of preparation including packaging and patient information leaflet (PIL) comparable to that of a licensed product from the UK | Low |
| Product from within an ICH country. Quality of preparation supported by documentation / Packaging and information leaflet in a language other than English. | Minor |
| Packaging and information leaflet unlikely to be in English / | Moderate |

| | |
|--|--------------|
| Complex manipulation required to administer | |
| Manufactured in a non-ICH country with little supporting documentation. Possible risk of counterfeiting / Highly complex manipulation required to administer | Major |
| <i>*ICH – International Conference on Harmonization (covering areas of pharmaceutical regulation; members include the EU, USA, Canada and Australia)</i> | |

5 Specific types of unlicensed medicines

5.1 Medicines prepared by a manufacturer, but not on sale in the UK

These products may be awaiting the grant of a Marketing Authorisation, be manufactured for clinical trials or for export, or may have been withdrawn from the UK market. Such products may be obtained from the manufacturer, or through a specialist importer.

If the medicine is to be used for the treatment of a particular patient, it may usually be obtained from the manufacturer on an individual patient basis. The manufacturer has no justification for demanding individual patient names, hospitals divulging such information may be breaking patient confidentiality. However, the Hospital should keep detailed records of the purchase of these products.

Products no longer marketed in the UK due to safety concerns should be deemed moderate risk as a minimum.

A clinical and product risk assessment will be required for all products within this classification and patients will need to be consented if the drug to be used has either a product or clinical risk assessment of moderate or major.

5.2 Unlicensed medicines obtained from a manufacturer or hospital pharmacy with a Specials Manufacturing License.

These medicines ("Specials") will have been specially prepared by the holder of a NHSPQA approved Manufacturers Specials License, or imported in response to, or in anticipation of the order of a doctor or dentist to meet the special needs of individual patients.

No clinical or product risk assessment, pharmacy dispensing record or patient consent required for any drug prescribed in this way. The product risk grading for these products will normally be graded as LOW.

5.3 Re-packed medicines

The Marketing Authorisation for a medicine regulates not only its formulation and manufacture but also the container in which it is sold. When the item is either repacked, it becomes an unlicensed product. However, this is of little significance to prescribers as the medicine has been manufactured and sold in accordance with its Marketing Authorisation.

No clinical or product risk assessment, pharmacy dispensing record or patient consent is usually required for any drug prescribed in this way.

6 Documentation

6.1 Introduction

Usually no patient consent or pharmacy record of dispensing is required for any unlicensed drug classified with a clinical and/or product risk assessment of low or minor. This includes all unlicensed drugs kept as stock on wards and units within an ICU. Only those unlicensed drugs prescribed which have a moderate or major clinical and/or product risk assessment need patient consent or relatives assent and a pharmacy dispensing record.

6.2 Recording in patients' notes

There must be a record in the patient's notes of the use of any unlicensed drug which is classified with a clinical and/or product risk of moderate or major and written consent is recommended.

6.3 Reporting of Adverse Drug Reactions

Doctors or pharmacists should report serious adverse drug reactions to the MHRA using the existing Yellow Card System (copies available in the BNF) and also to the Hospital Drugs and Therapeutic Committee.

Implementation date: January 2009

Review date: January 2011