



Use of unlicensed medicines in the UK

by Dipti Amin

Dipti Amin is the Pharmaceutical Services Manager at Durbin plc. Her pharmaceutical training and experience includes over eight years facilitating the importation of unlicensed medicines, and over 10 years in the NHS and retail pharmacy.

All medicines in the UK are governed by strict checks and guidelines to make sure they are safe and effective. Once all the required safeguards are satisfied, the medicine receives a marketing authorisation (a product licence). The medicine can then be prescribed for the specific indication granted in its product licence.

For a medicine to receive marketing authorisation, the pharmaceutical company has to:

- Conduct clinical trials in humans;
- Show that it works for the illness it was developed for and has a good safety profile;
- Manufacture it to a high standard.

This data is submitted to the Medicines and Healthcare products Regulatory Agency (MHRA), who grants a marketing authorisation once all the information is assessed and approved.

However, there are many occasions where clinicians feel the need to use a medicine that does not have a UK marketing authorisation. These days, there is greater access to information about pharmaceutical companies' drug pipelines and clinical trials – both in the media and online. This has led to an increased awareness by patients, physicians and patient organisations contributing to an increased demand for unlicensed medicines.

This article reviews the use and importation of unlicensed medicines, and the regulations governing the use of such medicines in the UK.

Unlicensed medicines

An unlicensed medicine is any medicine that does not have a UK marketing authorisation, and examples of their use include:

- Medicines that are manufactured outside the UK and have a marketing authorisation in the country of origin, but are awaiting a marketing authorisation in the UK;
- Medicines that are manufactured outside the UK and a UK licence has not been applied for e.g. where the prevalence of the disease in the UK is so low as to make the product not commercially viable;
- Medicines manufactured in the UK

that may not yet have been granted a UK marketing authorisation or may still be undergoing clinical trials;

- Medicines discontinued in the UK market;
- Medicines encountering UK supply shortages;
- Specials manufactured by a supplier with a manufacturer's special licence.

These unlicensed medicines can be imported/used in the UK for the 'special needs' of an individual doctor's patient. This is known as 'named patient' supply. Unlicensed medicines can only be prescribed by physicians if they are satisfied that there are no suitable licensed alternatives. Pharmacists can then dispense such medicines, while nurses and midwives can administer them to patients.

Importation of unlicensed medicines into the UK

The importer of an unlicensed medicine (that has a marketing authorisation in an EC country) must have a UK Wholesale Dealer's Licence (WDL). Where the medicine to be imported comes from a country outside of the EC, the importer must hold a Wholesale Dealer's Import Licence (WI) as well as a WDL. The MHRA is currently going through a process of incorporating these licences into a single Manufacturer's/Importer's Authorisation (MIA).

The importer has to notify the MHRA of their intention to import a particular medicine no later than 28 days before each importation, and supply the following information:

- The generic or brand name of the product;
- Formulation, strength and pack size;
- Name of the product licence holder;
- Country of origin.

There are strict guidelines governing the promotion of all medicines in the UK. Pharmaceutical companies, importers or distributors cannot promote an unlicensed medicine or a licensed medicine for any off-label use. The importer cannot advertise or publish a price list for unlicensed medicines even if requested by a pharmacist.

Once an unlicensed medicine *has* received a UK marketing authorisation, the importer can no longer import or supply the product. Similarly, if a UK supply shortage issue is resolved, the importer cannot continue supplying the unlicensed medicine.

Liability

The physician or the prescriber is responsible for the use of the unlicensed medicine and for any harm to the patient due to side-effects or adverse reactions. The medicine should be prescribed with the patient's consent.

Most of the initiation and dispensing of unlicensed medicines occurs in hospitals. However, once the patient has been discharged, the responsibility for repeat prescribing is passed to the GP. This leads to prescriptions for unlicensed medicines being presented to retail pharmacies.

The pharmacist's role is to ensure the suitability and quality of the unlicensed medicine. Therefore, the pharmacist has a duty of care to make certain these criteria are satisfied and to reduce any risks of counterfeit medicines entering the supply chain. Reputable importers should be used to assure product quality and full batch traceability. If the imported medicine is licensed in its country of origin, and if that country operates

similar standards of Good Manufacturing Practice (GMP) and regulatory control to the UK, then the product may be regarded as low-risk (e.g. products originating from EU countries, Australia and New Zealand). However, if the product supplied by an importer is from another country or it is an unlicensed medicine in its country of origin, then this should be regarded as high risk. If this is the case, the importer will need to perform a number of mandatory checks to ensure that the product has been manufactured in compliance with GMP and EU Transmissible Spongiform Encephalopathy (TSE) guidelines.

Patient information leaflets and over-labelling

There is no legal requirement in the UK for suppliers of unlicensed medicines to provide patient information leaflets written in English. However, the pharmacist has a duty of care to the patient to provide information on side-effects, adverse reactions and possible contra-indications. Unlicensed medicines that are not labelled in English pose a greater risk than those that are supplied in English. It is, therefore, prudent to use reputable suppliers of unlicensed medicines as these companies will work with the product licence holder and may facilitate English translations.

Reimbursement

Pharmacists can claim for reimbursement for unlicensed medicines supplied on a 'named patient' basis from the prescription pricing authorities (PPA) if the UK product is not available and there are no suitable alternatives either. The process for this is to send a copy of the invoice supplied by the importer to the PPA. Postage and packing can be claimed as an out-of-pocket expense.

Record-keeping

When a pharmacist receives a prescription for an unlicensed medicine, they will contact a specialist importer or distributor to confirm its availability. It is essential to choose an importer/distributor that can demonstrate audit trails through the entire supply chain. Equally, it is vital for the pharmacist to keep records for supplies of imported medicines e.g. the name of the product, patient name, date when supplied, quantity, batch number and the expiry, in case of a recall or an adverse event.

Regulations under review

The MHRA has started a review of the regulations governing the manufacture, importation, supply and administration of unlicensed medicines in the UK but the outcome of this review is not expected until the end of 2009. ■