Impregnated dressings: Drugs or devices?

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1 From 30 October 2005 the definition of a 'medicinal product' has been amended. The changes to the definition add focus to the mode of action by which medicinal products are expected to work.

2 When developing new products to treat the diabetic foot it is crucial to take the regulatory process into account and decide at an early stage if the product is going to be classified as a device or a drug substance.

3 The regulatory and reimbursement process to bring novel products to the market in Europe and the UK is becoming increasingly onerous for manufacturers.

KEY WORDS

- Medicinal product
- Medical device and drug substance
- Updated definition
- Mode of action
- Regulatory process

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Introduction

This article outlines the main legal and regulatory aspects concerning the registration and reimbursement of drugs and dressings in caring for the diabetic foot in the UK. When inventing or developing a novel product or treatment, it is essential to understand the regulatory system for both drugs and devices if a new product is to be brought to the UK market in a timely and cost-efficient manner. Key aspects of medicinal product and medical device registration and reimbursement issues are described.

From 30 October 2005 the definition of a 'medicinal product' has been amended. Article 1 of the original Directive, 2001/83/EC, defines a 'medicinal product' as (The European Parliament and The Council Of The European Union, 2001):

> ***'[a] Any substance or combination of substances presented as having properties for treating or preventing disease in human beings.***
>
> ***[b] Any substance or combination of substances which may be [used in or] administered to human beings [either] with a view to [...] restoring, correcting or modifying physiological functions [by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis].'***

The paragraph identifications ('a' and 'b') are not part of the definition and are added here solely for ease of reference. Changes to the definition that came into effect from 30 October 2005 are underlined and in square brackets to aid identification.

Medicinal products may well fall under both categories of the definition, but the European Court of Justice has confirmed that falling under either category is sufficient to classify a product as a medicinal product (The European Court of Justice, 1989).

> ***'Directive 65/65 provides two definitions of the term "medicinal product": one relating to presentation, the other to function. A product is medicinal if it falls within either of those definitions.'***

(Since February 2002 the definition of a medicinal product has been contained in the Codified Pharmaceutical Directive 2001/83/EC, and all references to Directive 65/65/EC [The European Parliament and The Council Of The European Union, 1965] should be read accordingly.)

The changes to the definition add focus to the mode of action by which medicinal products are expected to work. The Medicines and Healthcare products Regulatory Agency (MHRA) does not believe that the changes to the definition will have a major impact on the classification of products in general (personal communication, MHRA representative). It is likely that products on the medicines–device borderline are the most likely to be affected. The MHRA's Medicines Borderline Section will not be undertaking a general review of decisions in light of the change to the definition, but device companies should, in the author's opinion, seek advice in cases where they believe that a product may now fall outside medicines regulations.

What is a medical device?

The Medical Device Directive 93/42/EEC defines a medical device as follows (The European Parliament and The Council Of The European Union, 1993):

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1 For a product to be regarded as a medical device it must have a physical or mechanical primary mode of action, but may be assisted in achieving its intended action by pharmacological, immunological or metabolic means.

2 Impregnated dressings can be classified either drug or devices. As a general rule, the dressing would be regarded as a device, but the active substance being delivered would usually be considered a drug substance.

3 Many impregnated dressings have been registered as medical devices, but as a result no medicinal claims can be made. Thus it is difficult, and some would say impossible, to measure the relative efficacy of such products.

4 Whether new products are going to be classified as device or drug substance not only dramatically affects the development costs and time to market, but also has an important effect on reimbursement in the UK.

5 As a general guide it is much cheaper and faster to develop and bring devices to market via the CE marking process, compared with drugs.

'[...] any instrument, apparatus, appliance, material or other article, whether used alone or in combination, including the software necessary for its proper application intended by the

manufacturer to be used for human beings for the purpose of:

- ***diagnosis, prevention, monitoring, treatment or alleviation of disease,***
- ***diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap,***
- ***investigation, replacement or modification of the anatomy or of a physiological process,***
- ***control of conception,***

and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means.'

That is, for a product to be regarded as a medical device it must have a physical or mechanical primary mode of action, but may be assisted in achieving its intended action by pharmacological, immunological or metabolic means.

Thus a heparin-coated catheter is a medical device even though it contains a drug substance because the primary mode of action is mechanical (the channelling of body fluids). Interestingly, catheter patency solutions containing chlorhexidine, for example, are medical devices because the primary intended function is to maintain the physical and mechanical characteristics of the catheter or tube rather than to directly treat the ailment.

Devices designed to deliver a medicinal substance, such as impregnated dressings, can be classified as either a 'drug' or a 'device', depending on the claims made by the manufacturer. As a general rule a dressing would be regarded as a device, but the active substance being delivered would usually be considered a drug substance.

Many impregnated dressings have been registered as medical devices, but as a result no medicinal claims can be made. Thus it is difficult, and some would say impossible, to measure the relative efficacy of such products.

Developing new products for the diabetic foot

When developing new products to treat the diabetic foot it is crucial to take the regulatory process into account and decide at an early stage if the product is going to be designed to be classified as a device or a drug substance. This not only dramatically affects the development costs and time to market, but also has an important effect on reimbursement in the UK.

In simple terms, products that have the benefit of a marketing authorisation or drug approval are automatically reimbursed with regard to cost. On the other hand, medical devices, even with the benefit of a CE marking (visit www.dti.gov.uk/innovation/strd/cemark/page11646.html for a full explanation of CE marking [accessed 06.09.2006]), are not automatically reimbursed.

As a general guide, compared with drugs, it is much cheaper and quicker to develop and bring devices to market via the CE marking process. However, the reimbursed prices that can be charged for medical devices are generally lower and less profitable than those for drugs.

Medical devices that contain drug substances are normally placed in the Class III risk category (which is reserved for 'the most critical devices for which explicit prior authorization with regard to conformity is required for them to be placed on the market' [The European Parliament and The Council Of The European Union, 1993]). This means that the product must be assessed by both a Notified Body (such as the British Standards Institution [BSI]) and a pharmaceutical regulatory authority. This process can be expensive and slow, plus the added disadvantage is that listing in the Drug Tariff is not automatic.

Drug Tariff

The Drug Tariff is the Secretary of State's limited list of appliances, in vitro diagnostics and borderline substances that may be prescribed at the NHS's expense, although NHS hospital trusts are not bound by this limited list. However, failure to obtain listing in the Drug Tariff means that patients discharged from hospital will not be able to obtain further supplies, at the NHS's

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1 The Drug Tariff lists borderline substances that may be defined as substances that are not registered as drugs, but may be used as though they are drugs.

2 The National Institute for Health and Clinical Excellence (NICE) advises professionals as to which products and treatments are clinically and cost effective.

3 The advent of the Medical Device Directive has made it much cheaper and faster to bring new anti-bacterial substances to market. Thus there is now a much wider range of products for treating the diabetic foot, where infection is considered to be a serious problem.

4 New or advanced wound care products placed on the market as medical devices rarely have credible research to support their efficacy, compared with cheaper and more traditional dressings.

expense, from their GP or nurse prescriber.

Once a new medical device has obtained the benefit of a CE marking and it is going to be used on human beings then application has to be made for listing in the Drug Tariff.

Borderline products and issues

The Drug Tariff lists borderline substances that may be defined as those that are not registered as drugs but may be used as though they are drugs, subject to the approval of the Advisory Committee on Borderline Substances (ACBS; National Institute for Health and Clinical Excellence [NICE], 2006). Many foods for people with diabetes are ACBS listed.

National Institute for Health and Clinical Excellence

NICE advises healthcare professionals as to which products and treatments are clinically and cost effective. NICE was set up to avoid the problems of post code prescribing, where a treatment (usually expensive) was available in one trust but not in another.

NICE is often in the national press, as many expensive treatments indicated for life-threatening conditions are often denied even when they are properly licensed. NICE usually becomes involved where novel and expensive drugs, such as herceptin, are used outside their approved clinical indications.

Advanced wound care products

Many advanced wound care products are used to treat the diabetic foot. If they are registered as medical devices, their primary mode of action is mechanical or physical and thus they treat chronic wounds by secondary intent.

It is questionable as to whether any of the suppliers of such products can legally make credible claims of 'faster wound healing', especially where people with diabetes are involved. To legally make such claims, a marketing authorisation is required. Few manufacturers have bothered with the cost and delays of obtaining one. There is little high quality published evidence that any 'advanced wound care product' has benefits over cheaper and more traditional products.

Antibacterial substances

There are many new antibacterial wound irrigation solutions, registered as medical devices, that are under development or have recently been launched. The advent of the Medical Device Directive (The European Parliament and The Council Of The European Union, 1993) has made it much cheaper and faster to bring new antibacterial substances to market. Thus there is now a much wider range of such products for treating the diabetic foot, especially where infection is considered to be a serious problem.

Conclusions

The regulatory and reimbursement process to bring novel products to the market in Europe and the UK is becoming increasingly onerous for manufacturers. The commercial risks are therefore increased. New or advanced wound care products placed on the market as medical devices rarely have credible research to support their efficacy and efficiency, compared with cheaper, and more traditional, dressings.

Sadly, little, if any, serious research is being funded by manufacturers to develop genuinely novel treatments for the diabetic foot. It is perhaps the role of the healthcare professional involved in treating the diabetic foot to develop new concepts and treatment regimens for this condition. ■

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