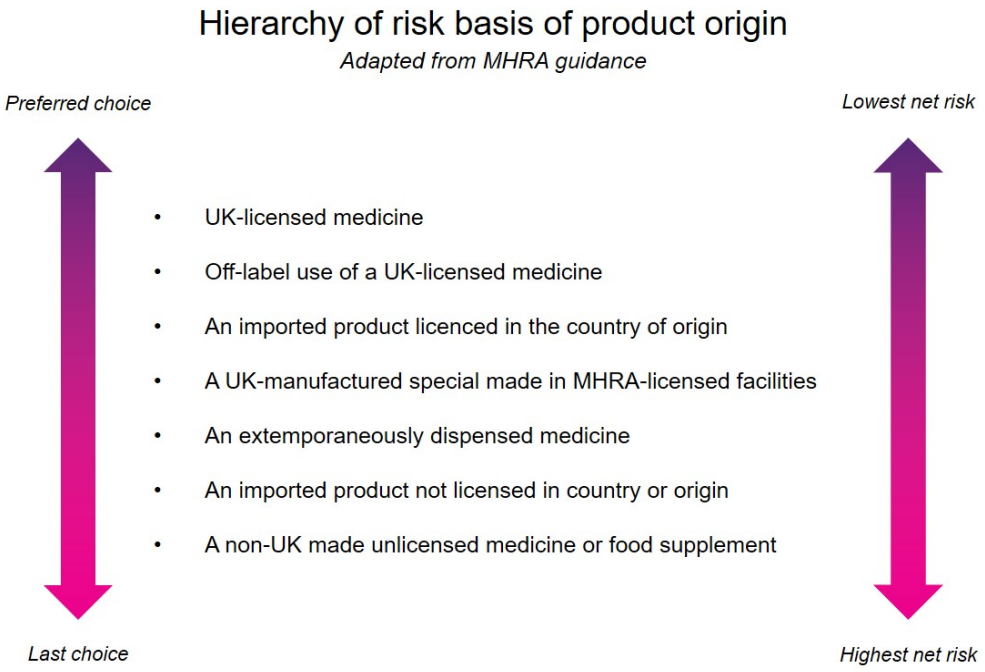
Policy position *the use of 'unlicensed specials' to treat NHS patients*

Summary

The ABPI recognises that there are occasions where the use of unlicensed medicines is required in the best medical interests of individual patients. As set out in medicines regulations and professional guidance, these circumstances should be limited to occasions where there is no suitable licensed alternative available.

Patients should always be informed of the unlicensed status of the medicine. The figure below gives some top-line information on key considerations on the prescribing of medicines outside of their license.



Where a medicine meeting a need previously only met by a special is granted a license, NHS Trusts should replace recommendations for specials with the licensed alternative, unless there are overwhelming clinical reasons not to.

Specials manufacturers should not supply specials in these circumstances without a clear indication from the physician that the licensed product is unsuitable for the patient. Patients should be informed of the availability of a licensed medicine.

On no account should unlicensed medicines be used where a licensed medicine is available for reasons of cost. Local NHS organisations advocating this are potentially compromising patient safety, undermining the medicines licensing system that exists to protect patients, and disincentivising the development of new medicines.

Background

What is a 'special'?

'Specials' is a term used for a range of medicines that do not hold a marketing authorisation in the UK, and which are offered to a patient when the physician has identified a clinical need that cannot be met by any available licensed alternative. It covers the following:

- Medicines manufactured by a holder of a Manufacturer's Specials (MS) license from the MHRA in multiple quantities with end-product analytical testing
- A bespoke medicine produced by a MS License holder that has not undergone end product analytical testing
- An extemporaneously prepared medicine made in a pharmacy under a pharmacist's direct supervision (a MS license is not required for this)
- A licensed medicine imported from another country which does not have a UK license
- An unlicensed medicine imported from another country

Regulatory framework

EU Directive 2001/83[1] sets out the legislative framework for medicines and its purpose to protect public health. It requires that only medicines with a positive risk-benefit ratio, determined through an evaluation of evidence of their safety, efficacy and manufacturing quality, may be granted a marketing authorisation (product license) and approved for use in patients.

In the UK, an unlicensed medicine may only be supplied in accordance with the provisions of Schedule 1 of The Medicines for Human Use (Marketing Authorisations Etc.) Regulations 1994.[2]

Schedule 1 provides an exemption from the need for a marketing authorisation for some medicines, because some patients may have special clinical needs that cannot be met by licensed medicines. To meet these special needs, the law allows the manufacture and supply of specials where:

- there is a bona fide unsolicited order;
- the product is formulated in accordance with the requirement of a doctor or dentist registered in the UK and it is for use by their individual patients on their direct personal responsibility; this process is under the supervision of the Royal Pharmaceutical Society (RPS).

If a special is manufactured in the UK, the manufacturer must hold a manufacturer's (specials) license issued by the MHRA. A special may not be advertised and may not be supplied if an equivalent licensed product is available which could meet the patient's needs. Good Manufacturing Practice must be followed, essential records kept, and suspected adverse reactions reported to the MHRA[3].

[1] Directive 2001/83, pages 67-128. (European Union, Nov 2004)
[2] Schedule 1 of The Medicines for Human Use (Marketing Authorisations Etc.) Regulations 1994 [SI 1994/3144]
[3] Guidance: Supply unlicensed medicinal products (specials) (HM Government, MHRA, Oct 2018)

Professional guidance supports the legal framework. The General Medical Council (GMC) advises[4] that before prescribers use medicines outside of their license they must be satisfied:

> *"…that it would better serve the patient's needs than an appropriately licensed alternative…"*

and

> *"… that there is a sufficient evidence base and/or experience of using the medicine to demonstrate its safety and efficacy…"*

The GMC Good practice in prescribing and managing medicines and devices (2013)[5] provides guidance in a section for prescribing of unlicensed medicines which states unlicensed medicines may be prescribed on the basis of an assessment of the individual patient, where concluded, for medical reasons, that it is necessary to do so to meet the specific needs of the patient.

The RPS gives similar advice[6] to pharmacists dispensing specials, saying that appropriate standard operating procedures should be in place for dispensing services, which include the supply of a product with a marketing authorisation, where such a product exists in a suitable formulation and is available, in preference to an unlicensed product.

There is a guidance by the RPS for prescribers of specials[7] which is based around principles that can be used to guide prescribing decisions and includes case studies that illustrate the challenges that are met to ensure that patients receive optimal treatment.

Use of specials on cost grounds

There are circumstances when NHS Trusts recommend the use of specials in preference to a licensed medicine for the same condition. In some cases, this is on the basis of relative cost. A judgment in 2012 in the European Court of Justice[8] has helped to clarify the legal position on government-sponsored organisations advocating the use of unlicensed medicines on cost grounds by finding that exceptions relating to special needs apply to therapeutic and not financial considerations.

Similarly, in 2018 is the case[9] specifically around the choice to prescribe an unlicensed medicine based on the grounds of cost, as evident in the scenario of the Judicial Review decision on access to medicines for wet Age-related Macular Degeneration (AMD). There are potentially significant implications for the regulation of medicines and patient safety arising from this judgment.

The ABPI position on the promotion of off-label or unlicensed use of medicines by healthcare bodies highlights the following:

- Off-label use of medicines is an important treatment choice for healthcare professionals in meeting the therapeutic needs of patients where no licensed medicine is available for that indication
- Off-label and unlicensed use of medicines presents a potentially greater risk to the patient, and therefore any decision to prescribe must carefully assess the benefit-risk for the patient to be treated
- Promotion of off-label or unlicensed use/supply for financial reasons, by healthcare bodies or governments, puts both patient safety and the continued robustness of the European regulatory framework at risk as well as establishes double standards for regulatory

[4] Good Practice in Prescribing Medicines (GMC, Sep 2008)
[5] Good practice in prescribing and managing medicines and devices (2013) (GMC, 2013)
[6] Good Practice Guidance on: The Procurement and Supply of Pharmaceutical Specials (RPS, Jun 2011)
[7] Prescribing Specials: Guidance for the prescribers of Specials (RPS, Apr 2016)
[8] Judgment in Case C-185/10 (Court of Justice of the European Union, Mar 2012)
[9] Judgment in Case No: CO/5288/2017 (Royal Courts of Justice, Sep 2018)

requirements that will undermine incentives for the development of new medicines and indications for existing medicines

Based on the above points, any approach that is in favour of off-label or unlicensed supply of a medicine for economic reasons only (that is, in the case where alternative medicines licensed for that indication are available) consequently puts the patient at a potentially higher level of risk and this stands in contrast with existing regulatory guidance in the UK and is not keeping with the system for the regulatory approval of medicines in Europe.

Therefore, it raises concerns as it relates to patient safety, and the role of the regulatory systems in protecting patients and ensuring safe use of medicines as well as risk management plans and ongoing pharmacovigilance after a medicine is licensed.

Pharmaceutical innovation

It costs over £1 billion and 12-15 years to research and develop a new medicine, to generate the evidence required by the regulatory authority and to put it through the licensing process. The use of specials in preference to licensed medicines undermines the regulatory process designed to protect patients and disincentivises the development of new medicines.

The ABPI only supports the use of unlicensed medicines where an appropriately licensed medicine would not meet a patient's specific needs not on the grounds of cost; where prescribing needs to be in accordance with standards set out by the MHRA and GMC.[5]