

# Professional Guidance for the Procurement and Supply of Specials

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# FOREWORD

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This professional guidance for the procurement and supply of pharmaceutical Specials is an update of Royal Pharmaceutical Society guidance first published in 2012. This guidance aims to support pharmacists and their teams to work with prescribers, patients and carers to ensure the safe and appropriate procurement and supply of Specials. Optimising the treatment of all patients for whom no suitable licensed medicine is available, regardless of the care setting where the patient is being treated.

The updated guidance reflects regulatory changes, such as the update to the Medicines and Healthcare Products Regulatory Agency Guidance Note 14, changes in clinical practice and the challenges that the constantly changing NHS environment presents. Increasingly, community and hospital pharmacists now buy Specials rather than preparing medicines extemporaneously within the pharmacy. There has also been steady growth in use of homecare services to dispense and supply ready to administer medicines, many of which are Specials, to patients at home. This update therefore also reflects an increased focus on governance to ensure that Specials are always procured and supplied safely and appropriately.

The use of Specials presents the NHS and patients with specific challenges, particularly when patients move between care settings. The importance of ensuring that patients and prescribers are aware of the complexities and risks associated with transferring the prescribing and supply of Specials across settings is also emphasised in this guidance.

Decisions about the prescribing, supply and procurement of Specials rely heavily on professional judgment based on understanding individual patient need. To reflect that we have re-designed the guidance to provide five principles that support professional practice, along with case studies that illustrate the challenges we have

to meet to ensure that patients receive optimal treatment. Whilst this guidance focuses on the use of Specials, the principles are broadly applicable to other unlicensed medicines that pharmacists may be required to supply.

To further support pharmacists (and prescribers) in the supply of unlicensed medicines, NHS Pharmaceutical Quality Assurance specialists are developing an Unlicensed Medicines Handbook that will contain more detailed support and resources for pharmacists and their teams.

To support the appropriate prescribing of Specials, the Royal Pharmaceutical Society will also be updating guidance for the prescribers of Specials. This guidance will support prescribers to make effective decisions about the prescribing of Specials and will be complementary to this guidance for pharmacists and their teams. Prescribers and pharmacists both have a responsibility to ensure that where Specials are prescribed they are the most appropriate choice and patients are supported to use them safely and effectively.

I hope that this professional guidance will support you in your daily practice and enable you to help your patients get the most from their medicines.



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# I. INTRODUCTION

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Specials are a category of unlicensed medicines that does not have either a centrally authorised Marketing Authorisation in the European Union, or a UK Marketing Authorisation and are manufactured, imported or distributed to meet the special clinical needs of an individual patient (see also Definitions).

A Special may only be supplied when there is no available licensed medicine which fully meets the patient's special clinical needs. Specials can be prescribed when it is judged by the prescriber and agreed with the patient or carer that, on the basis of available information, a Special is the most appropriate option for the patient<sup>1, 2</sup>.

Whilst there are several other categories of unlicensed medicines, this professional guidance relates primarily to the procurement and supply of Specials. Other categories of medicines not directly in the scope of this guidance include:

- Medicines used outside the terms of their Marketing Authorisation (commonly referred to as 'off-label' use);
- Medicines rendered unlicensed when the dosage form is manipulated, for example, crushed tablets/opened capsules (see separate RPS guidance<sup>3</sup>); and
- Extemporaneously dispensed medicines prepared in a pharmacy<sup>4</sup>.

Whilst this professional guidance focuses on procurement and supply only, it should not be viewed in isolation from the prescribing decision. A pharmacist shares with the prescriber accountability for supplying a Special to a patient. Pharmacists have a professional responsibility to liaise with the prescriber and the patient or carer to ensure that a Special is (and remains) the most appropriate choice; for example, a different licensed medicine in the same class or a different class of medicine may be suitable for the patient, a newly licensed medicine may have become available, or the patient's condition may have changed.

There is a range of diverse clinical situations where a Special may be judged to be the most appropriate option. For example, Specials may be the only available option for children and in some circumstances are routinely prescribed to achieve the lower doses required<sup>5</sup>. In dermatology and ophthalmology where a large number of Specials are in use, rationalised formularies have been produced to improve access to and improve the prescribing of Specials<sup>6, 7</sup>. For patients who require alternatives to solid dosage forms that are not available as a licensed oral liquid, for example those patients with PEG and naso-gastric tubes, a Special is one of a range of options available<sup>8, 9</sup>.

Prescribing any category of unlicensed medicine may carry benefits but is associated with the potential for additional risks compared to prescribing licensed medicines. Procurement and supply decisions will therefore depend heavily on pharmacists exercising their professional judgment for individual patients<sup>10</sup>. They must be able to demonstrate that they have acted with due diligence with regard to the patient's safety and requirement for effective treatment, and that they have taken all reasonable steps to ensure: procurement from an appropriate source; that the product is of appropriate quality; that relevant records are kept and adverse events are reported.

This is of particular importance when patients are having their care transferred from one care setting to another<sup>11</sup> where responsibility for prescribing and/or supplying the Special may change. In these cases there must be a clear transfer of information that ensures a safe, consistent and timely supply of the Special for the patient<sup>12, 13</sup>.

This professional guidance (which consists of five guiding principles) is aimed at supporting pharmacists and their teams to work with prescribers, patients and carers in the safe and appropriate procurement and supply of Specials.

Section 3 provides a definition of a Special and other terms used in this guidance. Readers should familiarise themselves with these definitions before reading the rest of this document.

## 2. FIVE PRINCIPLES FOR THE PROCUREMENT AND SUPPLY OF SPECIALS

The Royal Pharmaceutical Society (RPS) professional guidance consists of five guiding principles that support pharmacy teams with the procurement and supply of Specials.

The five principles are highlighted in figure 1. As represented in figure 1, the patient's experience is central to every decision that pharmacists make about the supply and procurement of Specials.

Under each principle there is a statement in italics that describes the principle itself. This is supported by a series of statements that describe examples of good practice that support the principle's application in practice.

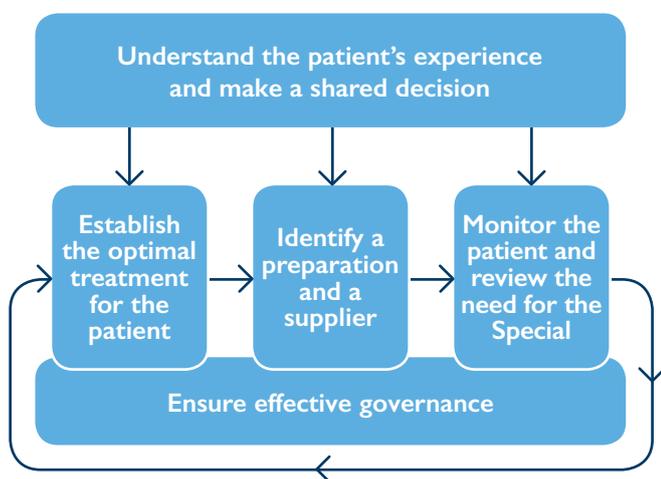


Figure 1: Five principles for the procurement and supply of Specials

### 1. ESTABLISH THE OPTIMAL TREATMENT FOR THE PATIENT

All treatment options are evaluated. Prescribers and pharmacists work together to ensure that Specials are only supplied when the patient has a special clinical need that cannot be met by an available licensed medicine (this special clinical need does not include reasons of cost, convenience or operational need<sup>1, 14</sup>).

1. Every reasonable effort is made by prescribers (with support from pharmacists) to identify a UK licensed medicine, or a licensed medicine in a similar class, that meets the patient's special clinical needs.

2. Specials are supplied only by exception and with the full knowledge of the prescriber and the patient. Pharmacists discuss with prescribers how together they ensure that prescribers are aware of the unlicensed status of a Special<sup>1</sup>.

3. Where it is essential to supply a Special, professional judgment is exercised to assess the risks and benefits of the various options. The most appropriate option will minimise the risk to the patient, bearing in mind the patient's special clinical circumstances and the urgency of the need for treatment.

Appendix 1 provides a brief guide to the product options available to the prescriber and the pharmacist and identifies gaps in assurance of quality, safety and efficacy in comparison to a licensed medicine. The guide can be used for risk assessment as an aid to decision making but it should be seen only as a guide. The final decision should be based on the patient's circumstances taking into account the risks and benefits of the available options, and what is known about the quality, safety, efficacy and availability of the medicine.

### CASE STUDY I

A patient with severe chronic plaque psoriasis on his elbows regularly attended an outpatient dermatology clinic. He had been using coal tar 2% in yellow soft paraffin twice daily to control his symptoms. However at his last appointment he reported that his symptoms were no longer controlled and after discussion with his doctor they agreed to increase the strength of his coal tar preparation.

The doctor initially prescribed coal tar 5% in yellow soft paraffin which could only be supplied as a Special. However after discussion with the pharmacist they agreed to change the prescription to a licensed preparation – coal tar 6% and in lecithin 0.4% cream (brand name Psoriderm 6% cream). This was a formulation in line with local formulary and British Association of Dermatologists guidance, and was potentially equally effective for the patient. It was also likely to be easier to obtain from a community pharmacy and would provide the patient with a consistent formulation.

### KEY LEARNING

This case study illustrates the importance of ensuring prescribers and pharmacists consider all options available to their patients before prescribing and supplying a Special. Considering all the available options resulted in an equally effective licensed medicine being prescribed for the patient.

## 2. UNDERSTAND THE PATIENT'S EXPERIENCE AND MAKE A SHARED DECISION

The patient's needs, values and preferences are discussed to ensure that the implications and practicalities of supplying and using Specials are understood, and that patients (or carers) are supported to adhere to their medicines<sup>15, 16, 17</sup>.

1. Pharmacists understand why the patient requires a Special and if the patient is taking or using the medicine themselves, or whether it is being administered to them and by whom.
2. When starting or taking over the supply of a Special, pharmacists obtain information from prescribers or pharmacy teams who have previously supplied the Special, as well as patients or carers. This will include details of the formulation and patient factors such as appropriate packaging, or the need for measuring devices for small doses.
3. Pharmacists (and their teams) transferring the supply of a patient's Special to another pharmacist ensure that the pharmacist taking over responsibility for supply has the information necessary to make a safe and effective supply to the patient.
4. Continuity of supply is supported so that patients do not run out of their medicines. Patients or carers (and prescribers) are advised about the ordering of repeat prescriptions, quantities needed, shelf life and in-use shelf life (when relevant), the likely timescales of the supply and who to contact if they run out of the Special.
5. Given that there may be increased risk of treatment failure with Specials, patients or carers are invited to contact their pharmacist if they have any questions or concerns.
6. Extra care is taken when advising patients or carers about the use of Specials if there has been a change of supplier or formulation that may impact on how the patient takes or uses their medicine.
7. When available, information leaflets are provided to the patient or carer<sup>i</sup>. If, as is often the case with Specials, written information is not available verbal advice is provided.

*i The medicines for children website has a range of patient information leaflets for children and parents*

### CASE STUDY 2

A patient with tuberculosis was discharged from hospital on a liquid formulation of ethambutol being taken via an enteral tube. Shared care arrangements were in place for the GP to continue prescribing. When at home, the patient requested another prescription from his GP the day before the supply ran out. The GP issued the prescription which was picked up by the patient's daughter (his carer) the next day. The prescription was then presented to the community pharmacist on Friday afternoon by which time the patient had finished the medicine supplied by the hospital.

Neither the patient nor the carer was aware that the ethambutol was a Special that would not be routinely stocked at his usual community pharmacy. The pharmacist was unable to obtain the ethambutol liquid at short notice so the patient missed one day of treatment. The patient's daughter had to take time off work to go back to the hospital on Saturday to obtain a supply until the community pharmacist was able to source the product.

Unfortunately the ethambutol liquid prescribed by the GP and supplied by the community pharmacist was a different concentration to the liquid the patient had been using in hospital. Whilst the new concentration was labelled correctly, the patient continued to take the same volume as previously and so received a suboptimal dose of ethambutol until the error was noticed.

### KEY LEARNING

This case study illustrates the importance of ensuring that when the responsibility for prescribing and/or supplying a Special is transferred, for example from a hospital setting to primary care, full information about the medicine is also transferred. When transferring responsibilities for the prescribing and supply of Specials, organisations must have processes in place to support full and timely communication. This might include template letters to be sent to GPs on discharge and/or direct contact with the patient's preferred community pharmacy.

The case study also illustrates the need for clear communication with patients and carers about the practical differences between licensed medicines and Specials, specifically about timescales necessary for the Special to arrive in the pharmacy and the impact this has on the ordering of repeat prescriptions. The need to consult with patients about any new supply of a Special is also illustrated here with the change in concentration of the ethambutol requiring the patient to take a different volume than they had previously.

### 3. IDENTIFY A PREPARATION AND A SUPPLIER

When procuring and supplying a Special, pharmacists ensure that patients receive medicine that is of appropriate quality, is appropriate for the patient's condition and personal circumstances, with minimal clinical risk.

1. No aspect of quality is assumed and all reasonable steps are taken to obtain evidence that the quality of the Special (whether it is manufactured under a Manufacturer's Specials Licence or imported) meets appropriate standards.
2. To ensure consistency (and bioequivalence) when dispensing a repeat supply (rather than a new treatment) pharmacists aim to use the same product specification and supplier if possible. Where this is not practical pharmacists assess the risks and benefits of available options and discuss with the prescriber if necessary.
3. Pharmacists and their teams agree with the supplier what they require to meet the prescription, this includes strength, formulation and, where relevant, requirements for excipients e.g. sugar-free or alcohol-free formulations, and flavourings. This is based on the pharmacist's understanding of the clinical needs of the patient. Where necessary the agreed formulation is confirmed to the manufacturer in writing.
4. Pharmacists and their teams agree with the supplier the documentation required to provide evidence that the Special meets the purchasing specification and the prescriber's requirements, is pharmaceutically appropriate, and suitable for the patient. For UK manufactured Specials this should include Certificates of Analysis or Conformity and for imported Specials may include Summaries of Product Characteristics and Patient Information Leaflets (translated if not already in English).

The responsibility for agreeing a product specification which meets a patient's special clinical need and the requirements of the prescription rests with the pharmacist.

The responsibility for providing medicines that comply with the product specification rests with the manufacturer.

5. Specials and their supporting documentation are checked on receipt to ensure that they meet the purchasing specification i.e. the prescriber's requirements, appropriate pharmaceutical quality, and are suitable for the patient. Supporting documentation may include Certificates of Analysis or Conformity and translated Patient Information Leaflets as appropriate.

#### CASE STUDY 3

A 4kg neonate was discharged from hospital on phenobarbital 20mg twice a day prescribed as 2ml twice a day of 50mg/5ml unlicensed alcohol-free phenobarbital suspension. When the GP came to prescribe a repeat supply a British Pharmacopoeia (BP) suspension of 15mg/5ml that was in the general practice prescribing system was prescribed as 6.8ml (20mg) twice a day. This was subsequently dispensed by the community pharmacist.

Four days later the child was taken to hospital with lethargy and increased fitting. The 15mg/5ml preparation contained 38% alcohol and the volume of 6.8ml administered to the neonate was similar to an adult having a glass or more of wine with each dose. As a neonate cannot metabolise alcohol as efficiently as an adult this would have resulted in lethargy and decreased seizure threshold which explained the increased fitting.

#### KEY LEARNING

This case study highlights the importance of new prescribers and pharmacists having a full product specification available when a patient transfers from one setting to another. The need for the original prescriber and pharmacist to share this information in a timely way is also highlighted.

## 4. MONITOR THE PATIENT AND REVIEW THE NEED FOR A SPECIAL

The appropriateness of continued prescribing of a Special is reviewed to ensure that it remains the best option and ongoing supply is justified by the patient's continued special clinical need.

1. For patients receiving regular prescriptions for continuing treatment, pharmacists and prescribers work together to periodically review the choice of medicines with the patient and/or carer to confirm whether there is a better alternative. For example, whether the medicine is still required, a newly licensed medicine has become available, there is a licensed medicine in a similar class or an alternative Special.
2. Unlike licensed medicines, the quality, safety and efficacy of Specials will not have been formally assessed by the MHRA therefore there may be an increased likelihood of adverse events or treatment failure. Where the pharmacist and prescriber feel it necessary, treatment with Specials should be monitored more closely. This will depend on individual patient circumstances, for example medicines toxicity, increased vulnerability of babies, children or older people.
3. Adverse reactions to the product are reported to the MHRA via the yellow card scheme (<http://yellowcard.mhra.gov.uk>) along with suspected product defects stating the manufacturer and indicating that the product is unlicensed. Reporting to manufacturers is also encouraged.

### BOX 1

#### RECORD KEEPING REQUIREMENTS FOR SPECIALS\*

Any person selling or supplying a Special must keep the following records for at least 5 years:

- The source from which and the date on which the person obtained the product;
- The person to whom and the date on which the sale or supply was made;
- The quantity of the sale or supply;
- The batch number of the batch of that product from which the sale or supply was made; and
- Details of any suspected adverse reaction to the product so sold or supplied of which the person is aware or subsequently becomes aware.

\* Regulation 170 of the Human Medicines Regulation 2012 [SI 2012/1916]

### CASE STUDY 4

A seventy two year old woman was admitted to hospital for the second time following a fall. Her sitting systolic blood pressure was as low as 50mmHg and she had peripheral neuropathy. Her blood pressure improved with fludrocortisone 100 micrograms but it was still inadequate to support her daily activities. Whilst in hospital, she was started on midodrine 5mg twice daily titrated up to 15mg three times daily. Prior to discharge her blood pressure improved to 135/72 mmHg.

Midodrine is used to treat postural (orthostatic) hypotension but at the time there was no UK Marketing Authorisation for this or any other indication.

Under a planned shared care arrangement the patient was advised to continue taking midodrine for three months until her next hospital appointment. The hospital informed the patient's GP that she was being discharged on a Special and shared details of the prescription. Prior to discharge the patient was advised that her prescription was for a Special and that she should speak to her community pharmacist about the implications that this might have for the timescales of the further supply.

At the patient's next outpatient appointment the prescriber and the patient decided to continue the midodrine, however a licensed preparation was now available so the prescription was changed to the licensed product.

### KEY LEARNING

This case demonstrates that there are situations where a patient's special clinical need cannot be met by an established licensed medicine and so a Special is chosen. In 2013 the National Institute for Health and Care Excellence published an evidence summary to support the use of midodrine<sup>18</sup>. This case study also illustrates the importance of reviewing and monitoring the patient regularly as in this case a licensed preparation that could meet the patient's special clinical need became available<sup>14</sup>.

## 5. ENSURE EFFECTIVE GOVERNANCE IS IN PLACE

Governance arrangements are in place to support the safe and effective procurement and supply of Specials in order to provide consistently safe and effective Specials to treat patients.

1. The pharmacy team procuring and supplying Specials have the knowledge, skills and competency to ensure that patients are able to get the best possible outcomes from using Specials. Option evaluation and assessment of risks are core competencies for pharmacists and their teams involved in making decisions about the purchase and supply of Specials.
2. The requirements set out in national, and local guidance, are taken into account before a Special is procured. Nationally this might include Drug Tariff guidance<sup>19</sup> and in Scotland the need for pharmacists to obtain prior authorisation from the relevant Health Board<sup>20</sup>. Locally this includes agreed guidelines or policies on joint-working that relate to the prescribing and supply of Specials.
3. Systems are in place and regularly reviewed to support the safe procurement and supply of Specials of an appropriate quality. These might include policies and procedures for the following:
  - Documenting discussions with the prescriber in relation to the unlicensed nature of the product and its suitability;
  - Sourcing and approval of manufacturers and suppliers, e.g. using a licensed Specials manufacturer;
  - Preparing product specifications and orders listing the formula of the product to ensure that the pharmacist has understood exactly what is required and communicated that accurately to the supplier;
  - Receipt of medicines and evaluating supporting documentation e.g. Certificates of Analysis, Certificates of Conformity, or stability information; and
  - Processes for the reporting of errors<sup>13</sup>.
4. Records are kept for five years in line with the specific MHRA requirements for Specials (see Box 1) and are available for inspection by the licensing authority<sup>ii</sup>.
5. In common with all procurement for the NHS, pharmacists and their teams, and their employers have a responsibility to use suppliers who provide value for money. Suppliers are periodically reviewed to ensure they are offering the best all round service, taking into account quality and safety of supply; a supply chain involving one or more third parties is potentially associated with additional risks.

### CASE STUDY 5

An older person patient presented a prescription for Sodium Chloride preservative free eye drops 5% 10ml. The pharmacist found one product which had a brand name and whilst checking the packaging found that there was a CE mark on it identifying the product as a Medical Device. The pharmacist checked their medicines ordering system and found that the product also appeared to be available as a Special.

The medicine was prescribed for the treatment of corneal oedema and it was important to start treatment as soon as possible. The pharmacist checked the information on the Medical Device packaging and confirmed that it was intended for the treatment of corneal oedema, but was unsure whether the Medical Device would be reimbursed on the NHS and so checked in the Drug Tariff to confirm that the product on the shelf was listed in Part IXA.

The Medical Device had been formulated with a delivery mechanism which assisted patients with limited manual dexterity. Following a discussion with the prescriber and the patient it was agreed that the Medical Device was suitable for the patient and also might be easier for them to use than the available Special. So taking everything into consideration, the pharmacist supplied one of the Medical Device products listed in the Drug Tariff. The prescription was endorsed to reflect this.

### BOX 2

#### A MEDICAL DEVICE OR A SPECIAL?

Some products such as eye drops, or eye ointment are available as both a Special and as CE marked Medical Devices (see definitions).

The decision about which of the two options to supply should be based on the patient's needs, the condition being treated, and the purpose for which the Medical Device is intended as indicated on the pack or pack insert. Further considerations include ease of administration for the patient, the formulation including presence or absence of sensitising excipients, and a validated, extended in-use shelf-life.

<sup>ii</sup> There may be other requirements for record keeping which also apply. See also Recommendations for retention of pharmacy records produced by East and South East England Specialist Pharmacy Services. <http://www.medicinesresources.nhs.uk/en/Communities/NHS/SPS-E-and-SE-England/Reports-Bulletins/Retention-of-pharmacy-records/>

### 3. DEFINITIONS

TERM	DEFINITION
Marketing Authorisation	The Human Medicines Regulations 2012 requires a medicine placed on the market in the UK to hold a Marketing Authorisation. Medicines with a Marketing Authorisation have been approved by the European Commission or MHRA and appropriate standards of quality, safety and efficacy are met provided the medicine is used in accordance with the terms of its Marketing Authorisation.
Special	<p>The Human Medicines Regulations 2012 provide exemptions from the requirement to hold a Marketing Authorisation in certain circumstances. A Special is an unlicensed medicine that does not have either a centrally authorised Marketing Authorisation in the European Union or a UK Marketing Authorisation and is manufactured imported or supplied to meet the special clinical needs of an individual patient.</p> <p>Specials can be obtained from:</p> <ul style="list-style-type: none"> <li>■ A licensed manufacturer manufacturing medicines or importing them from outside the EEA under a Manufacturer (Specials) Licence (see below); or</li> <li>■ A licensed wholesale dealer importing or distributing medicines from elsewhere in the UK/EEA under a Wholesale Dealer's Licence (see below).</li> </ul>
Manufacturer (Specials) Licence (MS)	<p>In the UK, only holders of a Manufacturer (Specials) Licence may manufacture Specials (see above). The MHRA inspects MS Licence holders' premises and processes to ensure the manufacturer is fully compliant with Good Manufacturing Practice (GMP). However, <b>there is no formal assessment and approval of the formulation, manufacturing method or stability of individual Specials</b> (nor is there any assessment of quality, safety or efficacy of the individual Special).</p> <p>Medicines may be manufactured in batches against a pharmacopoeial or other validated formulation, or formulated as a bespoke medicine for an individual patient. In many cases batches of Specials are tested prior to release and will be supplied with a Certificate of Analysis (see below). Bespoke medicines are usually provided with a Certificate of Conformity (see below) but are unlikely to be tested prior to release.</p> <p>Medicines made under a MS Licence must have the MS Licence number on the label (see BP general monograph for unlicensed medicines)<sup>21</sup>.</p>
Manufacturer's (Specials) Licence covering importation from outside the EEA	The holder of an MS Licence that also covers importation may import unlicensed medicines from outside the EEA. The intention to import a medicine must be notified to the MHRA, which may object to importation for reasons such as patient safety concerns, or the availability of a licensed medicine in the UK.
Wholesale Dealer Licence	The holder of a Wholesale Dealer Licence whose licence covers imports of unlicensed medicines from within the EEA, may import such medicines. The intention to import a medicine must be notified to the MHRA, which may object to importation for reasons such as patient safety concerns, or the availability of a licensed medicine in the UK.

TERM	DEFINITION
<b>Product specification</b>	<p>A product specification defines the quality requirements of the purchaser (acting on behalf of the prescriber) and should be agreed with the supplier. The product specification is the document against which the purchaser should be able to hold the manufacturer accountable for the quality of the medicine.</p> <p>What sort of information should a product specification for a UK manufactured Special contain?</p> <ul style="list-style-type: none"> <li>■ That the manufacturer is making the medicine in accordance with GMP under a MS Licence</li> <li>■ The formulation or, where this is commercially confidential, a list of ingredients and that the starting materials are of appropriate quality (pharmaceutical grade)</li> <li>■ That the manufacturing process ensures consistent product quality. Supportive evidence may include details of methods, in-process controls, and method of sterilisation (if applicable)</li> <li>■ The criteria for release of the medicine</li> <li>■ The justification/evidence for the shelf life and (where applicable) in-use shelf life</li> <li>■ How the product should be labelled, packaged and stored.</li> </ul>
<b>Certificate of Analysis</b>	<p>A Certificate of Analysis is a batch-specific certificate of finished product testing. It should detail: the tests performed; required results; actual results; the laboratory which issued it; and should be signed by an authorised person such as someone working in a quality discipline, such as, Quality Assurance or Quality Control.</p>
<b>Certificate of Conformity</b>	<p>A Certificate of Conformity is a declaration of conformity only, which is not supported by end product batch testing. A Certificate of Conformity will only state that the medicine was made under the MS Licence, according to GMP. Without an agreed product specification a Certificate of Conformity is of limited value.</p> <p>A Certificate of Conformity should be signed by an authorised person such as someone working in a quality discipline, such as, Quality Assurance or Quality Control.</p>
<b>Labelling</b>	<p>Specials manufactured in the UK under a MS Licence must be labelled in accordance with the BP monograph for unlicensed medicines. Patient information will not normally be available for these medicines.</p> <p>If a Special is imported and not already labelled in English then consideration should be given to overlabelling in English and obtaining a translated Patient Information Leaflet and/ or Summary of Product Characteristics from the importer.</p>
<b>Medical Device (CE marked): see also BOX 2</b>	<p>The MHRA regulates the approval process for medical devices but the system is very different to that for the regulation of medicines.</p> <p>All approved medical devices have a CE mark however the approval process used varies depending on the class of device. Class I devices are subject to less stringent requirements than Class 3 devices.</p> <p>More information about the regulation of medical devices can be found at:  <a href="https://www.gov.uk/topic/medicines-medical-devices-blood/medical-devices-regulation-safety">https://www.gov.uk/topic/medicines-medical-devices-blood/medical-devices-regulation-safety</a></p>

## 4. REFERENCES AND USEFUL RESOURCES

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### REFERENCES

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20. The Scottish Government. NHS Circular: PCA(P)(2015) 17 Pharmaceutical Services Amendments to Drug Tariff in Respect of Special Preparations and Imported Unlicensed Medicines. 21 January 2015. <http://www.sehd.scot.nhs.uk/pca/PCA2015%28P%2917.pdf>
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## USEFUL RESOURCES

- British National Formulary for Children.  
<http://www.evidence.nhs.uk/formulary/bnfc/current>
- The National Institute for Health and Care Excellence publishes evidence summaries for some off-label or unlicensed medicines. <https://www.nice.org.uk/about/what-we-do/our-programmes/nice-advice/evidence-summaries-unlicensed-or-off-label-medicines>
- NHS Greater Glasgow and Clyde Guidance on the Use of Specials in Primary Care. 2013. [http://www.glasgowlmc.co.uk/download/Clinical%20Guidelines%20&%20Referral%20Guidance/Prescribing/Specials/specials\\_guidance\\_-\\_1206.pdf](http://www.glasgowlmc.co.uk/download/Clinical%20Guidelines%20&%20Referral%20Guidance/Prescribing/Specials/specials_guidance_-_1206.pdf)
- NHS Greater Glasgow and Clyde. Specials A-Z. 2015. <http://www.ggcprescribing.org.uk/prescribing-resources>
- East of England NHS Collaborative Procurement Hub and NHS East of England. Information and guidance on the prescribing and use of unlicensed pharmaceutical specials. <http://www.prescqipp.info/resources/finish/196-full-specials-toolkit-commissioner-version/424-specials-toolkit-full-commissioner-ed>
- Centre for Pharmacy Postgraduate Education e-learning: Safer supply and use of Specials. 2015. <https://www.cppe.ac.uk/programmes//specials-e-01/>
- Details of registered licensed manufacturers and wholesale dealers can be found at [www.gov.uk](http://www.gov.uk)
- Details of Import Notifications can be found at [www.gov.uk](http://www.gov.uk)
- Details of NHS hospital pharmacy manufacturing units are listed in the British National Formulary. <http://www.evidence.nhs.uk/formulary/bnf/current>
- The Association of Pharmaceutical Specials Manufacturers <http://www.apsm-uk.com/>

## RESOURCES WITH RESTRICTED ACCESS TO NHS EMPLOYED STAFF:

- NHS Pro-File: <http://www.pro-file.nhs.uk/>
- Medusa: <http://medusa.wales.nhs.uk/>

# APPENDIX I: GUIDE TO PRODUCT OPTIONS WHEN NOT SUPPLYING A LICENSED MEDICINE\*

To be used to aid decision making and for risk assessment only. Prescribing and supply decisions must be driven by individual patient need.

What the MHRA does:	Origin of the medicine:	What prescribers and pharmacists should consider:
<ul style="list-style-type: none"> <li>MHRA/EMA assesses and approves individual products and the manufacturer's premises and processes</li> <li>Appropriate standards of quality, safety and efficacy are met</li> </ul>	EU or UK licensed medicine	<ul style="list-style-type: none"> <li>Use of the medicine in accordance with its Marketing Authorisation</li> </ul>
<ul style="list-style-type: none"> <li>MHRA assesses and approves individual products and the manufacturer's premises and processes</li> <li>Appropriate standards of quality are met</li> </ul>	Off-label (unlicensed) use of EU or UK licensed medicine	<ul style="list-style-type: none"> <li>Assessment of the safety and efficacy of off-label use</li> <li>Risks of using the medicine outside the terms of the Marketing Authorisation</li> </ul>
		What the pharmacist is responsible for:
<ul style="list-style-type: none"> <li>MHRA evaluates and assesses import notifications for individual medicines (see also definitions)</li> <li>The regulator in the country of origin assesses and approves individual products and the manufacturer's premises and processes: this may or may not be equivalent to the UK</li> </ul>	Imported product licensed in country of origin**	<ul style="list-style-type: none"> <li>Assessing clinical suitability</li> <li>Clinical suitability and licensed indications</li> <li>Sourcing from a country with an equivalent regulatory framework to the UK</li> <li>Checking that manufacturing standards are equivalent to EU GMP</li> <li>Controlling risks of medication error because of unfamiliar/foreign language packaging, labelling and leaflets</li> </ul>
<ul style="list-style-type: none"> <li>MHRA inspects and approves the MS Licence holder's premises and processes, but not individual products</li> </ul>	UK Special manufactured by MS Licence holder	<ul style="list-style-type: none"> <li>Assessing clinical suitability</li> <li>Checking manufacturer has an appropriate licence</li> <li>Ensuring product meets the purchasing specification</li> <li>Assess the evidence that supports the formulation and shelf life</li> </ul>
<ul style="list-style-type: none"> <li>No MHRA oversight. The medicine is made under the supervision of a pharmacist in response to a prescription</li> </ul>	Made under pharmacist supervision Extemporaneously prepared medicine	<ul style="list-style-type: none"> <li>Assessing clinical suitability</li> <li>Ensuring the medicine is made in a registered pharmacy</li> <li>Ensuring product meets the purchasing specification</li> <li>Assess the evidence that supports the formulation and shelf life</li> </ul>
<ul style="list-style-type: none"> <li>MHRA evaluates and assesses import notifications for individual medicines</li> <li>There may be no regulatory framework in the country of origin</li> </ul>	Imported medicine not licensed in country of origin	<ul style="list-style-type: none"> <li>Assessing clinical suitability</li> <li>Checking that manufacturing standards are equivalent to EU GMP</li> <li>Ensuring product meets the purchasing specification</li> <li>Obtaining evidence that the formulation and shelf life are validated</li> <li>Controlling risks of medication error because of unfamiliar/foreign language packaging, labelling and leaflets</li> </ul>

\*See also MHRA guidance note 14; appendix 2. \*\*Countries with an equivalent regulatory framework are European Economic Area countries, and countries with mutual recognition agreements. Medicines licensed in other countries may not be subject to safeguards equivalent to GMP. Discuss with Regional QA Specialist or MHRA if necessary; see useful resources.

For borderline substances and food supplements see Appendix 2.

# APPENDIX 2: PROCUREMENT AND SUPPLY OF FOOD SUPPLEMENTS AND BORDERLINE SUBSTANCES ON PRESCRIPTION

## FOOD SUPPLEMENTS

Under the EU Food Supplement Directive (EC/2002/46), a food supplement is defined as *any food the purpose of which is to supplement the normal diet and which is a concentrated source of a vitamin or mineral or other substance with a nutritional or physiological effect, alone or in combination and which is sold in dose form such as capsules, pastilles, tablets, pills and other similar forms, sachets of powder, ampoules of liquids, drop dispensing bottles, and other similar forms of liquids or powders designed to be taken in measured small unit quantities.*

The MHRA advises on whether products are medicinal and classifies them on the basis of the definition of a medicinal product which is set out in Regulation 2 of the Human Medicines Regulation 2012. In cases where there is a history of sale and widespread availability as food supplements, which predates Marketing Authorisations for medicinal products containing the same “active” ingredient, there may be scenarios where products containing comparable levels of active ingredient can be marketed both as food supplements and as medicines, depending on the claims made by the manufacturer. If a product claims to treat or prevent disease it is a medicine and must be manufactured as a medicine. Further information about classification of medicines can be found in the MHRA's Guidance Note 8 [https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/398998/A\\_guide\\_to\\_what\\_is\\_a\\_medicinal\\_product.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/398998/A_guide_to_what_is_a_medicinal_product.pdf)

The regulatory framework for the manufacturing of medicines and that for the production of food supplements are different. Medicinal products, whether licensed or unlicensed, must be produced in accordance with GMP, while food supplements must comply with all relevant aspects of food law and, in particular, EC/2002/46. Food law does not require or enforce compliance with GMP so any claims by a manufacturer that their food supplements have been made to GMP standards have not been validated.

## CASE STUDY 6

A hospital purchased vitamin D food supplement capsules. The manufacturer did not have a MS Licence but claimed to make the food supplements “under GMP”. The hospital had 10 capsules analysed by a Regional Pharmaceutical Quality Control laboratory and the content of the capsules was found to range between 70% and 130% of the label claim. As the capsules were required to treat patients with known vitamin D deficiency the hospital decided to purchase a licensed medicine with an equivalent level of vitamin D instead.

## KEY LEARNING

Content claims on food supplement labels must be based on averages from manufacturers' analysis, but there are no defined tolerances for content for any individual dose, and there is no requirement for routine finished product testing. Given this, prescribers must be aware of the potential for variation within and between batches when deciding whether food supplements meet the needs of their patients.

Manufacturers of food supplements may follow the principles of GMP, and in some cases may also manufacture medicines, however their certificate of GMP compliance from the MHRA does not cover the manufacture of food supplements, so claims such as “made under GMP” or “made in a MHRA licensed facility” are of limited relevance in the context of food supplement products.

A challenging situation which may face community pharmacists is to be presented with a prescription for a vitamin in a dose or presentation which is neither available as a licensed medicine nor readily available as a Special, in which case prescribing a food supplement may be the only practical option.

In this situation after first satisfying themselves that there is no appropriate and available licensed medicine, pharmacists are advised to check with their local medicines information service or other relevant local pharmacy teams who will have access to relevant national and local guidelines and other relevant information, and will be able to advise on the appropriate choice of product.

## BORDERLINE SUBSTANCES

Borderline substances that are detailed in Part XV of the Drug Tariff (NHS England and Wales) are not regarded by the MHRA to be medicinal products. They are regulated under food or cosmetics legislation. In the Scottish Drug Tariff refer to Part I Para 13.

The Advisory Committee on Borderline Substances (ACBS) issues advice as to the circumstances in which such substances may be used in the context of an underlying medical condition.

Prescribers and pharmacists are expected to satisfy themselves that any such 'borderline substances' can be safely prescribed and dispensed to patients and that patients are adequately monitored. Indications listed in Part XV of the Drug Tariff (NHS England and Wales) include:

- Disease-related malnutrition;
- Intractable malabsorption;
- Pre-operative preparation of malnourished patients;
- Post-operative support following total gastrectomy;
- Short bowel syndrome;
- Dysphagia;
- Proven inflammatory bowel disease; and
- Bowel fistulae.

The BNF lists the following nutritional borderline substances:

- Enteral Feeds (non-disease-specific);
- Nutritional supplements (non-disease-specific);
- Specialised formulae;
- Feed supplements;
- Feed additives;
- Foods for special diets; and
- Nutritional supplements for metabolic diseases.

# APPENDIX 3: A CHECKLIST FOR DISPENSING SPECIALS

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This check list is based on the five guiding principles in the RPS professional guidance that support the procurement and supply of Specials. This template can be used in conjunction with the full guidance document as a starting point for pharmacists and their teams to develop their own local checklists.

## WHAT IS THE PATIENT'S SPECIAL CLINICAL NEED?

1. Why is the patient being prescribed a Special?
2. Is there a need to make contact with the prescriber to discuss:
  - If the prescriber is aware that the prescription is for a Special?;
  - Alternatives to the Special? or;
  - The formulation of the product?

## UNDERSTAND THE PATIENT'S EXPERIENCE

3. If the patient has not had the Special before are there any specific patient requirements (e.g. special containers, measuring devices)?
4. Is there a need to discuss with the patient:
  - Likely timescales for the supply and the need to request a repeat prescription in good time?
  - How and when to order repeat prescriptions from their GP?
  - The shelf life/in-use shelf life of the Special? Is this on the label?
  - Quantities they need to order?
  - Why Specials are different to licensed products?
  - Changes to the supplier or formulation that may alter the way the Special is taken or used (e.g. a change in concentration)?

## IDENTIFY A PREPARATION AND SUPPLIER

5. Does the pharmacy previously supplying the Special need to be contacted to confirm the formulation (e.g. hospital, different community pharmacy)?
6. If the patient has had the Special before can the same supplier be used to ensure consistency?
7. Has the formulation been fully agreed with the supplier? Including any particular requirements (e.g. sugar free, alcohol free, flavourings?). Should this be confirmed with the supplier in writing?
8. Has information to support the quality of the Special been obtained? E.g. Certificate of Analysis or Conformity?
9. Have the supplier's details been entered into the patient's record?

## ENSURE EFFECTIVE GOVERNANCE

10. Has national and/or local guidance been followed?
11. Have all records been completed in line with MHRA and organisational requirements?
12. Have the organisation's relevant standard operating procedures been followed?

## MONITOR AND REVIEW

13. What are the arrangements for reviewing the patient's prescription?
14. Does the patient's condition or the Special mean that they require closer monitoring?
15. Is there any cause for concern about the patient's treatment?
  - Any adverse events?
  - Any indication of treatment failure?

# APPENDIX 4: ACKNOWLEDGEMENTS

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## SPECIALS EXPERT ADVISORY GROUP

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David Chandler	Chief Executive	Psoriasis and Psoriatic Arthritis Alliance
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Nanette Kerr	Chief Executive	Company Chemists' Association
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The Royal Pharmaceutical Society (RPS) is the professional body for pharmacists in Great Britain.

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