PrescQIPP Community Interest Company

Specials prescribing

Medicine optimisation projects in this area are aimed at optimising prescribing by reviewing the continued need for a special (an unlicensed medicine), offering an alternative licensed product or by suggesting how to contain prescribing of the special. This bulletin reviews the place in therapy of unlicensed specials and offers guidance and support materials for organisations considering reviewing prescribing of specials as a medicines optimisation project.

Recommendations

- Before prescribing a special consider if a medicine is needed at all.
- If a medicine is required, a stepped approach is suggested to choose an appropriate preparation, especially where an adult has difficulties swallowing:
  1. Licensed medicines administered as intended.
  2. Licensed medicines administered in an unlicensed manner (off-label).
  3. Imported products.
  4. Special-order products.
- A special should only be prescribed when there is no available licensed medicine which fully meets the patient's clinical needs.
- Decisions about the prescribing of specials should be based on professional judgement and an understanding of individual patient need as accountability for prescribing a special, rests with the prescriber.
- Review patient's prescribed specials to ensure that a special is (and remains) the most appropriate option for the individual.

Background

A special is an unlicensed medicine that does not have a UK Marketing Authorisation (MA). It is manufactured, imported or supplied to meet the special clinical needs of an individual patient.[1]

Medicines can also be used outside the terms of their MA. This is commonly referred to as 'off-label' use. For example, metformin is licensed for type 2 diabetes mellitus, but is also prescribed for polycystic ovary syndrome which is an unlicensed indication and so used 'off-label' for this indication.[1,2]

Imported products are unlicensed medicinal products sourced from outside the UK under an importers licence issued by the Medicines and Healthcare products Regulatory Agency (MHRA). These products have been specially sourced to meet a prescription ordered for individual patients without the need for the importer to hold MA for the medicinal product concerned.[3]

A special may only be supplied when there is no available licensed medicine which fully meets the patient's clinical needs. They 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.[1] The General Medical Council (GMC) advises that prescribers should usually prescribe licensed medicines in accordance with the terms of their licence.[4] However, prescribers may prescribe unlicensed medicines where, on the basis of an assessment of the individual patient, they conclude,

for medical reasons, that it is necessary to do so to meet the specific needs of the patient.[4] There are certain clinical situations where a special may be judged to be the most appropriate or only available option, for example:

- For children, e.g. they are routinely prescribed to achieve the lower doses required.[1]
- In dermatology, e.g. unlicensed creams and ointments containing tars, dithranol, salicylic acid, steroids and other active constituents in a range of concentrations and bases.[5]
- For patients intolerant or allergic to particular ingredient(s).[6]
- For patients who require alternatives to oral solid dosage forms that are not available as a licensed oral liquid.[1]

The GMC guidance states that prescribing unlicensed medicines may be necessary in the following instances:[4]

- There is no suitably licensed medicine that will meet the patient's need. Examples include, but are not limited to, where:
  - There is no licensed medicine applicable to the particular patient, for example, if the patient is a child and a medicine licensed only for adult patients would meet the needs of the child.
  - A medicine licensed to treat a condition or symptom in children would nonetheless not meet the specific assessed needs of the particular child, but a medicine licensed for the same condition or symptom in adults would do so.
  - The dosage specified for a licensed medicine would not meet the patient's need.
  - The patient needs a medicine in a formulation that is not specified in an applicable licence.
- A suitably licensed medicine that would meet the patient's need is not available. This may arise where, for example, there is a temporary shortage in supply.
- The prescribing forms part of a properly approved research project.
- There is a serious risk to public health and the MHRA has temporarily authorised the sale or supply of an unlicensed medicine, such as a vaccine or treatment, in response.

A prescription only medicine that is unlicensed in Northern Ireland has been supplied under the Northern Ireland MHRA Authorised Route (NIMAR).[4]

Considerations when prescribing specials

Currently, the following healthcare professionals can prescribe an unlicensed medicine: doctors; dentists; independent nurse and pharmacist prescribers and, in some circumstances, supplementary prescribers (who can be a pharmacist, nurse, midwife, community nurse, optometrist, physiotherapist, radiographer, or chiropodist/podiatrist). The following can prescribe a licensed medicine off-label: nurse independent prescribers, pharmacist independent prescribers, and optometrist independent prescribers. However, all healthcare professionals are subject to: their individual clinical competence; the professional codes and ethics of their statutory bodies; and the prescribing policies of their employers.[7] For nurse and midwife prescribers, these are in included in the Standards for proficiency for nurse and midwife prescribers. For pharmacists prescribers these are included in In practice: Guidance for pharmacist prescribers.

Decisions about the prescribing of specials rely heavily on professional judgement based on understanding individual patient need. As with licensed medicines accountability for prescribing a special, rests with the prescriber and where supplied by a pharmacy, the supplying pharmacist will share accountability with the prescriber for supplying a special to a patient.[1] Prescribing medicines outside the recommendations of their marketing authorisation alters (and probably increases) the prescriber's professional responsibility and potential liability. The prescriber should be able to justify and feel competent in using such medicines, and also inform the patient or the patient's carer that the prescribed medicine is unlicensed.[2] A clear, accurate and legible record of all unlicensed medicines prescribed should be made and the reasons for prescribing an unlicensed medicine, if prescribing does not follow common practice.[4]

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.[1]

However, with specials there are additional considerations for prescribers in any care setting.

Licensing

The MHRA in the UK is responsible for ensuring that medicines and medical devices are effective, safe and of an appropriate quality. The MHRA's primary aim is to safeguard public health through a system of regulation. Pharmaceutical manufacturers and distributors operating in the UK marketplace are subject to a system of licensing and inspection, which ensures that licensed medicinal products conform to internationally agreed standards, and that those medicines are manufactured, stored and distributed in compliance with the required regulatory standards.

The regulation of medicines in the UK market is undertaken by the MHRA in accordance with the Human Medicines Regulations 2012 (SI 2012/1916).[6] Unless exempt a medicinal product must be the subject of MA or a product licence before being placed on the market. Regulation 167 of the Human Medicines regulations 2012 provides an exemption from the need for a MA for a medicinal product which is supplied in certain circumstances. These include for use for a patient for whose treatment that person is directly responsible in order to fulfil the special needs of the patient and as long as the medicinal products meet the conditions specified in regulation 167. Regulation 167 include assurances around the manufacture and supply of the unlicensed special.

Unlicensed specials are not assessed through the MHRA MA process and so they have not been assessed as meeting appropriate standards of quality, safety and efficacy. Only holders of Manufacturer (Specials) (MS) Licence may manufacture Specials. The MHRA inspects MS Licence holders' premises and processes to ensure they are fully compliant with Good Manufacturing Practice (GMP). However, there is no formal assessment and approval of the formulation, manufacturing method or stability of individual specials.[1]

Legal

Unlicensed specials do not have MA or a product licence. The MA or product licence defines a medicine's terms of use which is outlined in its' Summary of Product Characteristics (SPC). The SPC includes such things as the indication(s), recommended dose(s), contraindications, and special warnings and precautions for use on which the licence is based. It is in line with such use that the benefits of the medicine have been judged to outweigh the potential risks.[7] Any use of a licensed medicine not in accordance with the SPC is an unlicensed or 'off-label' use.

Common examples of 'off-label' use include: unlicensed indication, unlicensed dose, unlicensed method of delivery, unlicensed route of administration, and many medicines prescribed for children and neonates. The term also includes licensed medicines which have been re-packed and supplied to, or received from, an external organisation. For example, bevacizumab (Avastin®) is licensed for treatment of various solid cancers, but is also used outside of its' MA, or "off-label" in ophthalmology.[7] The use of bevacizumab in the ophthalmology setting has not been subject to a formal regulatory assessment for safety, quality and efficacy. The preparation of bevacizumab for intravitreal use involves manipulation of the authorised medicine to produce multiple aliquots, usually in plastic syringes (so-called compounding). No relevant MA covers its use in this way and it is considered by the MHRA to be an off-label use. However, should a similarly compounded product be placed on the market for sale, the product would become an unlicensed medicine which would require a new or extended MA, or an exemption from the need for one.[7,8]

Good practice in prescribing guidance

The responsibility for prescribing unlicensed specials rests with the prescriber who signs the prescription - this is shared with the supplying Pharmacist.

The GMC has guidance for prescribers relating to unlicensed medicines. When prescribing an unlicensed medicine, you must:[4]

- Be satisfied that there is sufficient evidence or experience of using the medicine to demonstrate its safety and efficacy.
- Take responsibility for prescribing the medicine and for overseeing the patient's care, monitoring and any follow up treatment, or make sure that arrangements are in place for another suitable doctor to do so.
- Make a clear, accurate and legible record of all medicines prescribed and, where you are not following common practice, your reasons for prescribing an unlicensed medicine.

The Royal Pharmaceutical Society (RPS) outlines what pharmacists should consider when supplying a UK Special manufactured by an MS Licence holder, e.g. assess clinical suitability, check the manufacturer has an MS licence, assess the evidence that supports the formulation and shelf life.[1]

Patient information

The GMC guidance states that prescribers must give patients, or their parents or carers, sufficient information about the medicines they propose to prescribe, to allow them to make an informed decision.[4] This can be difficult as patient information leaflets are not routinely available for specials. Where necessary, the prescriber and supplying pharmacist should take additional steps to ensure the patient is informed about the medicine.[9]

In emergencies or where there is no realistic alternative treatment and such information is likely to cause distress, it may not be practical or necessary to draw attention to the licence. In other cases, where prescribing unlicensed medicines is supported by authoritative clinical guidance, it may be sufficient to describe in general terms why the medicine is not licensed for the proposed use or patient population. Prescribers must always answer questions from patients, or their parents or carers, about medicines fully and honestly. If an unlicensed medicine is prescribed where it is not routine or if there are suitably licensed alternatives available, the prescriber should explain this to the patient, and give their reasons for doing so.[4]

- The Royal College of Paediatrics and Child Health (RCPCH) offers practical and reliable advice including videos, leaflets and resources on their website Medicines for Children.
- The British Pain Society published - Use of medicines outside of their UK marketing authorisation in pain management and palliative medicine information for patients.
- Moorfields Eye Hospital NHS Foundation Trust. Unlicensed medicines FAQ's

Quality

The risks and benefits of using a special will differ in different patient groups, different medicines and in individual clinical circumstances. Prescribers need to take into account the safety, efficacy, quality and cost of the different specials available. Specials can be obtained from a range of sources by pharmacists and their teams and are not all manufactured in the same way. Unlike licensed medicines, the formulation of a special cannot be assumed to be consistent, with the quality, bioavailability and consistency of specials varying between suppliers and supplies, even where the same product is prescribed.[9] This can lead to potential differences in pharmacokinetics and clinical responses, which may have a negative impact on patient safety. This is particularly important for drugs with a narrow therapeutic index and in some patient groups, e.g. young children or transplant patients. In these cases, prescribers should be specific about the formulation and work with pharmacists to ensure that an appropriate special is always supplied.[9]

It is also important that new prescribers and pharmacists have a full product specification available, in a timely way, when a patient transfers from one healthcare setting to another.[9]

The RPS have a case study in their professional guidance on prescribing specials which illustrates the importance of this:[9]

"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."

Identifying a special

It can be difficult to identify a special at the point of prescribing.[9] The prescriber may not realise that they are prescribing a special when they select the medication from the clinical system or that a licensed alternative may be available.

Any pharmacist supplying a special should ensure that the prescriber is fully aware of the unlicensed status of the medicine and pharmacists working in general practice are well place to oversee the processes used by the practice to manage the prescribing of specials.[9]

For example, a patient with severe chronic plaque psoriasis had been using coal tar 2% in yellow soft paraffin twice daily to control his symptoms. The patient found that recently that strength no longer controlled the symptoms and an agreement to increase the strength of his coal tar preparation was made. The doctor initially prescribed coal tar 5% in yellow soft paraffin which could only be supplied as a special. After discussion with the pharmacist and the patient they agreed to change the prescription to a licensed preparation – coal tar 6% and lecithin 0.4% cream (brand name Psoriderm® 6% cream). As well as being licensed for this indication the formulation was in line with the local formulary and British Association of Dermatologists guidance. It was also likely to be easier for the patient to obtain from a community pharmacy and would provide a consistently formulated product.[9]

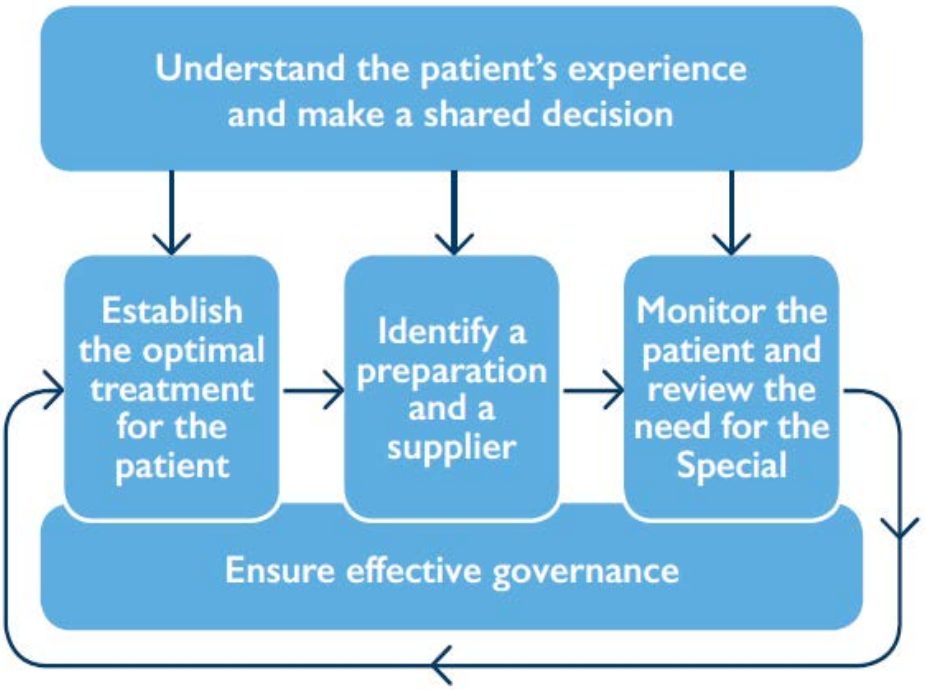
Five principles for prescribing specials

The RPS has published professional guidance and standards describing the five principles for the prescribing, procurement and supply of pharmaceutical specials.[1,9]

Categories of medicines not directly in the scope of these five principles include:[1]

- Medicines used outside the terms of their MA (commonly referred to as 'off-label' use).
- Medicines rendered unlicensed when the dosage form is manipulated, for example, crushed tablets/ opened capsules.
- Extemporaneously dispensed medicines prepared in a pharmacy.

Figure 1. Five principles for the prescribing, procurement and supply of specials[1,9]



1. Establish the optimal treatment for the patient

All treatment options are evaluated. Prescribers and pharmacists work together to ensure that specials are only prescribed/supplied when the patient has a special clinical need that cannot be met by an available licensed medicine of established safety, efficacy, and quality (this special clinical need does not include reasons of cost, convenience or operational need).

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 treatment options/supplying and using specials are understood, and that patients (or carers) are supported to adhere to their medicines.

3. Identify a preparation and a supplier

The risks and benefits of using a special will differ for different patient groups, different medicines and in individual clinical circumstances. Prescribers need to consider the safety, efficacy, quality and cost of the different specials available to patients. 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.

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.

5. Ensure effective governance is in place

Prescribers understand the rationale for using a special and the practical implications of prescribing before initiating, transferring, or taking over responsibility for prescribing. Governance arrangements are in place to support the safe and effective procurement and supply of specials to provide consistently safe and effective specials to treat patients.

These documents also contain a series of tips and case studies that describe examples of good practice that support the application of these principles in practice.[1,9]

The stepped approach to prescribing

Consider if a medicine is still needed at all. If a medicine is required, for example for patients with swallowing difficulties and unable to take solid dose forms, follow a stepwise approach to choose an appropriate preparation. Consider the:[10]

- Clinical suitability
- Product quality
- Licensed status
- Cost.

All decisions should be made on an individual basis. The patient should ideally be involved in the decision and provided with written and verbal administration instructions for each medicine they are prescribed. This is particularly important for patients who are moving between care settings.

When deciding whether to prescribe an unlicensed product, the first consideration should be to determine if a medicine is needed at all. Any unnecessary medicines should be stopped. If a medication is required, consider reducing the number of oral doses. Consider agents with a prolonged therapeutic effect, but modified or slow-release preparations may not suitable to be crushed or opened. If necessary, consider non-oral formulations such as transdermal patches or suppositories.[10]

If a medicine is required, a stepped approach is suggested to choose an appropriate preparation:[10]

1. Licensed medicines used as licensed

If possible, use a licensed medicine in a suitable formulation to meet the patient's needs. Licensed medicines are associated with less risk and are usually less expensive than special-order products.[10] Licensed strengths of solutions and solid dosage forms should be used wherever feasible, to avoid the prescribing of unlicensed strengths which would require a special. A different licensed medicine in the same class or a different class of medicine could be suitable for the patient. In addition a newly licensed medicine may have become available or the patient's condition may have changed.[1]

Other examples include:[10]

- Dispersible tablets or licensed liquid medicines can be used for patients who can safely swallow thin liquids (e.g. switch from gabapentin tablets to gabapentin oral suspension).
- Consider switching to a different agent in the same therapeutic class, to allow a licensed medicine to be used (e.g. switch from perindopril tablets to ramipril oral solution).
- Consider switching to a different route of administration to allow a licensed medicine to be used (e.g. switch from oral to transdermal hormone replacement therapy (HRT)).
- Ensure switches are undertaken appropriately, with patient monitoring if necessary.

Adults who can eat and drink normally, but dislike swallowing large tablets or capsules may manage small tablets and capsules, or large, scored tablets snapped in half. Good pill-swallowing techniques can help – examples are available on the NHS website.

The use of costly special-order products for these patients is not justified.[10]

Patients who can safely swallow thin liquids may have dispersible or effervescent tablets in water, oral liquids and crushed tablets or the opened contents of capsules with a drink or with food as appropriate. Pharmacists working in Primary Care Network (PCNs), for practices, Health Boards (HBs), Integrated Care Boards (ICBs) or community pharmacists may be able to suggest suitable licensed preparations for their patients.

2. Licensed medicine used 'off-label' (e.g. crushing a tablet or opening a capsule)

If there is no suitable licensed formulation, consider using a licensed medicine in an unlicensed manner or "off-label" manner, for example by crushing/dispersing tablets or opening capsules. Licensed medicines, even used 'off-label', may be associated with less risk and are usually less expensive than special order products.[10]

Not all tablets can be crushed or capsules opened and it is important to check beforehand with a pharmacy professional or appropriate reference source. Take into account the patient/carer's ability to administer medicines in this way and consider any risks to the carer from exposure to medicines such as cytotoxics or hormones.[10]

The prescriber should be aware of the route and method of administration of medicines they prescribe and if a medicine is to be used outside its licence, take responsibility for its use in this manner.[10]

Homecare and care home staff may only administer prescription medicines on the instruction of the prescriber and must be trained and competent to do so. If staff are to crush tablets or open capsules, or administer medicines via an enteral feeding tube, a written direction should be included in the patient's care plan.[10]

The MHRA acknowledges that, while it does not recommend "off-label" use, the use of licensed medicines "off-label" is preferred to the use of unassessed, unlicensed medicines.[6]

3. Imported products

If a UK product cannot meet the special need, then an imported medicinal product should be considered, which is licensed in the country of origin.[6]

4. Special-order products

Where the patient's needs cannot be met by licensed medicines, including 'off-label' use, consider using a special-order product ('Special'). Special-order medicines can be obtained when medicines are not commercially available in suitable licensed formulations. Special-order medicines, and extemporaneous preparations, are unlicensed and should only be considered for use when a patient's needs cannot be met by licensed medicines as they may increase the risk to both patient and prescriber. The products are not assessed for safety or efficacy by the regulatory authorities and prescribers assume greater liability for their use.[10]

Special-order medicines can be expensive, sometimes many times the cost of alternative licensed medicines. The cost to the NHS of some special-order products (those listed in Part VIIIB or Part VIIID of the Drug Tariff or Part 7S of the Scottish Drug Tariff) is fixed but the cost of others is unregulated.[10]

If a special is the only option, then the preference should be to use UK manufactured "specials", which are made in Good Manufacturing Practice (GMP) inspected facilities, but which are otherwise un-assessed (GMP inspection of "specials" manufacturers is not product specific). There may also be other products available which are unlicensed in the country of origin.[6]

According to the MHRA guidance the least acceptable options are products that are unlicensed in the country of origin, and which are not classed as medicines in the country of origin. For example, the use of products from countries where they are classed as supplements, not pharmaceuticals, and may not be made to expected standards of pharmaceutical GMP. These should be avoided whenever possible.[6]

Attachment 1 is a checklist to support prescribers and pharmacists when considering prescribing or supplying a special. It can also support discussions with specialists who initiate specials and request prescribing is continued in primary care. Once completed, to ensure effective governance and patient informed decisions, add the checklist to the patient's record. PrescQIPP have a Specials webkit which brings together all the PrescQIPP specials resources and suggests good practice and how to optimise the use of licensed medicines, alternatives and reviews to be done to support the reduced use of specials.

Other useful resources include:

- Neonatal and Paediatric Pharmacists Group (NPPG). Using standardised concentrations of liquid medicines in children' - includes commonly used liquid specials for children. It provides national standardisation of concentrations to reduce the risk of errors being made in the doses given to children and ideally allows doses for: 1kg patient to not be <0.2ml; 50kg patient to not be >10ml.

- NHS BSA ePACT2 Children's Standard Liquid Concentration dashboard - data on the extent to which liquid medicines prescribed in primary care for patients under the age of 18 follow the nationally recommended concentration for each drug.
- The NEWT Guidelines (subscription required)– guidance on alternatives available when a patient has swallowing difficulties or enteral feeding tubes.
- Handbook of Drug Administration via Enteral Feeding Tubes (subscription required)- guidance on the administration of drugs via enteral routes.
- BNF - Special-order manufacturers - includes a list of licensed hospital manufacturing.
- Medicines information services – Special Pharmacy Services (SPS) Medicines Advice for primary care based healthcare professionals, email: asksps.nhs@sps.direct; telephone: 0300 770 8564.
- The Royal College of Ophthalmologists. Ophthalmic Special Order Products
- Specialist Pharmacy Service - Choosing formulations of medicines for adults with swallowing difficulties
- Specialist Pharmacy Service - Medicines suitable for adults with swallowing difficulties
- Specialist Pharmacy Service Q&A - What injections can be given orally or via enteral feeding tubes?
- Specialist Pharmacy Service - Switching between liquid and tablet/capsule formulations – Which medicines require extra care?
- West Suffolk CCG - Specials and Unlicensed Medicines includes resources for patient use, prescribing guidance, requirements for prescribing and dispensing a special and safety and legal implications.
- NHS West Essex CCG - Unlicensed, Off-label medicines and specials prescribing guidance
- Coventry and Warwickshire - Medicines Optimisation Team Guidance on Possible Alternatives to Unlicensed Specials
- NHS Waltham Forest - Specials Quick Wins

Cost

In England and Wales, Part VIIIB of the Drug Tariff (Arrangements for payment for specials and imported unlicensed medicines with a price per unit above a minimum quantity), and Part VIIID (Arrangements for the payment for specials and imported unlicensed medicines with prices determined relative to a commonly identified pack size), set reimbursement prices on a selection of unlicensed specials and imports. The prices are set by the Department of Health and Social Care and are based on information of manufactured specials or imports submitted by suppliers that hold a Manufacturer Specials Licence or Wholesale Dealer Licence issued by the Medicine Healthcare products Regulatory Agency (MHRA).[11]

When an unlicensed special or an imported medicine which is listed in Part VIIIB or Part VIIID is prescribed, the pharmacy contractor will be reimbursed the set Drug Tariff price for dispensing the product, no matter how the product is sourced.[11]

Specials listed in Part VIIIB of the Drug Tariff have a minimum quantity, a price for that quantity and a price per subsequent ml/g/tab/cap unless in a special container. Most of the specials currently listed in this part are either liquids or creams.[3]

Currently the Drug Tariff states that bisoprolol 1.25mg/5ml oral solution costs £77.09 for 100ml (minimum quantity) and every 1ml extra will cost 24p.[3] So using bisoprolol 1.25mg/5ml oral solution as an example:

- If the quantity is below the Part VIIIB listed minimum volume, reimbursement will be the price for the minimum volume. For example, if 50mls of bisoprolol 1.25mg/5ml oral solution is ordered on prescription, the pharmacy will be paid £77.09.
- If the quantity is equal to the minimum volume, reimbursement will be the price for the minimum volume, e.g. if 100mls is ordered on prescription the pharmacy will be paid £77.09.

- If the quantity prescribed is more than this minimum volume, reimbursement will be paid on that price plus the 1ml list price for the additional amount prescribed, e.g. if 200mls of bisoprolol 1.25mg/5ml oral solution was ordered on prescription the pharmacy will be paid £77.09 for £100ml and every 1ml extra will cost 24p, therefore the total cost for 200mls would be £101.09.[3]

All the formulations in Part VIIID are solid dosage forms, i.e. tablets or capsules.

Both part VIIIB and VIIID, include additional information regarding the formulation, including if it is a standard formulation, sugar free, alcohol free, colour free, flavour free, lactose free or preservative free.[11]

For unlicensed specials or imports where the item is not listed in Part VIIIB or Part VIIID of the Drug Tariff (non-tariff specials), and where the product is obtained from a manufacturer under an MHRA specials licence, the pharmacy is required to endorse the names, quantities and cost of the ingredients used in preparing the product plus 'ED' for costs incurred in dispensing a product prepared under the Section 10 exemption from the Medicines Act 1968.[11] Different pharmacies may be charged different prices for the same specials and a pharmacy may be tied into a certain special supplier due to wider contracts.

An additional fee of £20.00 is paid to the pharmacy for dispensing unlicensed medicines including:[3]

- Preparations manufactured under an MHRA specials licence or sourced under an MHRA importers licence.
- Preparations prepared under the Section 10 exemption from the Medicines Act 1968.

For specials prescribed which are not included in the Drug Tariff, there is no set price and so the prescriber will be unaware of the cost at the point of prescribing. The cost of these specials can vary widely and can result in excessive and uncontrolled costs.

In the Scottish Drug Tariff, Part 7, there is a list of unbranded medicinal products and ingredients for which a price has been agreed for the current month.[12] Reimbursement arrangements for specialist preparations and imported unlicensed medicines depends on whether a reimbursement price is listed in Part 7S (Reimbursement of special preparations) of the Scottish Drug Tariff or not. Part 7S lists unlicensed specials obtainable from Specials Manufacturers, Part 7U (limited list of reimbursable unlicensed products) includes commercially available products that do not have a product licence.[13] If the preparation concerned is included in the list, then the reimbursement price paid to Scottish Pharmacy contractors, will be the price listed there. These Drug Tariff prices are set to include a handling allowance. Other than in exceptional cases, no further remuneration or reimbursement will be made and no out of pocket expenses may be claimed.[13]

A pharmacy contractor needs to seek reimbursement authorisation from the Scottish Health Board for all specials manufactured medicines, unlicensed or imported medications that are not listed in Part 7S or Part 7U of the Scottish Drug Tariff.

In Northern Ireland there is currently no Part VIIIB to the Drug Tariff. Therefore, there are no set reimbursement prices for any specials dispensed in Northern Ireland. Prescriptions for unlicensed medicines must be endorsed with invoice price less any discount or rebate.[14]

Newly licensed specials

As discussed, it can be difficult to identify a special at the point of prescribing and the prescriber may not realise that a licensed alternative product is available. There are an increasing number of licensed products coming on to the market when previously only a special unlicensed product has been available. This is particularly the case for medicines for children. Specials are often used in children as they could be judged to be the most appropriate or only available option to achieve the lower doses required. Licenced products now available for children which previously would have required prescribing a special include:

- Glycopyrronium bromide - Sialanar® 320micrograms/ml oral solution, which is licensed for symptomatic treatment of severe sialorrhoea (chronic pathological drooling) in children and adolescents aged three years and older with chronic neurological disorders.
- Melatonin - Slenyto® 1mg and 5mg prolonged-release tablets, which are licensed for the treatment of insomnia in children and adolescents aged 2-18 with Autism Spectrum Disorder (ASD) and / or Smith-Magenis syndrome, where sleep hygiene measures have been insufficient.
- Colecalciferol 1ml/2740IU (equivalent to 68.5micrograms/ml vitamin D3) oral drops solution - Fultium®-D3 Drops, which is licensed for the prevention and treatment of vitamin D deficiency. As an adjunct to specific therapy for osteoporosis in patients with vitamin D deficiency or at risk of vitamin D insufficiency for infants aged 0–11 years and adolescents aged 12–18 years.

The top 15 special order products

Table 1 lists the top 15 special order products by cost for PrescQIPP subscribers from June 2021 to May 2022. It is intended as a guide for healthcare professionals reviewing prescribing of specials and is not an exhaustive list of products available. Prices of medicines may vary depending on handling fees and changes in Drug Tariff price. Where a Drug Tariff price is referred to this applies to England and Wales.

***Exception Handler - Unspecified Item / Discount Not Deducted Item**

Table 1 includes two lines described as “Exception Handler – unspecified item” or Exception Handler – discount not deducted. Sometimes in England and Wales, a product description applied during the prescription pricing process will return these descriptors from the NHS Business Services Authority (NHSBSA). ’ This indicates that the product prescribed cannot be specified as it is not included in the Dictionary of Medicines and Devices.[16] The term ‘Exception Handler’ is used by the NHSBSA to indicate that the product could not be routinely processed.[17] Discount Not Deducted indicates that there is no discount on this product.[17] These items should be monitored as they can contribute to primary care specials spend. Patients receiving them should be reviewed to ensure they are receiving the most appropriate product for them.

Table 1: Top 15 special order products by cost (NHSBSA June 2021 – May 2022)[2,3,15,16]

Drug	Potential alternative (licensed, off-label or unlicensed)	Cost of alternative[3]	Total Cost June 2021 to May 2022	Total items June 2021 to May 2022	Cost per item (£) June 2021 to May 2022	DT special? [3,16]
Exception Handler Discount Not Deducted Item*	• These are products with unspecified drug codes & no discount applied.	N/A	£2,634,133	18,730	£141	No
Methadone 1mg/ml oral solution sugar free	• Unlicensed products being prescribed. • Licensed product to be prescribed as per drug tariff - methadone 1mg/ml oral solution sugar free and not as methadone 1mg/ml oral solution colour free sugar free.	100ml/£1.02	£1,841,732	284,630	£6	No
Sucralfate 1g tablets	• Review ongoing need for sucralfate. • Consider alternative drug treatment, e.g. PPI, H2 antagonist for GI ulcers. • Licensed alternative - sucralfate 1g/5ml oral suspension sugar free.	Sucralfate 1g/5ml oral suspension sugar free 200ml / £124.87	£1,812,444	6,822	£266	Yes
Exception Handler Unspecified Item*	• These are products with unspecified drug codes.	N/A	£1,722,929	108,481	£16	No
Colecalciferol 2,000unit tablets	• See PrescQIPP Bulletin 275: Vitamin D • Review ongoing need for colecalciferol. • Licensed alternatives of colecalciferol tablets available in different strengths.	Consider recommending self care as a 2000iu dose would be a maintenance dose for an adult. ColeDose D3 2,000unit 30 tablets / £3.86 HealthAid Vitamin D3 2,000unit 120 tablets / £7.25 SunVit-D3 2,000unit 28 tablets / £4.19 Urgent-D 2,000unit chewable 60 tablets / £4.31 Vitamin D3 Lemon Melts 2,000unit 120 tablets / £5.66	£1,660,031	15,139	£110	Yes

Drug	Potential alternative (licensed, off-label or unlicensed)	Cost of alternative[3]	Total Cost June 2021 to May 2022	Total items June 2021 to May 2022	Cost per item (£) June 2021 to May 2022	DT special? [3,16]
Co-proxamol 32.5mg/325mg tablets	• Safety issue withdrawn from the market worldwide. • Included in NHSE 'Items which should not routinely be prescribed in primary care guidance'. • See PrescQIPP Bulletin 194: Co-proxamol. • Review ongoing need for co-proxamol. • Consider switching patient to an alternative licensed pain medication. • If unable to stop co-proxamol, refer them to a specialist for a review of their pain management and support to switch to suitable alternatives.	Paracetamol 500mg 100 tablets/£2.34 Codeine 30mg 100 tablets/£3.29 Co-codamol 8mg/500mg 100 tablets/£3.53 Co-dydramol 10mg/500mg 100 tablets/£8.10	£1,647,469	5,383	£306	Yes
Cyanocobalamin 1mg modified-release tablets	• Recommended treatment for vitamin B12 deficiency is hydroxocobalamin 1mg/1ml solution for intramuscular (IM) injection ampoule administered, every two to three months once the patient is on maintenance treatment. • Vitamin B12 in larger oral doses may be effective, but the IM injection remains the treatment of choice. • Hydroxocobalamin is retained in the body longer than cyanocobalamin and therefore where administered by injection can be given at intervals of three months. • Licensed alternative - Cyanocobalamin 1mg tablets • BNF states that cyanocobalamin injection is less suitable for prescribing.	Hydroxocobalamin 1mg/1ml 5 amps/£5.73 Cyanocobalamin 1mg 30 tablets/£9.99 (Orobalin)	£1,338,820	228,087	£6	No
Sodium chloride 5% eye ointment	• Licensed alternatives: » Sodium chloride 5% eye ointment preservative free (Alissa Healthcare) » Sodium chloride 5% eye drops (Alissa Healthcare)	Sodium chloride 5% eye ointment preservative free (Alissa Healthcare) 5g/£22.50 Sodium chloride 5% eye drops 10ml/£25.25	£1,278,547	8,189	£156	Yes

Drug	Potential alternative (licensed, off-label or unlicensed)	Cost of alternative[3]	Total Cost June 2021 to May 2022	Total items June 2021 to May 2022	Cost per item (£) June 2021 to May 2022	DT special? [3,16]
Midazolam 10mg/ml oral liquid	• See PrescQIPP Bulletin 147: Buccal midazolam. • Licensed preparations are available, but may be prescribed off-label, refer to the SPC: » Midazolam 10mg/1ml oromucosal solution pre-filled oral syringes sugar free. » Midazolam 10mg/2ml oromucosal solution pre-filled oral syringes sugar free. » Midazolam 2.5mg/0.5ml oromucosal solution pre-filled oral syringes sugar free. » Midazolam 5mg/1ml oromucosal solution pre-filled oral syringes sugar free. » Midazolam 7.5mg/1.5ml oromucosal solution pre-filled oral syringes sugar free.	10mg/1ml oromucosal solution 1/£45.76 (Epistatus) 10mg/2ml oromucosal solution 4/£91.50 (Buccolam) 2.5mg/0.5ml oromucosal solution 4/£82.00 (Buccolam) 5mg/1ml oromucosal solution 4/£85.50 (Buccolam) 7.5mg/1.5ml oromucosal solution 4/£89.00 (Buccolam)	£1,210,188	2,714	£446	No
Midazolam 10mg/2ml oromucosal solution pre-filled oral syringes sugar free	• As midazolam 10mg/ml oral liquid above.	As midazolam 10mg/ml oral liquid above.	£1,016,434	10,404	£98	No
Potassium chloride 600mg (potassium 8mmol) modified release tab	• Was manufactured as Slow K (modified release), licensed for correction of hypokalaemia, now discontinued. • Licensed alternatives (modified release): » Aad K 600mg (8mmol) slow release tablets. » PotaChlor 600mg (8mmol) modified-release tablets. • Licensed alternatives (immediate release): » Potassium chloride 375mg/5ml (potassium 5mmol/5ml) oral solution sugar free. » Potassium chloride 600mg / Potassium bicarbonate 400mg (total potassium 12mmol) effervescent tablets.	375mg/5ml 500ml/£9.58 (Kay-Cee-L syrup) Potassium chloride 600mg/ Potassium bicarbonate 400mg 100 effervescent tablets/£9.95 (Sando-K) Aad K 600mg (8mmol) slow release 100 tablets/£67.29 PotaChlor 600mg (8mmol) modified-release 100 tablets/£67.28	£901,506	4,870	£185	No
Methadone 1mg/ml oral solution	• Unlicensed product being prescribed. • Licensed product to be prescribed as per Drug Tariff methadone 1mg/ml oral solution.	100ml/£0.99 500ml/£4.95	£629,739	98,550	£6	No

Drug	Potential alternative (licensed, off-label or unlicensed)	Cost of alternative[3]	Total Cost June 2021 to May 2022	Total items June 2021 to May 2022	Cost per item (£) June 2021 to May 2022	DT special? [3,16]
Levomepromazine 6mg tablets	• Licensed alternative - Levomepromazine 6mg tablets. • Macmillan Cancer Support advise that the licensed 25mg tablets can be quartered for a starting dose of 6.25mg. • Off-label oral use of licensed levomepromazine 25mg/1ml solution for injection ampoules.	6mg 28 tablets/£247.20 25mg 84 tablets/£20.26 (Nozinan) 25mg/1ml 10amp/£20.13 (Nozinan)	£578,791	1,938	£299	No
Phenobarbital 50mg/5ml oral solution	• Licensed alternatives: » Phenobarbital 15mg tablets. » Phenobarbital 15mg/5ml elixir. Contains 38% alcohol. Not suitable for young children and neonates and others for whom formulations containing alcohol would not be suitable. » Phenobarbital 30mg tablets. » Phenobarbital 60mg tablets. • The tablets may be crushed and mixed with water for administration. • BNF states: in children the RCPCH and NPPG recommend that, when a liquid special of phenobarbital is required, it is alcohol-free and the following strength is used: 50 mg/5 ml. • MHRA/CHM Advice - For category 1 drugs antiepileptics patients should be maintained on a specific manufacturer's product.	15mg 28 tablets/£24.25 15mg/5ml elixir 500ml/£83.01 30mg 28 tablets/£0.94 60mg 28 tablets/£8.07	£564,311	2,557	£221	Yes

Drug	Potential alternative (licensed, off-label or unlicensed)	Cost of alternative[3]	Total Cost June 2021 to May 2022	Total items June 2021 to May 2022	Cost per item (£) June 2021 to May 2022	DT special? [3,16]
Melatonin 5mg/5ml oral solution	• See PrescQIPP Bulletin 245: Melatonin • Review ongoing need for melatonin. • Licensed preparations are available, but may be prescribed off-label, refer to the SPC: » Melatonin 1mg modified-release tablets. » Melatonin 1mg/ml oral solution sugar free - should not be used in children and adolescents due to safety and efficacy concerns in relation to possible excipients. See PrescQIPP Bulletin 245: Melatonin for more information and consider melatonin 1mg modified-release tablets. » Melatonin 2mg capsules. » Melatonin 2mg modified-release tablets. » Melatonin 3mg capsules. » Melatonin 3mg tablets. » Melatonin 5mg capsules. » Melatonin 5mg modified-release tablets.	1mg MR 60 tablets/£41.20 (Slenyto®) 1mg/ml oral solution sugar free 150ml/£155.57 2mg 30 tablets/£15.30 (Adaflex®) 2mg 30 capsules/£57.50 (Colonis Pharma Ltd) 2mg MR 30 tablets/£15.39 (Circadin®) 3mg 30 capsules/£62.50 (Colonis Pharma Ltd) 3mg 30 tablets/£19.81 4mg 30 tablets/£20.23 (Adaflex®) 5mg 30 capsules/£105.00 (Colonis Pharma Ltd) 5mg 30 tablets/£23.27 (Adaflex®) 5mg MR 30 tablets/£103.00 (Slenyto®)	£466,692	2,548	£183	No

The Specials snapshot reports and visual analytics allows ICBs/HBs/PCNs/practices to identify their top special order products. The quarterly specials tariff watch is designed to help prescribers navigate the changes in Part VIIIB and Part VIIID of the drug tariff to facilitate cost-effective prescribing. It also includes the top ten list of potential highest savings. A 'Specials tariff watch opportunity detail' document is also available which shows the supporting data by ICB/HB where opportunities may exist, by specific drug and quantity.

The use of a licensed alternative product may be outside of its licence, or off-label. The MHRA acknowledges that, while it does not recommend "off-label" use, the use of licensed medicines "off-label" is preferred to the use of unassessed, unlicensed medicines.[6] Please refer to the SPC or manufacturer for licensing information.

For all the specials listed, the continued need for the special should be the first consideration when reviewing treatment.

See PrescQIPP's Polypharmacy and Deprescribing webkit and Bulletin 268: Improving Medicines and Polypharmacy Appropriateness Clinical Tool (IMPACT) for further guidance.

Savings

In England, approximately £49 million is spent annually on prescribing specials (unlicensed medicines). (NHSBSA (June – August 2022)

A 10% reduction in spend on specials in England could result in annual savings of £4.9 million. This equates to £7,974 per 100,000 population.

Summary

A special is an unlicensed medicine that does not have a UK Marketing Authorisation. It is manufactured, imported or supplied to meet the special clinical needs of an individual patient.[1] Medicines can also be used outside the terms of their Marketing Authorisation. This is commonly referred to as 'off-label' use.[1,2] Imported products are unlicensed medicinal products sourced from outside the UK under an importers licence issued by the MHRA.[3] If a medicine is required, a stepped approach is suggested to choose an appropriate preparation:[10]

1. Licensed medicines administered as intended
2. Licensed medicines administered in an unlicensed manner – off-label
3. Imported products – products licensed outside the UK
4. Special-order products

A special may only be supplied when there is no available licensed medicine which fully meets the patient's clinical needs.[1] Then, the five principles prescribing specials should be followed:[9]

1. Establish the optimal treatment for the patient
2. Understand the patient's experience and make a shared decision
3. Identify a preparation and a supplier
4. Monitor the patient and review the need for a special
5. Ensure effective governance is in place

Review individuals prescribed specials and whether there is a continued need for the special. Deprescribe those no longer needed. Consider offering an alternative licensed cost-effective product which is suitable for the individual if prescribing is to be continued.

References

1. Royal Pharmaceutical Society of Great Britain. Professional Guidance for the Procurement and Supply of Specials. December 2015. https://www.rpharms.com/Portals/0/RPS%20document%20library/Open%20access/Support/toolkit/specials-professional-guidance.pdf
2. Joint Formulary Committee. British National Formulary (online) London: BMJ Group and Pharmaceutical Press. August 2022. https://www.medicinescomplete.com/
3. NHS Business Services Authority. Drug Tariff. October 2022. https://www.nhsbsa.nhs.uk/pharmacies-gp-practices-and-appliance-contractors/drug-tariff
4. General Medical Council. Prescribing unlicensed medicines. April 2021. https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/good-practice-in-prescribing-and-managing-medicines-and-devices/prescribing-unlicensed-medicines
5. British Association of Dermatologists. Specials Recommended by the British Association of Dermatologists for Skin Disease. 2018. https://www.bad.org.uk/guidelines-and-standards/access-to-medicines/
6. Medicines and Healthcare products Regulatory Agency. The supply of unlicensed medicinal products ("specials"), MHRA Guidance Note 14. 2014. Last updated October 2018. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/373505/The_supply_of_unlicensed_medicinal_products__specials_.pdf
7. Medicines and Healthcare Regulatory Products Agency. Off-label or unlicensed use of medicines: prescribers' responsibilities. Drug Safety Update. December 2014. https://www.gov.uk/drug-safety-update/off-label-or-unlicensed-use-of-medicines-prescribers-responsibilities
8. Medicines and Healthcare products Regulatory Agency. Review of MHRA published statements on the supply and use of Avastin (bevacizumab) for intravitreal use. 19 September 2019. https://assets.publishing.service.gov.uk/media/5d8371f8ed915d522e416522/Review_of_MHRA_published_statements_on_the_supply_and_use_of_Avastin.pdf
9. Royal Pharmaceutical Society of Great Britain. Prescribing specials. April 2016. https://www.rpharms.com/Portals/0/RPS%20document%20library/Open%20access/Support/toolkit/professional-standards---prescribing-specials.pdf
10. Specialist Pharmacy Service. Choosing formulations of medicines for adults with swallowing difficulties. June 2021. Last updated 7 March 2022. https://www.sps.nhs.uk/articles/choosing-formulations-of-medicines-for-adults-with-swallowing-difficulties/
11. Pharmaceutical Services Negotiating Committee. Unlicensed specials and imports. July 2013. Last updated September 2022. http://psnc.org.uk/dispensing-supply/dispensing-a-prescription/unlicensed-specials-and-imports/
12. Public Health Scotland. Scottish Drug Tariff. October 2022. https://www.isdscotland.org/Health-Topics/Prescribing-and-Medicines/Scottish-Drug-Tariff/
13. The Scottish Government. Pharmaceutical Services Amendments to Drug Tariff in Respect of Special Preparations and Imported Unlicensed Medicines. August 2015. https://www.isdscotland.org/Health-Topics/Prescribing-and-Medicines/Scottish-Drug-Tariff/Drugs-and-Preparations-with-Tariff-Prices/docs/PCA2015-P-17.pdf
14. Business Services Organisation. The Northern Ireland Drug Tariff. October 2022. https://hscbusiness.hscni.net/services/2034.htm
15. NHS Derby and Derbyshire Clinical Commissioning Group. Specials and expensive liquids guidelines. June 2019. Updated September 2022. http://www.derbyshiremedicinesmanagement.nhs.uk/assets/Specials/Local_resources/Specials_and_expensive_liquids_guideline_(v6).pdf
16. NHS Business Services Authority. dm+d browser. https://services.nhsbsa.nhs.uk/dmd-browser/ October 2022.
17. NHS Business Services Authority. Information Services Frequently Asked Questions. https://www.nhsbsa.nhs.uk/sites/default/files/2017-03/Frequently_Asked_Questions.pdf

Additional PrescQIPP resources

Briefing	https://www.prescqipp.info/our-resources/bulletins/bulletin-301-specials-prescribing/
Implementation tools	
Data pack	https://data.prescqipp.info/views/B301_Specialsprescribing/FrontPage?%3Aembed=y&%3Aiid=1&%3AisGuestRedirectFromVizportal=y

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