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Prescribing Specials

Five guiding principles for prescribers

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About the NPC:

The NPC is an NHS organisation formed in 1996 and funded by the Department of Health. In April 2011 the NPC integrated into the National Institute for Health and Clinical Excellence (NICE). The NPC and NICE has a history of close working and this integration will add further strength to achieve the NPC aim, which is:

"to support the NHS, and those working for it, to improve quality, safety and value for money, in the use of medicines for the benefit of patients and the public."

The NPC work programme is designed to support the specific needs of commissioners, providers and individuals with an involvement in prescribing and medicines use. In order to improve the flexibility, accessibility and timeliness of its support, the NPC provides key NHS audiences with a range of choices for accessing outputs. This includes making use of opportunities provided by electronic learning environments, as well as more traditional approaches. Additional materials to complement this guidance are available through the NPC website: www.npc.nhs.uk

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1 Introduction

About Specials

Specials are special-order unlicensed medicines **made to meet the needs of an individual patient**. Unlicensed medicines may be prescribed in clinical situations where it is judged that, on the basis of available evidence, unlicensed use is in the best interest of the patient.[1,2] As with any medicine, prescription of unlicensed medicines is the responsibility of the prescriber. However, there are several additional considerations.[1,2,3]

- Specials **have not been assessed by the regulatory authority** for safety, quality and efficacy in the same way as licensed medicines, therefore they have no Summary of Product Characteristics (SPC) outlining the dose, contra-indications, storage and side-effect profile. Patient information leaflets are not routinely available for Specials.

- Specials can be obtained from a range of sources by pharmacists and are not all manufactured in the same way. This means that the **quality, bioavailability and consistency of Specials can vary** even where the same product is prescribed (**Appendix 1** contains some FAQs which explain about how Specials are made).

- **Specials can be difficult to identify at the point of prescribing**. See **Box 1**

- The way that the supply chain operates for Specials means that **costs for the same product can vary significantly**. Prescribers will not know the cost of a Special when it is prescribed.

Taken together, these factors mean that **prescribing a Special is associated with somewhat more risk** than prescribing a licensed medicine for a licensed indication. Prescribers should be satisfied that the patient's clinical needs cannot be met by a licensed medicine (for example, a different drug in the same class, or an alternative formulation).[1,2]

If another prescriber is asked to take over prescribing of a Special, they should be provided with all the information they need to ensure a safe and consistent supply of product for the patient.

The costs to the NHS of Specials may vary widely. For example, data supplied by NHS Business Services Authority Prescription Services shows net ingredient cost for the same strength, volume and quantity of unlicensed omeprazole liquid have ranged from £112.98 to £1113.13, and for hypromellose eye drops from £38.70 to £2882.10 (data for March 2011). In addition, in recent years the volume and costs of specials has risen. Data supplied by NHS Business Services Authority Prescription Services shows that for March 2009 the total items dispensed in primary care within England for Specials was 39,873 with a total net ingredient cost of £7,472,762 and in March 2011 total Items dispensed was 63,280 with a total net ingredient cost of £11,153,095. (See www.nhsbsa.nhs.uk/PrescriptionServices/3201.aspx)

What is in this guidance?

This guidance includes five guiding principles based on good prescribing practice that highlight specific issues to support prescribers in the safe and appropriate use of Specials. **Appendix 2** contains a quick practical checklist for prescribers to print out and use as a tool when prescribing.

When might a Special be appropriate?

There are a range of diverse clinical situations when Specials may be judged by the prescriber to be in the best interest of the patient on the basis of available evidence.

In children, Specials may be the only option for the prescriber for some conditions and in some circumstances are routinely prescribed. Liquid Specials may be manufactured to achieve the lower strengths or doses required, and not just to achieve the optimal form for administration. Overall, the risks of prescribing for children are higher than for adults[4,5] and so prescribers need to be vigilant at all times. It is important to ensure that a product is prescribed and supplied which ensures a consistent dose can safely be given, and that the practical aspects of supply are addressed.

In dermatology, there are a large number of Specials in use. In 2008, the British Association of Dermatologists reviewed the national use of dermatological Specials and subsequently produced a rationalised formulary to improve access to, and appropriate prescribing of, Specials.[6]

Patients having medicines administered using an enteral feeding tube generally need alternatives to solid dosage forms. There are a range of different alternatives available to prescribers for patients with feeding tubes, of which, Specials are one option.[7,8]

Specials may be initiated in general practice for patients who have, or develop, swallowing difficulties (for example, older patients or those at the end-of life either at home or in hospices). As with enteral feeding tubes there are a range of alternatives for these patients.

Box 1: Tips to help prescribers identify Specials

Specials can be difficult to identify at the point of prescribing and prescribers may be unaware that they are considering prescribing one. Here are some tips. If in doubt clinicians should discuss with pharmacist colleagues before prescribing:

- If a medicine is not in the British National Formulary (BNF) it could be a Special.*
- Dermatology products, eye drops and liquid preparations are more commonly formulated as Specials.
- Electronic prescribing systems may not identify Specials. Some systems may use the letter 'U' to indicate an unlicensed medicine, or misleadingly highlight the cost of Specials as 'zero'.
- Clinical systems can be used to highlight that a Special is being selected and potentially suggest alternatives.
- Community pharmacists may wish to check with prescribers if they think a prescriber is unaware they are prescribing a Special. Pharmacists have a responsibility to help ensure that prescribers are aware they are prescribing an unlicensed medicine.[9]
- In hospitals, clinical pharmacists may highlight to prescribers they are prescribing a Special.

** 'For some preparations the BNF and BNF for Children indicate whether the preparation needs to be obtained through a 'special-order' manufacturer, or a specialist importing company. Where an unlicensed drug is included in the BNF, this is indicated in square brackets after the entry. When the BNF suggests a use (or route) that is outside the licensed indication of a product ('off-label' use), this too is indicated. In the BNF for Children individual drug entries give an indication of the licensed status of the drug.'*

Box 2: Sources of more information?

Local, regional and national NHS organisations and professional bodies have developed a wide range of resources and support initiatives to help prescribers with the safe, rational and cost-effective prescribing of Specials. A summary of these resources and links to them can be found by clicking here.

Community pharmacists, medicines management teams or medicines information colleagues will be able to advise about local guidance or specific medicines.

2
Five guiding principles for prescribers

1. Establish a clinical need

Prescribers should be aware when they are prescribing a Special, or asking another professional to administer one. In general, Specials should only be prescribed when the patient has an individual clinical need that cannot be met by a licensed medicine of established efficacy, quality and stability.[1,3]

- As with all medicines, before initiating or continuing a prescription for a Special, prescribers need to review the overall clinical need for a medicine. In some cases, medicines review prior to converting to a Special will identify medicines which are not working or no longer needed.

- If there is still a clinical need for a medicine, there may be a range of licensed alternatives to prescribing an unlicensed Special.
  For example:
  - another licensed product in the same therapeutic class may be available in a suitable formulation for the patient
  - a different formulation of a licensed medicine may be available (such as dissolvable tablets, suppositories, patches)
  - using a UK licensed medicine outside the terms of its licence or 'off-label' (for example, outside defined indications, doses, routes of administration).

If there is no licensed alternative that meets the patient's clinical need, there may be a range of unlicensed options that can be considered for the patient.[1,2]
These include:

- prescribing a medicine licensed in a different country, but not the UK, that can be imported
- prescribing a Special (see **Appendix 1** for more details about the different sorts of Specials)
- crushing tablets or opening capsules licensed in the UK (where the formulation allows).

These unlicensed options all have their own risks, benefits and costs which need to be considered in each individual clinical situation. A wide range of information and advice is available for prescribers who may need to consider unlicensed medicines — see **Box 2**.

2. Identify medicines and preparations

The risks and benefits of using a Special will differ for different patient groups, different medicines and in individual clinical circumstances. Prescribers need to take into account the safety, effectiveness, quality and cost of all the options available to patients.

- In the absence of a licensed medicine, prescribers need to be satisfied that there is a good rationale for using an unlicensed medicine before it is prescribed.

- For commonly prescribed Specials, an Area Prescribing and Medicines Management Committee (or equivalent Drug and Therapeutics Committee), with local clinical input, can provide a decision-making forum to evaluate usage and develop a local formulary.

- Pharmacists can obtain a Special in a variety of ways (see **Appendix 1).** Unlike licensed medicines, the consistency of a Special cannot be assumed. **Different supplies of the same Special may have a different formulation, stability and potentially bioavailability**.

- The clinical implications of sourcing decisions will vary from patient group to patient group. For example, in some patient groups, such as young children or transplant patients who are taking medicines with a narrow therapeutic index, **formulation and consistency of dose is critical. In these cases, prescribers should be specific about the formulation**.

- There can be significant variation in the final price paid by the NHS for the same Special. This price variation depends on which supply route is chosen by community pharmacies. The Royal Pharmaceutical Society has issued guidance for pharmacists when sourcing Specials to help ensure good practice.[10] Prescribers should discuss with pharmacy colleagues the costs associated with prescribing and supply of Specials, including where they are concerned about variations in price.

3. Make a shared decision with the patient (or carer)

Prescribers should discuss treatment options with patients and carers, and ensure that they are aware of the implications and practicalities of each option.

- **Prescribers need to use their professional judgement in consultation with the patient, carers, a pharmacist and other relevant healthcare professionals** to guide their prescribing decisions.

- The prescriber should be aware of whether the patient is taking the medicine themselves, or whether it is being administered to them and by whom.

- Prescribers and patients (or carers) need to understand the practical implications of maintaining an ongoing supply and continuity of treatment; this may require active management. For example, where shelf lives are short, a longer timescale may be required to source one appropriate Special. This will have implications for quantities prescribed and the ordering of repeat prescriptions.

- Patients (or carers) should be aware when prescribed medicines are unlicensed and given appropriate information about what this means for their treatment.[3] As patient information leaflets are not routinely available for Specials, the prescriber and supplying pharmacist will need to take additional steps to ensure that the patient is informed about the medicine. The Medicines for Children website provides some information leaflets about the use of medicines in children, some of which may be Specials (www.medicinesforchildren.org.uk).

4. Ensure effective prescribing governance

Prescribers should understand the rationale for using a Special and the practical implications of prescribing before initiating, transferring, or taking over responsibility for prescribing.

- There can be additional risks and complexities associated with the transfer of prescribing and dispensing responsibilities for Specials and overall there is likely to be less professional familiarity with these products.

- When a secondary or tertiary care prescriber requests a primary care prescriber to continue (or initiate) a Special, they should ensure that the rationale, formulation and ongoing monitoring requirements for the Special are communicated to the new prescriber. When taking over the prescribing of a Special from secondary or tertiary care colleagues, the primary care prescriber should ensure that they are aware of the clinical need for, and implications of, continuing to prescribe the Special.

- Where consistency of formulation is particularly important, secondary or tertiary care prescribers should ensure that details of the formulation are communicated to the primary care prescriber, who can liaise with community pharmacy colleagues to ensure a consistent supply.

- Prescribers should record the Special prescribed and, where not following common practice, the reason for choosing this medicine in the patient's notes.[3]

5. Monitor and review on an ongoing basis

Prescribers should have systems in place to ensure the need for the Special is regularly reviewed, both in terms of the continued need for a Special product and in the context of the need for a medicine overall.

- Unlike licensed medicines, the effectiveness of Specials may not have been formally proven, so prescribers should ensure that the effectiveness of the Special is monitored.

- The patient's clinical needs may change, or new licensed products may become available which mean that a Special is no longer the best option for the patient. For example, as children grow they may be able to take licensed preparations or, patients who have had a stroke and have experienced difficulties swallowing, may find that their gag reflex returns.

- Prescribers may therefore want to review Specials on a more regular basis than licensed medicines, for example, by allowing for a smaller number of repeat prescriptions.

- As with licensed medicines, any unwanted effects should be reported to the MHRA through the yellow card scheme (http://yellowcard.mhra.gov.uk/).

- Specials can be expensive. To ensure best value for the NHS, prescribers should regularly review the costs of their Specials prescribing. **Box 3** gives some tips on how prescribing can be reviewed.

Box 3: Tips for commissioners to help prescribers review their Specials prescribing
• Some local NHS organisations have worked locally with GP practices to audit Specials prescribing. This can be linked to the Quality and Outcomes Framework. Examples of local practice can be found here.
• Commissioners can use the ePACT system to produce local data on the prescribing of Specials. East of England NHS collaborative procurement hub has produced a guide for Commissioners on how to use ePACT.[11]
• Commissioners can share resources and collaborate to develop prescribing prompts that give better value alternatives to common Specials, or they may wish to use a commercial decision support system.
• Local NHS organisations have identified alternative options to the prescribing of expensive Specials. Examples of local practice can be found here.

References

1. Medicines and Healthcare products Regulatory Authority. Guidance note 14. *The Supply of unlicensed medicinal products for individual patients*.
2. Medicines and Healthcare products Regulatory Authority. *Off-label or unlicensed use of medicines: prescriber's responsibilities*. April 2009.
3. General Medical Council. *Good Practice in Prescribing Medicines. Supplementary Guidance.* September 2008.
4. Wong IC, Ghaleb MA, Franklin BD, et al. *Incidence and nature of dosing errors in paediatric medications.* Drug Safety 2004;27(9):661-70
5. Conroy S, Sweis D, Planner C, et al. *Interventions to reduce dosing errors in children*. Drug Safety 2007; 30(12):1111-1125
6. British Association of Dermatologists. *List of accepted unlicensed dermatological preparations*. 2008 www.bad.org.uk/Portals/_Bad/Specials/BAD%20Specials%20Booklet.pdf
7. Bradnam V, White R. *Handbook of Drug Administration via enteral feeding tubes*. Pharmaceutical Press, 2007.
8. Betsi Cadwaladr University Health Board (Eastern Division) (Previously North East Wales NHS Trust). *The Newt Guidelines for administration of medication to patients with enteral feeding tubes or swallowing difficulties.* Smyth J Ed. 2nd ed. 2010.
9. General Pharmaceutical Council. *Standards of conduct, ethics and performance*. September 2010. www.pharmacyregulation.org/pdfs/other/gphcstandardsofconductethicsandperflo.pdf
10. Pharmacy Professional. *Dealing with Specials. Good practice guidance on the procurement and supply of pharmaceutical specials*. Royal Pharmaceutical Society, June 2010.
11. NHS East of England and East of England NHS Collaborative Procurement Hub. *Information and guidance on the prescribing and use of unlicensed pharmaceutical specials.* 2010.

Abbreviations

MHRA – Medicines and Healthcare products Regulatory Agency

CQC – Care Quality Commission

SPC – Summary of Product Characteristics

Appendix 1: Specials FAQs

Why are medicines licensed in the UK?

Medicines can only be marketed in the UK if licensed by the appropriate regulatory body. The regulatory body ensures a rigorous assessment of the safety, quality and efficacy of a medicinal product in the UK, prior to granting a marketing authorisation (formerly called a product licence, hence the term licensed medicines).

Do all medicines prescribed in the UK need to be licensed?

No. There are clinical situations when the use of **unlicensed medicines** may be judged by the prescriber to be in the best interests of the patient on the basis of available evidence.

Healthcare professionals may regard it necessary to prescribe, or advise on the use of an unlicensed medicine. This may be when no licensed suitable alternative is available, or when a licensed medicine is used outside the terms defined by the licence.

What are the Specials referred to in this document?

Specials are unlicensed medicines prescribed to meet the special (clinical) needs of individual patients on the direct personal responsibility of the prescriber.

How can they be legally made?

The Specials exemption[1] allows holders of a Manufacturer's ("Specials") Licence, issued by the MHRA, to manufacture and supply unlicensed medicines. It also allows the holder of a wholesale dealer's licence or, wholesale dealer's import licence issued by the MHRA, to import and supply unlicensed medicines.

In addition, an exemption to the Medicines Act 1968 (Section 10) allows the preparation of unlicensed medicines in a registered pharmacy by, or under the supervision of a pharmacist. This is known as extemporaneous preparation and allows pharmacists to make small amounts of 'custom-made' medicines.

Are all 'Specials' the same?

No. To hold and maintain a "Specials" Licence, manufacturers have to meet and retain minimum quality standards for their premises and procedures, as dictated and monitored by the MHRA. Specials that are made by a manufacturer with a Manufacturer's ("Specials") Licence can be (although are not always) made in batches, when the clinician requires, with some end product analytical testing.

Extemporaneously prepared medicines tend to be 'bespoke' medicines with no end product testing. They can be made in any registered pharmacy under the supervision of a pharmacist. If the holder of a Manufacturer's ("Specials") Licence premises is also a registered pharmacy, they can manufacture Specials under either of these exemptions.

How can a prescriber be sure about the quality of Specials?

Specials produced on a batch basis by manufacturers with a Manufacturer's ("Specials") Licence should have a certificate of analysis for the final product. Where the Special is not batch produced there should be a certificate of conformity, which is a signed statement from the manufacturer that they believe the product complies with the purchaser's specification. It would be good practice for the pharmacist dispensing the Special medicine to request this documentation.[8]

For extemporaneously prepared Specials, unless the manufacturer has a Manufacturer's ("Specials") Licence, there is unlikely to be any documented evidence of quality.

Where can a prescriber get more information about the manufacture of Specials?

- Association of Specials Manufacturers www.acsm.uk.com
- Special order manufacturers listed in the BNF www.bnf.org.uk
- Jackson M, Lowey A. Handbook of extemporaneous preparation. Pharmaceutical Press 2010 (www.pharmpress.com/product/9780853699019/handbook-of-extemporaneous-preparation)

[1] The exemption to meet the "special needs" of individual patients provided by Schedule 1 of the Medicines for Human use (Marketing Authorisations Etc) Regulations 1994 No 3144.

Appendix 2: Prescribing Specials: a quick checklist for prescribers

1. Establish a clinical need

Prescribers should be vigilant when they are prescribing a Special, or asking another professional to administer one. In general Specials should only be prescribed when the patient has an individual clinical need which cannot be met by a licensed medicine of established efficacy, quality and stability.

Does the patient need a medicine? Is it essential for this patient?

Is there a licensed preparation which could meet the patient's needs, for example soluble tablets, liquid formulations, or patches?

What are all the unlicensed alternatives? Is local guidance available?

2. Identify medicines and preparations

The risks and benefits of using a Special will differ for different patient groups, different medicines and in different individual clinical circumstances. Prescribers need to take into account the safety, effectiveness, quality and cost effectiveness of all the options available to patients.

What is the rationale for using an unlicensed medicine? Is there evidence or accepted practice to support usage?

Is the dose critical? Is the patient a child? Does the medicine have a narrow therapeutic window? Is there a requirement to specify the exact formulation?

What is the best value-for-money? Is there any local guidance?

3. Make a shared decision with the patient or carer

Prescribers should discuss treatment options with patients and carers and ensure that they are aware of the implications and practicalities of each option.

What are the practical implications of prescribing? What is the shelf-life? How often will prescriptions be needed? How long does it take to obtain?

Will the patient be taking the medicine themselves or will it be administered? Are there any implications for the choice of product?

4. Ensure prescribing governance

Prescribers should understand the rationale for using a Special and the practical implications of prescribing before initiating, transferring, or taking over responsibility for prescribing.

If initiating prescribing, how long is the patient expected to need this medicine?

If asking someone to continue prescribing, are communications with the new prescriber optimised?

If continuing the prescribing of a Special, do prescribers know the formulation and source of the initial supply? Is there a need to ensure consistency of dose by specifying the formulation?

5. Ensure ongoing monitoring and review

Prescribers should have systems in place to ensure the need for the Special is regularly reviewed, both in terms of the continued need for a Special product and in the context of the need for a medicine overall.

How often will the patient be reviewed?

Who will do the review?

Appendix 3: Acknowledgements

Expert group			
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British Medical Association

Royal Pharmaceutical Society (through expert group membership)

UK Clinical Pharmacists Association

National Pharmacy Association

Pharmaceutical Services Negotiating Committee

Association of Commercial Specials Manufacturers

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