

Prescribing and Clinical Effectiveness Bulletin

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ALTERNATIVES TO PRESCRIBING UNLICENSED PHARMACEUTICAL 'SPECIALS'

Key Points

- Special-order products (more commonly known as “specials”) are made-to-order unlicensed medicines designed to meet the needs of individual patients. The vast majority of prescribed specials are oral liquids formulated for patients who have difficulty taking tablets or capsules or those with swallowing difficulties; other types of specials include specially formulated ointments, creams, eye preparations or unlicensed tablets or capsules.
- In November 2011 the Department of Health published new arrangements for the reimbursement of specials (see Part VIII B of the *Drug Tariff*). As a consequence, a number of specials, capturing the majority of high-cost, high-volume items, were listed in the *Tariff* for the first time along with set reimbursement prices. The initial *Tariff* list was relatively small, but the list, and associated reimbursement prices, will be reviewed regularly with the potential for the list to be expanded as appropriate. Only the formulations and strengths specified in the *Tariff* are subject to set reimbursement prices; other strengths and formulations remain subject to non-*Tariff* reimbursement. Where a special is indicated and an appropriate product is available on the *Tariff* list, that product should be prescribed.
- Specials are unlicensed and, like any unlicensed medicine, should ONLY be prescribed where a licensed alternative does not meet the clinical needs of the patient. A prescribing pathway is detailed in the *Bulletin* that recommends stepwise consideration of (1) the full range of licensed formulations; (2) alternative medicines from the same therapeutic class; (3) licensed medicines used in an unlicensed manner; and (4) medicines licensed abroad, before consideration of (5) unlicensed specials.
- Prescribers are potentially liable for any adverse event or harm arising from the use of an unlicensed special and are professionally accountable for their judgement in prescribing an unlicensed product for their patient. Patients (or their carers) should be fully aware that they are being prescribed an unlicensed product and should give their consent to treatment; this should be fully documented in the patient’s notes.
- Specials are often expensive; even those listed in Part VIII B of the *Drug Tariff* can be significantly more expensive than licensed alternatives. For specials not listed in the *Drug Tariff*, there are no legal price restraints. Prescribers are unlikely to know the cost of the special at the point of prescribing and are advised to check, where possible, with their local community pharmacist or dispensary staff prior to issuing a prescription.
- This guidance has been developed by PACEF in consultation with both primary and secondary care and should be in use on both sides of the interface. Where a special is initiated or recommended from within secondary care, prescribers should ensure that all appropriate alternatives have been considered before continuing to prescribe.
- Prescribers should ensure that the continued prescription of a special is regularly reviewed and justified for each individual patient.
- The PCT Prescribing and Medicines Optimisation Team are currently working with individual practices to help to identify inappropriate prescribing of specials and to

recommend appropriate alternatives. If you have any queries about a particular special or need advice on possible alternatives in a particular situation do not hesitate to contact your local community pharmacist or PCT prescribing adviser.

- **Appendices to this *Bulletin* provide practical guidance on possible alternatives to unlicensed specials, advice on dispersing and crushing tablets or opening capsules and details the products currently specified on the *Drug Tariff* List.**

Introduction

This edition of the *PACE Bulletin* updates and expands on advice originally issued in *PACE Bulletin* Vol. 4 No. 17 (Nov 2010). It incorporates new material derived from Part VIII B of the *Drug Tariff* entitled *Arrangements for payment for specials and imported unlicensed medicines*.

Special-order products (more commonly known as “specials”) are made-to-order unlicensed medicines designed to meet the needs of individual patients. They are usually made by “special-order” manufacturers, occasionally by hospital manufacturing units and, rarely, by community pharmacies. The vast majority of prescribed specials are oral liquids specially formulated for patients who have difficulty taking solid dosage forms such as tablets or capsules; other types of specials include specially formulated ointments, creams and eye preparations. This issue of the *Bulletin* provides updated answers to the following questions:

- (1) When is it appropriate to prescribe a special?
- (2) What alternatives are available?
- (3) What are the medico-legal implications of prescribing specials?
- (4) What are the implications of the *Drug Tariff* Specials List launched in November 2011?

The main focus of the advice is on adults who have genuine difficulties taking solid dose forms, usually due to swallowing difficulties.

What’s the problem with specials?

While the prescribing of specials may be entirely appropriate for certain individual patients and some specific patient groups (e.g. neonates and young infants), prescribers need to consider the following risks associated with the use of specials in comparison to alternative options:

(1) Specials are unlicensed

Like any other unlicensed medicine, specials should ONLY be prescribed where a licensed alternative does not meet the clinical needs of the patient. Prescribers are potentially liable for any adverse event or harm arising from the use of a special and are professionally accountable for their judgement in prescribing a special for their patient. Patients should be fully aware that they are being prescribed an unlicensed product at the point of prescribing and this should be fully documented in the patient’s notes.

(2) Specials are not subject to the same level of quality control and stability testing as licensed products

Unlike licensed medicines, unlicensed specials have not been subject to clinical trials nor have they been assessed for safety, quality and efficacy by the licensing authority. They usually have a limited shelf-life (as little as seven days in some cases) and may also require refrigeration. It is advisable to check the likely expiry date with the community pharmacist or dispensary staff at the time of prescribing to ensure that a suitable quantity commensurate with the product’s shelf-life is prescribed.

While a Certificate of Analysis (COA) or a Certificate of Conformity (COC) should be available for every special, these certificates only provide a basic level of quality assurance. A COA provides evidence that critical parameters have been confirmed by retrospective physical, chemical or microbiological assay of a sample of the final product (i.e. the product has been analysed to show that the correct drug at the correct strength is present at the time of analysis). A COC is a signed statement by the manufacturer that they believe the product complies with the purchaser's specification.

Different manufacturers may use different formulations for what appears nominally to be the same product. This can lead to lack of bioequivalence between formulations and has resulted in anecdotal reports of harm (e.g. poor suspension of clobazam has resulted in seizures due to inadequate dosing).

(3) Specials are expensive

Even specials listed in Part VIII B of the *Drug Tariff* can be significantly more expensive than licensed alternatives (see below). For specials not listed in the *Drug Tariff* there are no legal price restraints resulting in a wide variation in cost for the same item depending on the supplier and the method of procurement. The average cost per special item across NHS Lincolnshire is £129; this compares to an average cost of just £7 for any prescribed item. The cost and volume of specials prescribed continues to rise; the projected per annum spend on specials in NHSL at current usage is £1.61 million (£134,000 per month). The largest cost recorded for a single liquid special item in Lincolnshire was in excess of £13,000 (in April 2010). Prescribers are unlikely to know the cost of a special at the point of prescribing and are advised to check, where possible, with their local community pharmacist or dispensary staff prior to issuing a prescription.

Drug Tariff Part VIII B; Arrangements for payment for specials and imported unlicensed medicines

In November 2011 the Department of Health introduced new arrangements for the reimbursement of specials. As part of these arrangements, a number of specials, capturing the majority of high-cost, high-volume items, were listed in the *Drug Tariff* (Part VIII B) along with set reimbursement prices. At present, 26% of all specials prescribed in Lincolnshire (by volume) are included in Part VIII B of the *Tariff*. The initial *Tariff* list was relatively small, but the list, and associated reimbursement prices, will be reviewed regularly with the potential for the list to be expanded as appropriate. Only the formulations and strengths specified in the *Tariff* are subject to set reimbursement prices; other strengths and formulations remain subject to non-*Tariff* reimbursement. The aim of the new arrangements is to create a more transparent system for reimbursing specials, linking the cost of reimbursement to the cost of the product, while providing value for money for the NHS. Having a *Tariff* price for key specials should create an incentive for providers of pharmaceutical services to procure specials in a manner that ensures value for money for the NHS and simplified reimbursement arrangements for the contractor.

While the *Tariff* specials list has standardised the reimbursement prices of some high-volume, high-cost specials, it must be emphasized that *Tariff* specials remain relatively expensive products. The average cost per item of a *Tariff* special in Lincolnshire is £137; this is higher than the average cost for a non-*Tariff* special (£127). In general, all specials, both *Tariff* and non-*Tariff*, remain expensive treatment options and should only be considered when other alternatives are deemed to be inappropriate.

What are the new paperwork requirements for non-*Tariff* specials?

For specials not listed in the *Drug Tariff*, the contractor (this applies to community pharmacists and dispensing doctors) or his representative must stamp, date, initial and

endorse the Certificate of Analysis (COA)/Certificate of Conformity (COC) that comes with the special with the invoice price less discount and add the prescriber's details. At the end of each month, the contractor must send a copy of the appropriately endorsed COA/COC to the PCT of the prescriber which will allow the PCT to match expenditure to the special supplied. A letter was issued from the PCT Contracting Team in December 2011 giving the full details of these new arrangements. Please contact the PCT Contracting Team or your PCT prescribing adviser if you need further advice.

Prescribing specials

The following pathway should be followed when faced with a patient with swallowing difficulties or for whom a solid dose form is not otherwise appropriate. It is also useful for those patients in whom an unusual solid dose formulated special or topical special is being considered:

Step 1: Is the medicine still needed?

Take the opportunity to review the patient's current medication and assess continuing need.

Step 2: Can I use an alternative licensed formulation?

Once continuing need has been established, review the availability of licensed formulations of the medicine required. These could include: oral liquids, soluble or effervescent tablets, orodispersible, granule or melt formulations. Alternative routes of administration could be considered where licensed products exist (e.g. transdermal patches etc). Wherever a licensed alternative is available, this should be preferred. Monitoring of prescribing data reveals that it is relatively common for an unlicensed special to be prescribed even where a licensed alternative is available.

Step 3: Is an alternative licensed agent in the same therapeutic class available?

If there are no appropriate licensed formulations of the preferred medicine, are there appropriate licensed formulations of an alternative agent or agents in the same class (e.g. where an oral liquid formulation of an SSRI antidepressant is required, consider those SSRIs available as licensed liquids rather than SSRIs only available as unlicensed liquid specials).

Step 4: Can I use a licensed medicine in an unlicensed manner?

Where none of the options detailed in Steps 1 to 3 provide a practical solution, consideration should be given to using a licensed medicine in an unlicensed manner (e.g. dispersing, crushing or dissolving tablets, opening capsules etc). Manipulation of a licensed product in this way will be outside of the product's marketing authorisation. However, for many solid dose formulations there will be evidence and clinical experience detailed in reputable sources confirming that formulation manipulation of this nature can take place without compromising the effectiveness of the medicine (see Appendices 2 and 3). Using an unlicensed medicine or a licensed medicine in an unlicensed manner is allowed by the Medicines Act if, in the view of the prescriber, this is necessary to fulfil the needs of an individual patient. MHRA advice is that it is preferable to use a licensed medicine in an unlicensed manner rather than a medicine licensed for purpose abroad or an unlicensed medicine like a liquid special (see below). Some formulations (e.g. enteric coated tablets, modified release formulations, cytotoxic, immunosuppressant, antibiotic and hormonal preparations) should not usually be crushed. Similarly sublingual or buccal tablets should not be crushed as this might reduce their bioavailability. As a general rule, chewable tablets should not be crushed or dispersed either unless there is specific information to the contrary. Fractional doses, often required in the treatment of neonates, infants and young children are most accurately given using licensed oral liquids or unlicensed liquid specials. Ultimately, whatever decision is taken must be taken based on best evidence (see Appendices 2 and 3), sound pharmaceutical advice (from either your local community pharmacist or PCT prescribing adviser) and be made in the best interests of the patient.

Step 5: Is a medicine licensed for purpose in another country available?

If there are no appropriate licensed formulations of the preferred medicine and no alternative formulations of a medicine within the same class, consider whether there is an appropriate medicine or formulation licensed abroad (for example, Bio-melatonin). In terms of the MHRA *Hierarchy of risk on the basis of product origin* (see below), this is preferable to using a completely unlicensed special. Prescribers are likely to require specialist advice from their local community pharmacist, their own suppliers or their local PCT prescribing adviser in order to determine what is available and from where.

Step 6: Consider using an unlicensed special

Where all of the options detailed in steps 1 to 5 yield no appropriate alternative, prescribing of an unlicensed special should be considered.

Applying the pathway: two worked examples

Proton Pump Inhibitors

A patient with swallowing difficulties requires an oral formulation of a proton pump inhibitor (PPI). The licensed options are as follows:

Licensed options	Dose	Cost (28 days)
Lansoprazole orodispersible tablets (Zoton FasTab) 15mg	15mg daily	£2.99
Lansoprazole orodispersible tablets (Zoton FasTab) 30mg	30mg daily	£5.50
Omeprazole multi-unit pellet system tablets (Losec MUPS) 10mg	10mg daily	£7.75
Omeprazole multi-unit pellet system tablets (Losec MUPS) 20mg	20mg daily	£11.60
Esomeprazole gastro-resistant granules 10mg (Nexium Granules)	10mg daily	£25.19

The unlicensed specials listed in Part VIII B of the Drug Tariff are as follows:

Unlicensed options	Dose	Cost (28 days)
Omeprazole oral suspension 10mg in 5ml	10mg daily	£275.99 (£147.85 for 75ml)
Omeprazole oral suspension 20mg in 5ml	20mg daily	£171.28 (£183.51 for 150ml)

For adult patients with swallowing difficulties, any of the licensed options are significantly lower in cost than unlicensed omeprazole oral suspension. Lansoprazole orodispersible tablets (Zoton FasTab) are preferred first line. Esomeprazole granules (Nexium) are licensed for children over 1 year of age and are dramatically lower in cost than omeprazole oral suspension. The *BNF for Children 2011/12* advocates Losec MUPS dispersed in water or the contents of omeprazole capsules or Losec MUPS mixed with fruit juice or yoghurt as options in children. It is recognised that children's doses, particularly when calculated from body weight, can necessitate the use of omeprazole oral suspension in order to give the exact dose required. It is emphasized that omeprazole oral suspension (available as an unlicensed liquid special) should not be considered as a first line option for patients requiring a PPI who experience swallowing difficulties.

Statins

A patient with swallowing difficulties requires an oral formulation of a statin. The licensed options are as follows:

Licensed options	Dose	Cost (28 days)
Atorvastatin chewable tablets (Lipitor Chewable Tablets) 10mg	10mg once daily	£12.88
Atorvastatin chewable tablets (Lipitor Chewable Tablets) 20mg	20mg once daily	£24.64
Simvastatin oral suspension 20mg in 5ml	20mg at night	£98.43 (£105.47 for 150ml)
Simvastatin oral suspension 40mg in 5ml	40mg at night	£150.38 (£161.12 for 150ml)

Careful consideration will need to be given to the cost-effectiveness of statin treatment within this context. Where treatment is indicated, atorvastatin chewable tablets are preferred. Lipitor Chewable Tablets are licensed in adults, adolescents and children aged 10 years or older. The cost of licensed simvastatin oral suspension exceeds NICE cost-effectiveness thresholds and should only be used exceptionally. Unlicensed special formulations of statins may be even more expensive than this and should not usually be prescribed.

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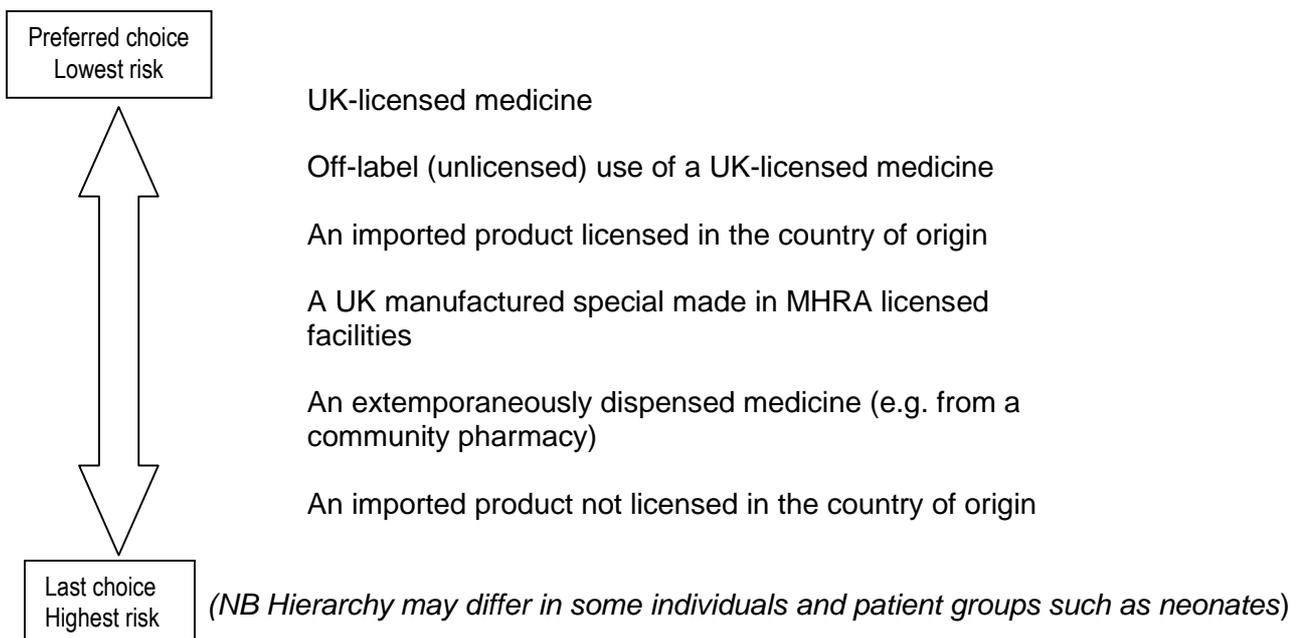
Stephen Gibson
Head of Prescribing and Medicines Optimisation

Richard Glet
Prescribing Adviser

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Appendix 1

Medicines and Healthcare products Regulatory Agency (MHRA): *Hierarchy of risk on basis of product origin* (adapted from MHRA guidance)



Appendix 2: Dispersing and crushing tablets or opening capsules

1. Dispersing or crushing tablets or opening capsules should not be seen as a routine way of administering medication to patients with swallowing difficulties, but as an option within the context of the stepwise process outlined above.
2. Many preparations are unsuitable for dispersing or crushing (e.g. enteric coated tablets, modified release preparations, sublingual or buccal tablets, chewable tablets (not usually recommended), solid dose formulations of cytotoxic, immuno-suppressant, antibiotic and hormonal drugs).
3. Crushing tablets or opening capsules should never be used to attempt covert administration in a non-compliant patient or against the wishes of a patient who refuses medication. Like any other method of administration, administering medicines in food or liquid should only be done with the patient's knowledge and consent.
4. Dispersing or crushing tablets or opening capsules should not be used to administer a proportion or fraction of a dose (e.g. for neonates or small children); within this context a licensed oral liquid formulation of the required medicine in an appropriate strength is preferred.
5. Where a licensed formulation of the required drug or an alternative drug in the same therapeutic class is unavailable, an unlicensed liquid special formulation is recommended.
6. Care staff in nursing or residential care may only administer medicines in an unlicensed manner on the specific instructions of the prescriber; to facilitate this, a written direction must be documented in the patient's care plan. Similarly, use of an unlicensed special must be documented in the same way.
7. When crushing / dispersing tablets and opening capsules:
 - Any manipulation of tablets or capsules should be done immediately before administration.
 - Where it is possible (see Appendix 3), dispersing a tablet in liquid should be done in preference to crushing it.
 - If dispersing tablets in water this may take several minutes. Unless there are specific instructions to the contrary, tablets should be dispersed in a small volume of water (e.g. 10 to 30mls), using a medicine administration pot or egg cup. Do not use boiling water to try to encourage dispersal of tablets as this might degrade the drug.
 - For medicines that are suitable for crushing, crush using a pestle and mortar, a tablet crusher or between two metal spoons. Tablets should NOT be crushed in plastic containers as the drug may adhere to the plastic.
 - The equipment used to crush tablets should be rinsed with the rinsings administered in addition to the crushed tablet to ensure that the total dose is taken.
 - Only disperse/crush medicines one tablet at a time; do not mix different medicines together.
 - Crushed tablets or capsule contents may be mixed with a teaspoon of cold food (e.g. yoghurt, jam) to mask the taste and for ease of swallowing.
 - Patients should be advised to rinse their mouth with water after taking crushed tablets/opened capsules to reduce the risk of any local irritation or anaesthetic action in the mouth.
 - Medicines should only be administered in food or liquid with the patient's knowledge and consent.
8. If a tablet is crushed or dispersed in water, or a capsule opened, clear instructions should be given. In most cases when crushed or dispersed, the product becomes unlicensed, but the use of a licensed product (manufactured to the highest pharmaceutical standards) in an unlicensed way is likely to be associated with a lower risk than using an unlicensed special manufactured to less exacting standards.
9. Most dispersed tablets can be flushed down PEG or other standard bore enteral tubes without problem - please contact your local community pharmacist or PCT prescribing adviser for further advice.

Appendix 3: Information on commonly prescribed specials and possible alternatives

These recommendations are taken from standard reputable sources on the administration of solid dose medicines to patients with swallowing difficulties or to those who need to have medicines administered via enteral tubes (see References). **The following alternatives are suggestions and may not be appropriate for some patients (e.g. young children requiring small fractional doses, and those who are unable to manipulate medicines).** It will not always be possible to avoid using a special.

'Special order' product	Possible alternatives
Allopurinol liquid special	Tablets may be dispersed or crushed. Allopurinol is insoluble in water but tablets will disperse if shaken in ≈10mls water to produce a milky suspension
Amiodarone liquid special	Tablets may be crushed and mixed with water or fruit juice; taste is very bitter. Tablets disperse very slowly if not crushed. Alternatively mix crushed tablets with jam if taken orally.
Amisulpride 25mg / 5ml liquid special*	A licensed solution (100mg/ml) is available (Solian) and comes with a dosing pipette allowing 50mg (0.5ml) to be accurately measured. <i>Tariff</i> specials are available, but should only be used where alternatives are considered inappropriate.
Amitriptyline HCl liquid special 10mg in 5ml*	A licensed solution containing 25mg in 5ml or 50mg in 5ml is available. Consider using 12.5mg (2.5ml) measured with an oral syringe. <i>Tariff</i> specials are available, but should only be used where alternatives are considered inappropriate. Both an oral solution and an oral suspension are available on <i>Tariff</i> , the oral solution is lower cost.
Amlodipine liquid special*	Tablets may be dispersed or crushed. They readily disperse in water. <i>Tariff</i> specials are available, but should only be used where alternatives are considered inappropriate. Both oral solutions and oral suspensions are available (5mg in 5ml and 10mg in 5ml strengths); the oral solutions are lower in cost.
Atenolol liquid special	Available as a licensed 25mg in 5ml SF oral solution. Alternatively the tablets can be crushed and mixed with water
Atorvastatin liquid specials	Atorvastatin chewable tablets (10mg and 20mg) are the preferred licensed equivalent (licensed in children aged 10 years and over, adolescents and adults) (see worked example). Alternatively atorvastatin tablets may be dispersed in water or crushed. Tablets will disperse slowly in water to produce a fine milky suspension. The suspension is light sensitive; do not delay administration.
Azathioprine 25mg or 50mg or 125mg in 5ml *	Cytotoxic – do not crush. Tablets are usually film coated and will disperse in water within 5 minutes to give a yellow milky dispersion. A <i>Tariff</i> special is available (50mg in 5ml oral suspension), but should only be used where alternatives are considered inappropriate.
Bendroflumethiazide liquid specials*	Tablets (2.5mg / 5mg) may be crushed or dispersed in water to produce a milky suspension. A <i>Tariff</i> special is available (2.5mg in 5ml oral suspension), but should only be used where alternatives are considered inappropriate.

'Special order' product	Possible alternatives
Bisoprolol fumarate liquid specials	Some brands are film coated but may be crushed. Some patient information leaflets may advise against crushing or chewing presumably because of the film coating. They disperse in water to produce a fine suspension.
Captopril liquid specials *	Tablets (12.5mg, 25mg and 50mg) can be crushed or will disperse readily in water. <i>Tariff</i> specials are available, but should only be used where alternatives are considered inappropriate. Captopril 5mg in 5ml oral solution is lower cost than oral suspension.
Carbamazepine 500mg/5ml liquid special	Carbamazepine is available as a licensed 100mg/5ml sugar-free oral suspension instead of the 500mg/5ml liquid 'special'. Chewable sugar-free tablets are also available in 100mg and 200mg strengths. Consider these if clinically appropriate.
Carbimazole 5mg or 10mg in 5ml	Tablets can be crushed (the active drug is contained within the central core of the tablet; the coloured compression coat is inert). Tablets will disperse in water only with vigorous shaking to produce a fine dispersion
Chloral hydrate liquid special 200mg / 5ml (chloral elixir, paediatric) or 500mg / 5ml (chloral mixture) *	A licensed elixir is available (Welldorm) containing 143.3mg/5ml. <i>Tariff</i> specials are available (500mg in 5ml), but should only be used where alternatives are considered inappropriate.
Chlortalidone liquid special	Tablets can be dispersed in water
Clobazam liquid special *	Tablets (10mg) can be dispersed in water or crushed. May taste unpleasant - could put in fruit juice or soft food to mask taste. <i>Tariff</i> specials are available, but should only be used where alternatives are considered inappropriate.
Clonazepam 2.5mg /ml, 2mg /5ml and 500mcg / 5ml liquid special	Tablets (500 mcg and 2mg tablets) can be crushed or will disperse in water within 5 minutes to produce a coarse dispersion. A new licensed formulation containing 500mcg in 5ml has recently become available.
Clopidogrel liquid special	Clopidogrel tablets are film-coated but can be crushed and mixed with water (e.g. 10ml). The resulting suspension can be flushed down feeding tubes without blockage.
Co-careldopa liquid special	Consider changing to co-beneldopa dispersible tablets, (co-beneldopa 25/100, Madopar Dispersible tablets 125 or co-beneldopa 12.5/50, Madopar Dispersible 62.5). Non-MR Sinemet tablets (co-careldopa) disperse readily in water. Take care to administer the whole dose; there is a tendency for settlement to the bottom of the container or syringe.
Co-dydramol liquid special 10/500 in 5ml *	Consider use of co-codamol 8/500 or 30/500 dispersible tablets (but high sodium content). Licensed liquid preparations of dihydrocodeine (10mg in 5ml) and paracetamol (250mg/5ml) are available that could be prescribed separately. <i>Tariff</i> specials are available, but should only be used where alternatives are considered inappropriate.
Dantrolene sodium liquid special	Open capsules (25mg) and mix contents with orange juice (to maintain acidity)
Diazepam liquid specials	Licensed solutions available containing 2mg / 5ml or 5mg / 5ml

'Special order' product	Possible alternatives
Diltiazem HCl liquid special 60mg / 5ml	Consider whether amlodipine tablets (which can be crushed) can be used in place of diltiazem. 60mg diltiazem MR tablets designed for dosing three times a day may be crushed and although this is likely to affect the pharmacokinetics, it is unlikely to cause adverse effects. Slozem capsules (once daily) may be opened and the pellets taken with soft food without crushing. Pellets may block smaller sized enteral tubes.
Diltiazem 2% cream *	Anoheal [®] brand of diltiazem 2% cream is available directly from SLA Pharm 01923 681001, 2 day order to delivery schedule & 18 month shelf life. GTN 0.4% ointment (Rectogesic [®]) is a licensed alternative. <i>Tariff</i> specials are available, but should only be used where alternatives are considered inappropriate.
Dipyridamole liquid special *	Licensed liquid preparation contains 50mg in 5ml. For stroke prevention, consider opening MR capsules and mix granules with yoghurt or similar soft food. Do not crush or chew the granules. Granules may block enteral tubes. Clopidogrel is now preferred to dipyridamole in stroke prevention; patients currently receiving a dipyridamole liquid special for this indication could benefit from review. <i>Tariff</i> specials are available, but should only be used where alternatives are considered inappropriate.
Doxazosin mesilate liquid special	Non-MR tablets can be crushed or dispersed in water to give a coarse dispersion
Enalapril liquid special	A licensed liquid formulation of ramipril is available and is the preferred option; patients currently receiving an enalapril liquid special could benefit from review. Alternatively, enalapril tablets can be crushed or dispersed in water to create a fine suspension.
Ferrous sulphate liquid special 60mg in 5ml (12mg iron in 5ml) *	Licensed iron preparations available e.g. Fersamel syrup (ferrous fumarate 140mg (45mg iron) / 5ml (if for tube administration dilute with an equal volume of water to reduce viscosity). Ironorm Drops (ferrous sulphate 125mg (25mg iron) /ml). <i>Tariff</i> specials are available, but should only be used where alternatives are considered inappropriate.
Folic acid liquid special	Licensed preparation contains 2.5mg / 5ml. Alternatively tablets can be crushed and mixed with water.
Gabapentin liquid special 250mg or 500mg or 600mg in 5ml *	Capsules can be opened (100mg, 300mg or 400mg) and contents dissolved in water/fruit juice or sprinkled on food. 100mg caps are fiddly due to small size. <i>Tariff</i> specials are available, but should only be used where alternatives are considered inappropriate; 250mg in 5ml oral solution is lower cost than oral suspension.
Gliclazide liquid special *	Standard release tablets can be crushed and mixed with water if required. <i>Tariff</i> specials are available, but should only be used where alternatives are considered inappropriate.
Glyceryl trinitrate ointment 0.2% *	Glyceryl trinitrate ointment 0.4% (Rectogesic [®]) is a cheaper licensed alternative. <i>Tariff</i> specials are available, but should only be used where alternatives are considered inappropriate.
Haloperidol liquid specials *	Licensed sugar-free solutions 1mg/ml, 2mg/ml available. Alternatively, capsules can be opened and contents dispersed in water. <i>Tariff</i> specials are available, but should only be used where alternatives are considered inappropriate; 1mg in 5ml oral solution is less costly than oral suspension.

'Special order' product	Possible alternatives
Hydrocortisone liquid special	10mg or 20mg tablets can be crushed and mixed with food. They will disintegrate readily in water. Hydrocortisone 10mg tablets are scored
Hypromellose 0.25% eye drops *	Although not expensive and Tariff listed, licensed alternatives are available. 0.3%, 0.5% and 1% licensed eye drops available in bottles; licensed preservative-free 0.3% unit dose drops also available (Lumecare, Tears Naturale, Artelac). <i>Tariff</i> specials are available, but should only be used where alternatives are considered inappropriate.
Isosorbide mononitrate liquid special	Standard release tablets can be crushed. Consider GTN patches
Levothyroxine liquid specials	Licensed solutions are available (25mcg, 50mcg and 100mcg in 5ml). Tablets can be crushed and/or dispersed in water.
Lisinopril liquid special *	A licensed liquid formulation of ramipril is available and is the preferred option; patients currently receiving a lisinopril liquid special could benefit from review. Alternatively, lisinopril tablets can be dispersed in water to give a fine dispersion or they can be crushed and taken with food. <i>Tariff</i> specials are available, but should only be used where alternatives are considered inappropriate; oral solution is less costly than oral suspension.
Lorazepam liquid special *	1mg and 2.5mg tablets can be crushed and/or dispersed in water. Tablets can also be administered sublingually. <i>Tariff</i> specials are available, but should only be used where alternatives are considered inappropriate; 1mg in 5ml oral solution is less costly than oral suspension.
Magnesium glycerophosphate tablets (97.2mg Mg ⁺⁺ = 4mmol/tab)	Magnaphate 4mmol tablets is a cheaper alternative (4mmols equal to 97.2mg of magnesium and 1g of magnesium glycerophosphate); tabs may be chewed or swallowed whole & are scored so they can be broken into quarters. Available from Arjun products.
Melatonin special-order tablets / capsules/ liquid*	Consider Circadin [®] (UK license for short term use in people aged 55 and over but long-term use and/or use in younger people is unlicensed) or Bio-melatonin (import; licensed in some European countries). Both are much cheaper alternatives to specials. <i>Tariff</i> specials are available, but should only be used where alternatives are considered inappropriate; melatonin 5mg in 5ml oral solution is less costly than oral suspension.
Meloxicam liquid special	Tablets are film coated but will disperse in water to give a clear suspension with a virtually neutral taste.
Metformin liquid special (500mg in 5ml)	500mg or 1g sachets are available as a licensed product (Glucophage). This is the lowest cost option for patients with swallowing difficulties (Note: sachets should be taken in 150ml water) A licensed SF oral liquid 500mg in 5ml is available that is cheaper than the special.
Methyldopa liquid special 250mg in 5ml	Tablets can be crushed and dispersed in water for oral administration; unsuitable for enteral tube administration because the tablet coating may not dissolve and may block the tube.

'Special order' product	Possible alternatives
Midazolam liquid special 10mg / ml (buccal or mucosal)	Midazolam oromucosal solution 5mg/ml (Buccolam) in 2.5mg/5mg/7.5mg/10mg pre-filled syringes is a recently licensed product that has been approved in Lincolnshire for the emergency treatment of status epilepticus after specialist initiation. To minimise risks and potential confusion existing patients on unlicensed midazolam 10mg/ml buccal solution (Epistatus) should remain on this until they or their clinician consider it to be appropriate to change or stop. All new patients requiring midazolam for this indication should be initiated on midazolam 5mg/ml oromucosal solution (Buccolam) at an appropriate dose dependent upon age. Liquid midazolam formulations should only be initiated on specialist advice; no formal shared care guideline is required. To avoid confusion liquid midazolam preparations should always be prescribed by brand. <i>Tariff</i> specials are available, but should only be used where alternatives are considered inappropriate.
Omeprazole liquid special 10mg or 20mg in 5ml *	Consider lansoprazole orodispersible tablets as the most cost-effective alternative. Omeprazole MUPS dispersible tablets are also an option; they disintegrate to give a dispersion of small granules (may block fine bore feeding tubes <8Fr). Do not crush or chew dispersible tablets. Esomeprazole granules (Nexium) are licensed for children over 1 year of age and are also dramatically lower in cost than omeprazole oral suspension (see worked example). Alternatively, omeprazole capsules may be opened and sprinkled on food, or mixed with yoghurt or jam but the granules must not be crushed or chewed. Omeprazole liquid specials are formulated with sodium bicarbonate and may prove unpalatable for young children. <i>Tariff</i> specials are available, but should only be used where alternatives are considered inappropriate.
Ondansetron liquid special	A licensed ondansetron syrup SF 4mg/5ml is available (contains sorbitol). Zofran Melt (4mg & 8mg oral lyophilisates) can be allowed to disperse on the tongue and swallowed. Plain tablets will disperse slowly in water
Oxybutynin liquid special	Licensed liquid unavailable until March 2013 at earliest. Licensed patches available or standard release tablets can be crushed and mixed with water.
Paracetamol liquid special 500mg in 5ml *	Use paracetamol dispersible tablets or paracetamol 250mg/5ml suspension. <i>Tariff</i> specials are available, but should only be used where alternatives are considered inappropriate.
Phenytoin liquid special 90mg in 5ml *	Licensed phenytoin liquid contains 30mg / 5ml. <i>Tariff</i> specials are available, but should only be used where alternatives are considered inappropriate.

'Special order' product	Possible alternatives
Pregabalin liquid special	A new licensed oral liquid is now available (20mg/ml) and is the preferred option; patients currently receiving an unlicensed pregabalin liquid special should be reviewed. Pregabalin capsules can be opened and contents mixed with water or food (may have unpleasant taste).
Quetiapine liquid special *	Standard release tablets can be crushed and mixed into soft food (e.g. yoghurt). Bitter taste, yoghurt is the best vehicle. <i>Tariff</i> specials are available, but should only be used where alternatives are considered inappropriate.
Ramipril liquid specials	A licensed liquid formulation of ramipril is available (2.5mg in 5ml) and is the preferred option; patients currently receiving an unlicensed ramipril liquid special should be reviewed. Ramipril tablets disperse within 2 – 5minutes in water to give a fine dispersion which settles quickly but may be flushed down an 8Fr NG tube. Ramipril capsules can be opened and mixed with food or water
Riluzole liquid special 50mg in 5ml (£900)	The tablets are film coated but can be crushed and mixed with water or food. Use within 15 minutes
Ranitidine liquid special	150mg and 300mg licensed effervescent tablets available. Also 75mg/5ml SF licensed oral solution available.
Rosuvastatin liquid specials	The tablets are film coated and will disperse in water within 5 minutes to give a pale pink, milky dispersion that flushes down an 8Fr NG tube without blockage. Atorvastatin chewable tablets (10mg and 20mg) are the preferred licensed equivalent (licensed in children aged 10 years and over, adolescents and adults) (see worked example). Licensed preparations of simvastatin oral suspension are now available from Rosemont containing 20mg in 5ml and 40mg in 5mls. See sections on atorvastatin and simvastatin for further information.
Sertraline liquid special *	Film coated tablets that may be difficult to disperse or crush. Consider changing to an alternative SSRI available as a liquid preparation (e.g. citalopram 40mg/ml oral drops or fluoxetine 20mg in 5ml). <i>Tariff</i> specials are available, but should only be used where alternatives are considered inappropriate.
Sildenafil liquid special	Tablets can be crushed and dispersed in water or mixed with food. Vardenafil orodispersible tablets 10mg (Levitra) provide a licensed alternative.
Simvastatin liquid specials	Atorvastatin chewable tablets (10mg and 20mg) are the preferred licensed equivalent (licensed in children aged 10 years and over, adolescents and adults). Licensed preparations of simvastatin oral suspension are now available from Rosemont containing 20mg in 5ml and 40mg in 5mls; they are cheaper than specials but still expensive (see worked example). Simvastatin tablets can be slowly dispersed in water or crushed. All of these options are preferable to an unlicensed simvastatin liquid special.
Sodium bicarbonate liquid special 420mg/5ml (8.4%) *	<i>Tariff</i> specials are available, but should only be used where alternatives are considered inappropriate.
Spironolactone liquid specials *	Tablets can be crushed and will disperse in water. <i>Tariff</i> specials are available, but should only be used where alternatives are considered inappropriate.
Terbinafine liquid special	Tablets can be crushed and will disperse in water

'Special order' product	Possible alternatives
Tolterodine liquid special	Standard release tablets can be crushed and mixed with water or food. They will disperse in water within a minute.
Venlafaxine liquid special 37.5mg or 75mg in 5ml	Standard release venlafaxine tablets may be crushed and taken with food. They will disperse slowly in water, but may require shaking. The modified release capsules can be opened and the contents emptied out into smooth food (eg yoghurt). The capsule contents must not be crushed or chewed.
Warfarin liquid special	There is a licensed 5mg in 5ml oral suspension which should be used in preference to liquid specials of other strengths. Tablets may be crushed and taken with food. Most brands of tablets will disperse in water within 5 minutes if shaken.
Zolpidem liquid special *	Tablets can be crushed and mixed with water.
Zopiclone liquid special *	Do not crush zopiclone tablets (they are difficult to crush, taste very bitter and the bioavailability may be affected). Consider temazepam oral liquid 10mg in 5ml or zolpidem tablets which can be crushed and mixed with water. <i>Tariff</i> specials are available, but should only be used where alternatives are considered inappropriate.

* *Tariff* Specials available (see Appendix 4).

References

- White R, Bradnam V. *Handbook of drug administration via enteral feeding tubes* 2nd ed. London: Pharmaceutical Press 2011.
- Picton C et al., *Prescribing Specials: five guiding principles for prescribers*. National Prescribing Centre July 2011
- Dowell G., *Alternatives to prescribing unlicensed pharmaceutical special-order products*. NHS Coastal West Sussex v13 March 2012
- Anon. *Information and Guidance on the Prescribing and Use of Unlicensed Pharmaceutical Specials*. East of England NHS Collaborative Procurement Hub. January 2010.
- Anon., The use of 'specials' in primary care. *Drug & Therapeutics Bulletin* 2010; 48: 110-112
- Anon., *Dealing with Specials. Good Practice Guidance on: The Procurement and Supply of Pharmaceutical Specials* [Royal Pharmaceutical Society Guidance] Pharmacy Professional June 2010 pp27-32 updated June 2011
- NHS Lincolnshire *PACE Bulletin* 2012; 6(5): 4. Midazolam 5mg in 1ml Oromucosal Solution (Buccolam)
- NHS Lincolnshire *PACE Bulletin* 2010; vol 4 (17): Use of Unlicensed Pharmaceutical 'Specials'
- British National Formulary* 63 March 2012. Pharmaceutical Press.
- MIMS* June 2012 Haymarket Business Media
- Drug Tariff* June 2012. The Stationery Office

Appendix 4: Specials and imported unlicensed medicines listed in Part VIII B of the Drug Tariff (July 2012)

Amisulpiride 25mg/5ml oral solution
 Amisulpiride 25mg/5ml oral suspension
 Amitriptyline 10mg/5ml oral solution
 Amitriptyline 10mg/5ml oral suspension
 Amlodipine 10mg/5ml oral solution
 Amlodipine 10mg/5ml oral suspension
 Amlodipine 5mg/5ml oral solution
 Amlodipine 5mg/5ml oral suspension
 Azathioprine 50mg/5ml oral suspension

Bendroflumethiazide 2.5mg/5ml oral suspension
Bisacodyl 2.74mg/ml rectal solution
Captopril 25mg/5ml oral solution
Captopril 25mg/5ml oral suspension
Captopril 5mg/5ml oral solution
Captopril 5mg/5ml oral suspension
Chloral hydrate 500mg/5ml mixture BP 2000
Clobazam 10mg/5ml oral suspension
Clobazam 5mg/5ml oral suspension
Co-dydramol 10mg/500mg/5ml oral suspension
Colecalciferol 15,000units/5ml oral solution
Dexamethasone 0.1% eye drops
Dexamfetamine 5mg/5ml oral solution
Dexamfetamine 5mg/5ml oral suspension
Diltiazem hydrochloride 2% cream
Dipyridamole 100mg/5ml oral suspension
Ergocalciferol 3,000units/ml oral solution
Ferrous sulphate 60mg/5ml oral solution
Flecainide 25mg/5ml oral solution
Flecainide 25mg/5ml oral suspension
Gabapentin 250mg/5ml oral solution
Gabapentin 250mg/5ml oral suspension
Gabapentin 400mg/5ml solution/suspension
Gliclazide 80mg/5ml oral suspension
Glyceryl trinitrate 0.2% ointment
Glycopyrronium bromide 1mg/5ml oral solution/suspension
Haloperidol 1mg/5ml oral solution
Haloperidol 1mg/5ml oral suspension
Hypromellose 0.25% eye drops
Ketamine 50mg/5ml oral solution
Ketamine 50mg/5ml oral suspension
Lisinopril 5mg/5ml oral solution
Lisinopril 5mg/5ml oral suspension
Lorazepam 1mg/5ml oral solution
Lorazepam 1mg/5ml oral suspension
Lorazepam 500microgram/5ml oral solution
Lorazepam 500microgram /5ml oral suspension
Magnesium glycerophosphate 121.25mg/5ml (5mmol/5ml) oral solution
Magnesium glycerophosphate 121.25mg/5ml (5mmol/5ml) oral suspension
Melatonin 5mg/5ml oral solution
Melatonin 5mg/5ml oral suspension
Midazolam 10mg/ml oral solution
Omeprazole 10mg/5ml oral suspension
Omeprazole 20mg/5ml oral suspension
Omeprazole 5mg/5ml oral suspension
Paracetamol 500mg/5ml oral suspension
Phenobarbital 50mg/5ml oral solution
Phenobarbital 50mg/5ml oral suspension
Phenytoin 90mg/5ml oral suspension
Primidone 50mg/5ml oral suspension
Quetiapine 100mg/5ml oral suspension
Quetiapine 12.5mg/5ml oral suspension
Sertraline 50mg/5ml oral suspension
Sodium bicarbonate 420mg/5ml (1mmol/ml) oral solution
Sodium chloride 292.5mg/5ml (1mmol/ml) oral solution

Sodium chloride 5% eye drops
Sodium chloride 5% eye ointment
Spironolactone 25mg/5ml oral suspension
Spironolactone 5mg/5ml oral suspension
Spironolactone 50mg/5ml oral suspension
Tacrolimus 2.5mg/5ml oral suspension
Tacrolimus 5mg/5ml oral suspension
Topiramate 25mg/5ml oral suspension
Topiramate 50mg/5ml oral suspension
Zopiclone 3.75mg/5ml oral solution
Zopiclone 3.75mg/5ml oral suspension