# Unlicensed Medicines & Unlicensed Uses

Doctors can prescribe unlicensed medicines, or licensed medicines for unlicensed uses (off-label/off license prescribing). In these situations the doctor is legally responsible for the medicine. They may be called upon to justify their actions in the event of an adverse reaction. Doctors are expected to take “reasonable care” in common law, and to act in a way which is consistent with the practice of a responsible body of their peers of similar professional standing.

The General Medical Council guidance on Good Practice in Prescribing Medicines (January 2013) gives the following information for doctors (http://www.gmc-uk.org/guidance/ethical_guidance/prescriptions_faqs.asp)

**Prescribing unlicensed medicines**

You can prescribe unlicensed medicines but, if you decide to do so, you must:

1. Be satisfied that an alternative, licensed medicine would not meet the patient's needs.
2. Be satisfied that there is a sufficient evidence base and/or experience of using the medicine to demonstrate its safety and efficacy.
3. Take responsibility for prescribing the unlicensed medicine and for overseeing the patient's care, including monitoring and any follow up treatment.
4. Record the medicine prescribed and, where you are not following common practice, the reasons for choosing this medicine in the patient's notes.

**Prescribing medicines for use outside the terms of their licence (off-label)**

1. You may prescribe medicines for purposes for which they are not licensed. Although there are a number of circumstances in which this may arise, it is likely to occur most frequently in prescribing for children. Currently pharmaceutical companies do not usually test their medicines on children and as a consequence, cannot apply to license their medicines for use in the treatment of children. The use of medicines that have been licensed for adults, but not for children, is often necessary in paediatric practice.

2. When prescribing a medicine for use outside the terms of its licence you must:
   a) Be satisfied that it would better serve the patient's needs than an appropriately licensed alternative.
   b) Be satisfied that there is a sufficient evidence base and/or experience of using the medicine to demonstrate its safety and efficacy. The manufacturer's information may be of limited help in which case the necessary information must be sought from other sources.
   c) Take responsibility for prescribing the medicine and for overseeing the patient's care, monitoring and any follow up treatment, or arrange for another doctor to do so.
   d) Make a clear, accurate and legible record of all medicines prescribed and, where you are not following common practice, your reasons for prescribing the medicine.

**Information for patients about the licence for their medicines**

1. You must give patients, or those authorising treatment on their behalf, sufficient information about the proposed course of treatment including any known serious or common side effects or adverse reactions. This is to enable them to make an informed decision.
2. Some medicines are routinely used outside the scope of their licence, for example in treating children. Where current practice supports the use of a medicine in this way it may not be necessary to draw attention to the licence when seeking consent. However, it is good practice to give as much information as patients, or those authorising treatment on their behalf, require or which they may see as significant. Where patients, or their carers express concern you should also explain, in broad terms, the reasons why medicines are not licensed for their proposed use. Such explanations may be supported by written information, including the leaflets on the use of unlicensed medicines or licensed medicines for unlicensed applications in paediatric practice produced by the Royal College of Paediatrics and Child Health/Neonatal and Paediatric Pharmacists Group Standing Committee on Medicines.
3. However, you must explain the reasons for prescribing a medicine that is unlicensed or being used outside the scope of its licence where there is little research or other evidence of current practice to support its use, or the use of the medicine is innovative.

**The medicines detailed in the table below do not have a license in the UK or are being used outside the licensed indications and primary care prescribers may be asked to prescribe them. GPs are not obliged to prescribe unlicensed medicines if requested by a consultant. If they choose to, then check the 'evidence for use' column before prescribing. If you require references, please contact the East Anglia Medicines Information Centre (01473 704431). This document is reviewed and updated regularly.**

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**Most recent revision – 07 September 2018**

**ULM = unlicensed medicine, ULU = unlicensed use**

| Drug | Indication | Evidence for use / Other info |
|---|---|---|
| Acetylcysteine (NAC) capsules and effervescent tablets<br><br>**ULM** | Mucolytic and for fibrosing alveolitis | Generally not considered effective for treating the pulmonary manifestations of cystic fibrosis. Evidence for efficacy in meconium ileus and distal obstruction syndrome lacking. Acetylcysteine + prednisolone and azathioprine is a recommended option for treating idiopathic pulmonary fibrosis. (1,3, 8) |
| Albendazole tablets<br><br>**ULM** | Helminth infections | Albendazole is a benzimidazole carbamate anthelminthic structurally related to mebendazole and with similar activity. (1) Spectrum of activity broader than mebendazole. (3)<br><br>Evidence supports use in Ascariasis, Cutaneous larva migrans, Cysticercosis, Echinococcosis, Gnathostomias, Hookworm, Loiasis, Lymphatic filariasis, Microsporidiosis, Strongyloidiasis and Trichuriasis (1, 2)<br>Drug of choice against Echinococcosis because its degree of systemic absorption and penetration into hydatid cysts is superior to mebendazole. (3) |
| Alendronic acid | Early breast cancer (preventing recurrence and improving survival) | See “bisphosphonates” |
| Azithromycin | Cystic fibrosis (CF) – long term treatment<br><br>Non-CF bronchiectasis: long-term treatment | NICE ESUOM Nov 2014 - A Cochrane review included 10 studies (n=959) with various dosing regimens, the most common being 250−500 mg 3 times weekly. In 4 studies (n=549), azithromycin statistically significantly improved forced expired volume in 1 second over 6 months compared with placebo. Azithromycin doubled the rate of being free of exacerbations over 6 months compared with placebo; however, the data were heterogeneous and should be interpreted with caution. The need for oral antibiotics was statistically significantly reduced with azithromycin, but there were limited data on the need for intravenous antibiotics and other secondary outcomes. Adverse events were uncommon and not obviously associated with azithromycin. There is little published evidence to determine the safety of azithromycin when used for over 6 months - Link<br><br>NICE ESUOM Nov 2014 - Two RCTs found that compared with placebo, azithromycin reduced the rate of pulmonary exacerbations needing antibiotics in adults with non-CF bronchiectasis over 6-12 mths. However, the evidence for other outcomes is unclear. The improvement in exacerbations must be balanced against the risk of experiencing adverse events and the development of antibiotic resistance. Gastrointestinal adverse events occur very commonly (≥ 1 in 10) with azithromycin treatment. |

| Drug | Indication | Evidence for use / Other info |
|---|---|---|
| ULU | | However, in the trials few people discontinued treatment due to adverse events. There is little published evidence to determine the efficacy and safety of azithromycin when used for non-CF bronchiectasis for more than 6-12 months - Link |
| Antidepressants – tricyclic (amitriptyline, nortriptyline, imipramine etc.) ULU | Adjunct to other analgesics, neuropathic pain | Evidence favours efficacy. May not be effective for acute pain. Use sub-antidepressant doses. Extensive use for 25 yrs. (1, 3) |
| Benzbromarone ULM | Hyperuricaemia, including chronic gout | Reduces plasma levels of uric acid by blocking renal tubular reabsorption. May also increase the intestinal elimination of uric acid. Restrict to patients allergic or intolerant of other uricosuric drugs. Not used to treat acute gout attacks. Withdrawn in many countries due to reports of hepatotoxicity. (1, 2, 3) |
| Biotin (Vitamin H) 5mg tablets ULM | Deficiency of biotinidase or holocarboxylase synthetase (enzymes responsible for recycling & incorporation of biotin); long term TPN can induce biotin deficiency | Biotinidase deficiency is an inherited metabolic disorder. (1) Doses in BNF for Children. (8) |
| Bisphosphonates | Early breast cancer (preventing recurrence and improving survival) | NICE ES10 March 2017<br>Full summary available on NICE website at [link]<br>In all women in the EBCTCG meta-analysis (n=18,766), the absolute 10-year risk with bisphosphonates compared with control was reduced by 1.4% for distant recurrence, 1.1% for bone recurrence, and 1.7% for breast cancer mortality. There was no statistically significant reduction in the risk of all-cause mortality or all breast cancer recurrence.<br>Bisphosphonate use had no statistically significant effect on distant recurrence other than bone recurrence, or on locoregional recurrence (in the same site as the original tumour or in the regional lymph nodes) or contralateral breast cancer (in the opposite breast).<br>Subgroup analyses suggested that benefits were independent of the type and dosage of bisphosphonate, the tumour characteristics and the use of concomitant chemotherapy. No subgroup analyses assessed bisphosphonates according to women's estimated risk of breast cancer recurrence or mortality.<br>The MHRA has issued guidance on the use and safety of bisphosphonates, which summarises important safety issues with bisphosphonates, including oesophageal reactions, osteonecrosis of the jaw, atypical femoral fractures and adverse effects on renal function. |
| Botulinum toxin type A injection | Chronic anal fissure | NICE ESUOM June 2013 - 2 systematic reviews and 4 RCTs suggests that botulinum toxin type A injection is less effective than surgery, no better or |

| Drug | Indication | Evidence for use / Other info |
|---|---|---|
| ULU | | worse than topical glyceryl trinitrate (mostly 0.2% ointment) or isosorbide dinitrate, and no better than placebo or lidocaine at healing anal fissure - Link |
| Budesonide nebules<br>Children: 1 mg/day<br>Adults: 2 mg day, typically in a divided dose<br>ULU | Eosinophilic Esophagitis | Swallowed rather than inhaled for an initial duration of 8 weeks to coat the oesophagus and provide topical medication delivery. First-line pharmacologic therapy for treatment of eosinophilic esophagitis. (Recommendation strong, evidence high). (11) |
| Calcium carbonate dispersible tablets<br>ULU | Antacid; supplement in deficiency states; hyperphosphataemia in patients with chronic renal failure or associated secondary hyperparathyroidism | Short term use when used as an antacid because of risks of rebound acid secretion and metabolic acidosis. Effective phosphate binders, doses adjusted according to serum phosphate concentrations. (1, 3)<br><br>Available from specials manufacturers. |
| Carbamazepine tablets or liquid<br>ULU | Neuropathic pain; management of aggression, agitation and behavioural disturbances in dementia | Licensed for pain of trigeminal neuralgia, evidence also favours efficacy in other types of neuropathic pain in adults and children. (1, 3, 8)<br><br>NICE ESUOM March 2015 - 4 very small short-term RCTs (total n=97) with many limitations give conflicting results about the efficacy of carbamazepine for managing aggression, agitation and behavioural disturbances in people with dementia. Larger, longer-term RCTs are required to confirm its efficacy and safety for this use - Link |
| Cetirizine 10mg tablets<br>ULU | Chronic urticaria | NICE ESUOM July 2014 - 2 small RCTs & 2 double-blind crossover studies (n=76) suggest that cetirizine 20mg daily may improve weals and itching in adults with severe chronic urticaria refractory to standard doses of antihistamines. Symptoms remain in a proportion of people and the studies have many limitations. Cetirizine 20mg appears to be well tolerated. The benefits may outweigh the risks for those quality of life is significantly impaired by the condition. No data are available from high quality studies on the use of doses > 20mg - Link<br><br>Doubling the standard licensed dose of a non-sedating antihistamine is widely recommended by the British Association of Dermatologists and the British Society for Allergy and Clinical Immunology for urticaria not responding to therapy - Link |
| Chloral hydrate alcohol free liquid & suppositories<br>ULM | Sedation & insomnia | Used in the short-term management of insomnia (2 wks) and has been used for sedation and as a sedative for premedication. Use as a hypnotic, particularly in children, is now limited. (1, 3, 8)<br>Available from specials manufacturers & importers. |

| Drug | Indication | Evidence for use / Other info |
|---|---|---|
| Chlorothiazide oral liquid 250mg in 5ml<br>**ULM** | Heart failure, hypertension, ascites, diabetes insipidus, chronic hypoglycaemia | Doses in BNF for Children. (8)<br><br>Available from specials manufacturers & importers |
| Clodronate | Early breast cancer (preventing recurrence and improving survival) | See “bisphosphonates” |
| Clonidine tablets<br>**ULU** | Attention deficit hyperactivity disorder (ADHD) in children and young people | NICE ESUOM March 2013 – 2 small, short term RCTs provide weak evidence for use. Adding clonidine to existing stimulant therapy is associated with an increase in moderate to severe side effects, most notably sedation and drowsiness – Link |
| Clopidogrel<br>**ULU** | Transient ischaemic attack (TIA) | NICE ESUOM 2013 – No relevant RCTs or observational data were identified that assessed clopidogrel monotherapy efficacy in people who have had a TIA. Limited RCT evidence was identified for the use of clopidogrel in combination with aspirin for TIA – Link |
| Co-enzyme Q10 **ULM** | Various | See “Ubiquinone” |
| Colesevelam tablets<br>**ULU** | Bile acid absorption | NICE ESUOM Oct 2013 – 2 small case series (n=45 & n=5) showed improved andomiz/gastrointestinal symptoms. A RCT in 24 women with andomiz-predominant IBS had no improvement in outcomes, 4 had evidence of bile acid malabsorption. The study may have been underpowered to detect any differences. Well tolerated; most frequent adverse effects are flatulence and constipation – Link |
| Colistimethate sodium – nebulised powder and injection<br>**ULU** | Non-cystic fibrosis (CF) bronchiectasis | NICE ESUOM Jan 2014 – 4 small case series (total n=148) provide weak evidence for the effectiveness in people with non-CF bronchiectasis and P. aeruginosa. Nebulised or inhaled colistimethate sodium is very commonly associated with adverse respiratory effects, including cough, andomi, bronchospasm and sore throat – Link |
| Corticotropin (Acthar) gel<br>**ULM** | Stimulates corticosteroid release | Can be used to treat medical conditions where systemic corticosteroid therapy is indicated. Such use is now fairly limited.<br><br>Only available as an injection, individual responses to therapeutic corticotropin vary considerably and doses must be adjusted accordingly. (1, 3) |
| Desmopressin tablets<br>**ULU** | Nocturia and nocturnal polyuria in men with lower urinary tract symptoms (LUTS) | NICE ESUOM April 2013 – 2 RCTs show a reduction in number of nightly voids, increased duration of sleep until first void and improved quality of life. Use can result in hyponatraemia and water intoxication in the presence of inappropriate fluid intake – Link |
| Diltiazem cream 2%<br>  <br>Diltiazem for anal fissure | Anal fissure | Evidence to support use favours efficacy. (1, 3)<br><br>NICE ESUOM Jan 2013 – no statistically significant difference between topical diltiazem and glyceryl trinitrate in adults, limited evidence indicates a reduced frequency of headaches – Link |

| Drug | Indication | Evidence for use / Other info |
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| ULM | | Guidance sheet available from Ipswich Hospital pharmacy dept – see attached. |
| Docetaxel infusion<br><br>ULU | Hormone-sensitive metastatic prostate cancer | NICE ESUOM Jan 2016 – RCT data suggest that docetaxel improves overall survival and time to disease progression in men with hormone-sensitive metastatic prostate cancer. Two RCTs found that, compared with androgen deprivation therapy (ADT) alone, docetaxel combined with ADT statistically significantly improved overall survival by around 10–15 months in this population. No statistically significant difference was seen between the groups in another, smaller RCT. Time to disease progression was statistically significantly longer with docetaxel plus ADT compared with ADT alone in all 3 RCTs. These findings are reinforced by a meta-analysis of the RCTs. The toxicity of docetaxel is well-established. Nevertheless, most participants in the RCTs tolerated the planned number of docetaxel treatment cycles – Link |
| Domperidone tablets<br><br>Domperidone for lactation 2014<br><br>ULU | Promote lactation and promote tolerance of enteral feeds in children and young people | Lactation promotion – evidence available to support use which supports efficacy. (3, 4, 6)<br>Guidance sheet available from Ipswich Hospital pharmacy dept – see attached.<br><br>NICE ESUOM July 2013 – 1 small (n=22) partially blinded, andomized crossover study has shown a statistically significant benefit in the short term for domperidone improving gastric emptying times in very low birth weight preterm neonates receiving enteral feeds. No relevant studies were found in children and young people – Link<br><br>April 2014 – MHRA guidance on risk of cardiac side effects – Link<br>Use of domperidone in children update – Link<br>Use of domperidone for lactation update – Link |
| Eculizumab infusion<br><br>ULU | Prevention of recurrence of C3 glomerulopathy post-transplant | NICE ESUOM June 2015 – No evidence was found to determine whether prophylactic use of eculizumab is effective and safe for preventing recurrence of C3 glomerulopathy after kidney transplantation. There are 10 case reports for using eculizumab to treat C3 glomerulopathy in people who had experienced recurrence of the condition post-transplant. Eculizumab improved or andomized signs of C3 glomerulopathy in 7 cases. A partial response was seen in 1 case, and it was ineffective in 2 cases. More evidence is needed to better assess the safety and efficacy of eculizumab in this heterogeneous condition and to determine which patients are most likely to respond treatment – Link |
| Eculizumab infusion | C3 glomerulopathy in the native kidney | NICE ESUOM Dec 2015 – the evidence for using eculizumab to treat C3 glomerulopathy in people with their own, native kidneys is limited to 20 case reports. Eculizumab improved or andomized signs |

| Drug | Indication | Evidence for use / Other info |
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| ULU | | of C3 glomerulopathy in 15 cases. An initial response followed by subsequent deterioration was seen in 3 cases, and treatment was ineffective in 2 cases.<br>More evidence is needed to better assess the safety and efficacy of eculizumab in this heterogeneous condition and to determine which patients are most likely to respond treatment – Link |
| Erythromycin tablets<br>ULU | Gastroparesis in adults | NICE ESUOM June 2013 – limited evidence, 1 small single-blind, crossover study (n=13) has found a statistically significant benefit for erythromycin in the short term for improving symptoms of gastroparesis compared with metoclopramide – Link |
| Ethinyloestradiol 2mg capsules<br>ULM | Menopause symptoms; castration, or primary ovarian failure; prostate cancer; decreased estrogen level secondary to hypogonadism | Effective for menopause symptoms, decreased estrogen level secondary to hypogonadism, castration, or primary ovarian failure and palliative treatment in prostate cancer. (1, 3)<br><br>Available from specialist importers. |
| Fexofenadine 180mg tablets<br>ULU | Chronic urticaria | Doubling the standard licensed dose of a non-sedating antihistamine is widely recommended by the British Association of Dermatologists and the British Society for Allergy and Clinical Immunology for andomized not responding to therapy – Link |
| Fludrocortisone tablets<br>ULU | Postural hypotension in adults | NICE ESUOM Oct 2013 – limited evidence from 2 small short-term studies that fludrocortisone improves postural blood pressure and orthostatic symptoms. In another slightly larger study fludrocortisone had no effect on supine blood pressure or wellbeing in a population with chronic fatigue syndrome – Link |
| Flunarizine 5mg capsules<br><br><br><br><br><br><br><br><br><br>ULM | Complex epilepsy / alternating hemiplegia of childhood<br><br><br><br><br><br>Migraine prophylaxis | Evidence is inconclusive – some individual studies have reported benefit; a systematic review concluded that although flunarizine might have a weak effect on seizure frequency the evidence was not convincing. The withdrawal rate was significant, probably due to poor tolerability; therefore it should not be recommended as adjunctive therapy. (1, 3)<br><br>NICE ESUOM Sept 2014 – the evidence (including 2 RCTs & Cochrane review) suggests flunarizine is as effective as propranolol or topiramate at reducing the frequency of migraines in adults. In children, it was more effective than placebo, and as effective as dihydroergotamine. Nimodipine, propranolol or aspirin. All of the studies in children were small and of poor quality. The most common adverse effect of flunarizine is weight gain – Link<br><br>Available from specialist importers. |

| Drug | Indication | Evidence for use / Other info |
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| Fluoxetine<br><br>**ULU** | Hypersexuality | NICE ESUOM July 2015 – No RCTs which evaluate the use of fluoxetine in the treatment of hypersexuality were found, nor any studies that compared fluoxetine with any of the hormonal treatments licensed to treat hypersexuality. Limited evidence from 3 small, short-term observational studies suggests that fluoxetine may improve some measurements of hypersexuality and sexual preoccupation in men who have either been convicted of a sexual offence or who have a paraphilia or a non-paraphilic sexual addiction. However, these studies had a number of limitations which make it difficult to draw conclusions on the use of fluoxetine for this indication – Link. |
| Fluticasone inhaler (nebules or nasules)<br>Children: 88-440mcg/day in a divided dose<br>Adults 880-1760mcg/day in a divided dose **ULU** | Eosinophilic esophagitis | Swallowed rather than inhaled for an initial duration of 8 week to coat the esophagus and provide topical medication delivery. First-line pharmacologic therapy for treatment of eosinophilic esophagitis. (Recommendation strong, evidence high). (11) |
| Fosfomycin trometamol granules<br><br>**ULM** | Multidrug resistant urinary tract infections | NICE ESUOM July 2013 – 4 small observational studies showed a clinical success rate (resolution of symptoms after treatment) of 77.8% - 94.2%. In 2 comparative studies, outcomes were similar in people whose UTIs were treated with fosfomycin trometamol and other antibiotics. No data on adverse events were available from the studies. More robust studies are needed to further evaluate the safety and efficacy of fosfomycin trometamol for this indication – Link<br><br>Available from specialist importers. |
| Fumaric acid esters 30mg & 120mg tablets<br><br>**ULM** | Moderate/severe chronic plaque psoriasis | Evidence available to support use. (1) Approved for use by NHS Suffolk.<br><br>Available from specialist importers. |
| Gentamicin 0.3% eye ointment<br><br>**ULM** | Eye infection | Gentamicin ophthalmic solution and ointment are effective in treating ocular bacterial infections including conjunctivitis, keratitis, keratoconjunctivitis, corneal ulcers, blepharitis, blepharoconjunctivitis, acute meibomianitis, and dacryocystitis caused by susceptible microorganisms. (1, 3) |
| Gentamicin 0.1% cream<br><br>**ULM** | Skin infection | Topical use may lead to the emergence of resistance and is considered inadvisable. (1) Licensed in the USA for primary skin infections e.g. impetigo contagiosa, superficial folliculitis, ecthyma, furunculosis, sycosis barbae, and pyoderma gangrenosum; and secondary skin infections including infectious eczematoid dermatitis, pustular acne, pustular psoriasis, infected seborrheic dermatitis, infected contact dermatitis (including poison ivy), infected excoriations, and bacterial superinfections of fungal or viral infections. (3) |

| Drug | Indication | Evidence for use / Other info |
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| Glycopyrronium tablets / solution / suspension<br><br>**ULM** | Gastric & salivary secretion reduction; hypersalivation; hyperhidrosis | Evidence favours efficacy (1, 3)<br>NICE ESUOM July 2013 – moderate evidence for reduction of ***hypersalivation (sialorrhoea)*** or drooling in children and young people with a neurological condition, and adults with Parkinson's disease, compared to placebo. Limited evidence of efficacy in adults with schizophrenia and clozapine-induced hypersalivation. Antimuscarinic adverse effects most commonly reported, e.g. dry mouth. No evidence for long-term efficacy or safety - Link<br><br>NICE ESUOM July 2013 – weak evidence from case series to support reduced sweating in people with ***hyperhidrosis.*** The most commonly reported adverse effects are antimuscarinic, e.g. dry mouth. No andomized controlled trial evidence – Link<br><br>Available from specialist importers. |
| Ibandronic acid | Early breast cancer (preventing recurrence and improving survival) | See "bisphosphonates" |
| Infliximab IV infusion<br><br>**ULU** | Pulmonary sarcoidosis | NICE ES Dec 2016 – one RCT (n=138) and 3 uncontrolled, non-comparative observational studies (n=60) showed that infliximab improved mean percent of predicted forced vital capacity (FVC) at week 24 by 2.5% compared with placebo, ($p<0.05$) and improved mean percent of predicted FVC or vital capacity (VC, not forced) from baseline by about 7% respectively. Observational studies have many limitations and better quality evidence is needed. The evidence supports British Thoracic Society guidance that immunosuppressants have a limited role in pulmonary sarcoidosis because there are insufficient high-quality studies to confirm their place in therapy and they have significant adverse effects. Immunosuppressants should be used only when disease is refractory to standard treatments and when there are no pharmacological alternatives - Link |
| Infliximab IV infusion | Refractory pulmonary sarcoidosis | NICE ES Jan 17 - 10 observational studies (155 cases) assessed the effects of infliximab for treating active, unstable, extrapulmonary sarcoidosis (primarily in the nervous system (34%) or skin (25%)) in people who had found corticosteroids and other immunosuppressants to be ineffective, or who could not tolerate these treatments (refractory sarcoidosis). Of these cases, extrapulmonary sarcoidosis resolved in a third and improved in around half. Observational studies are subject to bias and confounding and have many limitations affecting their application to clinical practice. Adverse events seen in the studies reflected those listed in the summary of product characteristics. According to specialists involved in this evidence summary, infliximab may be an option for some |

| Drug | Indication | Evidence for use / Other info |
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| **ULU** | | patients with severe, refractory extrapulmonary sarcoidosis (particularly cutaneous or neurological sarcoidosis); for example, those affected by disabling or disfiguring disease, or whose life expectancy is likely to be reduced - Link |
| Isoniazid liquid<br>**ULM** | TB | Mainstay of the primary treatment of pulmonary and extrapulmonary tuberculosis. (1)<br>Available from specials manufacturers. |
| Ivermectin 3mg tablets<br>**ULM** | Onchocerciasis, lymphatic filariasis, other worm infections, strongyloidiasis and Mansonella infections, difficult to treat scabies. | Considered a drug of choice for the treatment of Onchocerciasis; Safe and effective in the treatment of nondisseminated strongyloidiasis of the intestinal tract; Effective in treating symptomatic Mansonella ozzardi infections, based on limited evidence (1-3)<br>NICE ESUOM Mar 2014 - appears to be effective for treating people with classical or crusted scabies. Differences in treatment regimens and the length of follow-up make interpreting comparisons with topical treatments difficult. Transient exacerbation of pruritus may occur at the start of treatment - Link<br>Available from specialist importers. |
| Ketamine injection / liquid<br>**Injection – ULU/ULM**<br>**Oral liquid - ULM** | Pain | Evidence for use limited, used in neuropathic or other pain unresponsive to conventional analgesics. May have a role in sedation and/or analgesia in pediatric patients before procedures. (1, 3, 8)<br>NICE ESUOM Feb 2014 - 2 small, short-term, placebo-RCTs and 1 n-of-1 trial provide no good quality evidence for the use of oral ketamine to treat chronic pain in adults. Only 1 phase I pilot study in young people was identified - too small and short-term to draw any firm conclusions about the efficacy and safety for treating chronic pain in young people. Frequently associated with adverse effects that result in treatment discontinuation - Link<br>Supply of 10mg/ml and 100mg/ml injection not available until March 2015. Unlicensed ketamine (esketamine) may be used instead - Link |
| L-Arginine 1g capsules<br>**ULM** | Hyperammonaemia | Of doubtful clinical usefulness in controlling increased ammonia levels in liver disease. (1, 3) |
| Lauromacrogol 400 injection (Aethoxysklerol)<br>**ULM** | Varices | Injection sclerotherapy for recurrent varicose veins following surgery, and thread veins. Evidence available to support use. (1) |
| Lidocaine 4% topical solution **ULU** | Pain relief in paediatrics | Evidence to support use. (1, 8) |
| Lidocaine & hydrocortisone mouthwash<br>**ULM** | Oral inflammation and ulceration following radiotherapy | Used when aphthous ulcers are widespread and recurrent. (9)<br>Available from specials manufacturers. |
| Lorazepam tablets buccally **ULU** | Acute anxiety | Rapidly absorbed sublingually, short term treatment. (9) |

| Drug | Indication | Evidence for use / Other info |
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| Magnesium glycerophosphate 4mmol tablets and 1mmol/ml liquid<br><br>Magnesium L-Aspartate 10mmol sachet<br><br>**ULM** | Hypomagnesaemia | Magnesium salts can be given by mouth for the treatment of chronic or asymptomatic magnesium deficiency. (1, 3)<br>Magnesium salts are poorly absorbed from the GI tract, but magnesium oxide, hydroxide and trisilicate are converted by acid gastric juice into soluble magnesium chloride which is absorbed. Magnesium oxide capsules have improved palatability compared to the hydroxide and trisilicate preparations.<br><br>NICE ESUOM Jan 2013 - The evidence for use of magnesium glycerophosphate is from 3 case reports describing its use for preventing recurrent hypomagnesaemia in adults after intravenous treatment - Link<br><br>Available from specials manufacturers. |
| Melatonin tablets / capsules / liquid<br><br>**NB. 2mg MR tablets (Circadin) and 3mg Bio-Melatonin tablets are EU licensed preparations**<br><br>**ULM** | Insomnia & ADHD | Evidence for use in sleep disorders is inconclusive. Improves sleep in blind patients, neurologically disabled children and the elderly. (1, 3, 8)<br><br>NICE ESUOM Oct 2012 – there is limited evidence for melatonin for sleep disorders in children & young people with ADHD - Link<br><br>MHRA will only authorize **import** of other preps in very exceptional circumstances, unlicensed capsules and liquid available from UK specials manufacturers without issue from MHRA. |
| Mepacrine 100mg tablets<br><br>**ULM** | Antiprotozoal for giardiasis & treatment of discoid and subcutaneous lupus erythematosus (SLE) | Evidence available to support use for giardiasis which indicates mepacrine is effective. (1, 2, 3)<br>Evidence for SLE is favourable - promotes energy and decreases fatigue in 2 to 4 weeks; maximal benefits in 6 to 8 weeks. (1, 3) |
| Metformin tablets<br><br>**ULU** | Polycystic ovary syndrome (PCOS) | Evidence available to support use. Metformin restores menstrual cyclicity and ovulatory function among insulin-resistant women with PCOS (1, 3, 6)<br><br>NICE ESUOM Feb 2013 - no good evidence that regimens containing metformin are statistically significantly different from co-cyprindiol in controlling hirsutism in women with PCOS who are not planning pregnancy – Link |
| Methadone tablets & liquid<br><br>**ULU** | Neuropathic pain in cancer patients | Evidence favours efficacy. (1, 3) |
| Methoxypsoralen gel, bath lotion & tablets<br><br>**ULM** | Psoriasis | Effective - evidence to support use. (1, 3) |
| Methylprednisolone tablets or IV injection<br><br>**ULU** | Treatment of relapse in multiple sclerosis (MS) | Drug of choice for the treatment of MS relapses but there is no clear evidence supporting an optimum therapeutic regime. (1, 3)<br><br>Guidance sheet available from Ipswich Hospital pharmacy dept – see attached. |

| Drug | Indication | Evidence for use / Other info |
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| Methylprednisolone (Depomedrone) epidural injection<br>**ULU** | Radicular pain | Role of epidural corticosteroids in sciatica unclear. Evidence of efficacy lacking or conflicting, guidelines do not recommend for routine use. (1) |
| Metoclopramide 10mg tablets<br>**ULU** | Promote lactation | Evidence favours efficacy. Promotes lactation in mothers with inadequate milk production, should be used as an adjunct to mechanical methods and the duration of therapy should probably be limited to 7 to 14 days. May be less effective in prolonged and complete lactation failure, especially in mothers who have failed to lactate for 30 days or more (1, 3, 6)<br><br>Information sheet available from West Suffolk Hospital pharmacy dept – see attached. |
| Mexiletine capsules or injection<br>**ULU** | Neuropathic pain | Possibly effective in the treatment of diabetic neuropathy. Conflicting data and nebulous results regarding efficacy have been reported. (1, 3) |
| Midazolam hydrochloride or maleate (Epistatus) 10mg/ml buccal solution<br>**ULM** | Status epilepticus | NICE guidance considers buccal midazolam an alternative to rectal diazepam for initial management of status epilepticus in the home setting or where intravenous access is not possible. (1)<br><br>**Midazolam hydrochloride 5mg/ml (Buccolam) is a licensed product.** |
| Midodrine 2.5mg, 5mg & 10mg tablets<br>**ULM** | Hypotension | Midodrine effective in the treatment of secondary hypotension & symptomatic orthostatic hypotension. Benefits reported in patients with hypotension caused by psychotropic drugs and anaesthetic agents, spinal cord injury, hypotension due to kidney/pancreas transplantation, systemic infection, and haemodialysis. (1, 3, 10)<br><br>NICE ESUOM Feb 2013 - Two double-blinded RCTs provide some limited evidence that midodrine may improve some patient-rated symptoms of postural hypotension, e.g. syncope & low energy levels - Link<br><br>Guidance sheet available from Ipswich Hospital pharmacy dept – see attached. |
| Modafinil tablets<br>**ULU** | Fatigue in multiple sclerosis (MS) | Evidence inconclusive for effectiveness of decreasing fatigue in patients with MS. (1, 3)<br><br>NICE ESUOM March 2013 - Two small placebo-controlled RCTs did not find any statistically significant evidence that modafinil (up to 200 mg or 400 mg daily in the respective trials) improved fatigue in adults with MS (of any disease pattern) at 8 weeks or 35 days respectively - Link<br><br>Guidance sheet available from Ipswich Hospital pharmacy dept – see attached. |
| Modafinil tablets | Excessive daytime sleepiness in Parkinson's | NICE ESUOM Sept 2015: Limited evidence from 4 small, short duration RCTs (total n=89) found a |

| Drug | Indication | Evidence for use / Other info |
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| ULU | disease (PD) | statistically significant reduction in daytime sleepiness with modafinil treatment in people with PD in 3 of these studies compared to placebo. The NICE guideline on PD which was published in 2006 and is currently being updated, recommends that modafinil may be considered for excessive daytime sleepiness in people with PD. This was based on 3 of the RCTs included in this evidence summary. Since the guideline was published, it has become apparent that modafinil is associated with serious psychiatric, cardiovascular and skin adverse effects. In 2010 a safety review by the European Medicines Agency (EMA) concluded that the benefits of modafinil outweighed the risks only in the treatment of narcolepsy - Link |
| Mycophenolate<br>ULU | Scleroderma<br><br>Systemic lupus erythematosus (SLE) | NICE ESUOM July 2014 - Observational studies suggest mycophenolate improves skin symptoms and may stabilise lung function in people with systemic sclerosis. The most common adverse effects were gastrointestinal tract disturbances and infections. Observational studies have limitations, and RCTs, particularly comparing mycophenolate with other treatments for scleroderma, are needed to clarify efficacy and safety in this condition - Link<br><br>NICE ESUOM Nov 2014 - a Cochrane review of RCTs/quasi-RCTs suggests that mycophenolate is as effective as cyclophosphamide at inducing remission in lupus nephritis, but with a lower risk of ovarian failure. In lupus nephritis maintenance therapy, mycophenolate was more effective than azathioprine for preventing relapse, with no increase in clinically important adverse events. Data in non-renal SLE mainly came from observational studies; further RCTs assessing the efficacy and safety in people with non-renal SLE are needed - Link |
| Nabilone capsules<br>  <br>Nabilone<br>ULU | MS | One report of reduction in spasticity and nocturia, and improvement in mood and well-being, in a patient with MS who received nabilone 1 mg every second day. (1)<br><br>Guidance sheet available from Ipswich Hospital pharmacy dept – see attached. |
| Naltrexone tablets<br>ULU | Central post stroke pain | No evidence to support use. |
| Oestrogens (conjugated) + bazedoxifene | Oestrogen deficiency symptoms in postmenopausal women | NICE ES Dec 2016 - an RCT (n=332), showed after 12 weeks that conjugated oestrogens & bazedoxifene 0.45 mg/20 mg statistically significantly reduced the average daily number of moderate and severe hot flushes from baseline |

| Drug | Indication | Evidence for use / Other info |
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| ULU | | compared with placebo. In another RCT (n=664) in women with vulvar or vaginal atrophy, at week 12, there were statistically significant improvements compared with placebo in some but not all primary outcomes in the conjugated oestrogens and bazedoxifene 0.45 mg/20 mg group. Statistically significant improvements in certain elements of quality of life compared with placebo were seen in both RCTs. No active comparator was included, making it difficult to establish the effectiveness of conjugated oestrogens and bazedoxifene 0.45 mg/20 mg compared with existing treatments. Because of the small number of women exposed and short duration of exposure, the available safety data do not allow for assessment of whether the incidence of rare but important adverse events including cardiovascular or cerebrovascular events, venous thromboembolism or cancer (including breast or ovarian cancer) are increased in women taking conjugated oestrogens and bazedoxifene compared with placebo, or other treatments - Link |
| Omega-3 fatty acid medicines<br>ULU | Schizophrenia | NICE ESUOM Sept 2013 - Inconclusive evidence from 8 placebo-controlled RCTs. Safety data from the short-term RCTs suggested that omega-3 fatty acids were well tolerated - Link |
| Ondansetron<br>ULU | Management of vomiting in children and young people with gastroenteritis | NICE ESUOM Oct 2014 - A Cochrane review found oral or intravenous (IV) ondansetron increased the proportion of children and young people who stopped vomiting compared with placebo. Oral ondansetron reduced the proportion of children and young people needing IV fluid therapy and reduced the immediate hospital admission rate compared with placebo. Ondansetron was associated with increased episodes of diarrhoea - Link |
| | Management of Nausea and Vomiting of Pregnancy and Hyperemesis Gravidarum | There is evidence that ondansetron is safe and effective, but because data are limited it should be used as second-line therapy.<br>Studies on the safety of ondansetron are mixed. A large retrospective analysis of data from the Danish birth registry of 608 385 pregnancies found no increased risk of major birth defect, stillbirth, preterm labour or small-for-gestational age. However, a case–control study with 4524 cases and 5859 controls found a two-fold increased risk of cleft palate (adjusted OR 2.37, 95% CI 1.18–4.76), although the authors suggest that this association may be due to chance due to the large number of variables investigated. Data from the Swedish Medical and Birth Register demonstrated a small increased risk of cardiovascular defects and cardiac septal defects (OR 1.62, 95% CI 1.04–2.14, and risk ratio 2.05, 95% CI 1.19–3.28, respectively). For these reasons, the use of ondansetron should be |

| Drug | Indication | Evidence for use / Other info |
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| ULU | | limited to patients who are not adequately managed on the aforementioned antiemetics and preferably used after the first trimester of pregnancy. Three small randomised studies have shown ondansetron to be superior to doxylamine and pyridoxine in reducing nausea and vomiting, equally effective but with fewer adverse effects than metoclopramide and more effective at reducing severe vomiting than metoclopramide. (13, Link) |
| Oxybutynin<br>ULU | Hyperhidrosis | NICE ES10 March 2017 – 4 studies investigated oxybutynin 2.5 mg to10 mg for treating hyperhidrosis in adults. Three studies found that more people treated with oxybutynin reported an improvement in symptoms of hyperhidrosis compared with those treated with placebo; the difference between the groups was statistically significant in all studies. Volume of sweating was measured in the fourth study, which found that the oxybutynin group had statistically significant reductions in sweating from baseline, whereas the placebo group did not. 3 studies assessed quality of life, which found that people treated with oxybutynin reported greater improvements compared with placebo; all differences between groups were statistically significant. The studies included here have many limitations, e.g. all were small (32-140 participants), of short duration (2 to 6 weeks) and did not compare oxybutynin to other active treatments. NICE has not published a guideline on managing hyperhidrosis but the CKS on hyperhidrosis suggests systemic therapies, including oral antimuscarinics, as treatment options for people whose hyperhidrosis is not adequately managed through lifestyle modifications and antiperspirants. (Link) |
| Oxycodone capsules, liquid or injection<br>ULU | Neuropathic pain | Evidence favours efficacy for post herpetic pain. (1, 3) |
| Pamidronate | Early breast cancer (preventing recurrence and improving survival) | See “bisphosphonates” |
| Papaverine 60mg in 2ml injection<br>ULM | Erectile dysfunction | Evidence of efficacy for intracavernosal use alone or combined with phentolamine. Dose-related priapism potentially serious. Penile fibrosis, fixed drug reactions, hepatotoxicity, and discomfort on injection are other complications. (1, 3) |
| Paraldehyde/olive oil 50:50 enema<br>ULM | Status epilepticus in paediatrics | Use largely been superseded by other drugs. It is still occasionally used to control status epilepticus resistant to conventional treatment. Given rectally or intramuscularly it causes little respiratory depression and is therefore useful where facilities for resuscitation are poor. (1, 8)<br><br>Available from specials manufacturers. |

| Drug | Indication | Evidence for use / Other info |
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| Pentosan polysulphate sodium<br>**ULM** | Interstitial cystitis | NICE ESUOM April 2015 - A RCT published in 2014 found no statistically significant difference between pentosan polysulfate sodium (pentosan) and placebo for the treatment of pain, urinary urgency, frequency and nocturia in people with the chronic bladder condition interstitial cystitis. A meta-analysis of older RCTs that used inconsistent methods for assessing symptoms found that pentosan was more effective than placebo in reducing some symptoms of interstitial cystitis. There are limited data comparing pentosan to other active treatments for interstitial cystitis - Link |
| Phenobarbitone alcohol free oral liquid – various strengths<br>**ULM** | Epilepsy in babies | Use in children based on best practice guidelines and advice from a network of clinical experts. (8)<br>Available from specials manufacturers. |
| Pirenzepine 50mg tablets<br>**ULM** | Resistant hypersalivation in patients receiving clozapine | A selective $M_1$ tertiary amine antimuscarinic that displays a preferential action on the gastric mucosa thus causing a reduction in the secretion of gastric acid; it also reduces the secretion of pepsin. At therapeutic doses it has few other antimuscarinic actions. (1, 3) |
| Povidone iodine 5% eye drops<br>**ULM** | Antiseptic and disinfectant prior to surgical procedures | Effective for prepping of the periocular region (lids, brow, and cheek) and irrigation of the ocular surface (cornea, conjunctiva, and palpebral fornices). (3)<br><br>Available from specials manufacturers. |
| Praziquantel 500mg tablets<br>**ULM** | Broad spectrum anthelmintic | Effective drug used in the treatment of cysticercosis, taeniasis, diphyllobothriasis, hymenolepiasis, schistosomiasis, and intestinal, liver, and lung fluke infections. (1, 3)<br><br>Available from special order manufacturers or specialist importers. |
| Prednisolone tablets<br>**ULU** | Anti-inflammatory agent | Prednisolone soluble tablets have increased significantly in cost in recent years. It has been established that plain prednisolone tablets dissolve satisfactorily in a small amount of water and the resultant solution tastes the same, regardless of whether a plain or soluble tablet is used. Administration of prednisolone in this manner is routinely adopted by hospitals, both locally and nationally, and is promoted widely by CCGs. There is only a limited number of clinical situations (for example patients with fine-bore enteral feeding tubes) where prescribing of soluble tablets or oral solution may be justified. (14) |
| Prednisolone metasulphobenzoate enema<br>**ULU** | Anti-inflammatory agent | Administered rectally retention enemas contain the equivalent of 20 mg of prednisolone per 100 ml. (1) |
| Probenecid 500mg tablets<br>**ULU** | Prevention of nephrotoxicity associated with nephrotoxic drugs eg. cidofovir, cisplatin | Effective in inhibiting renal impairment. (1, 3) |

| Drug | Indication | Evidence for use / Other info |
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| Promethazine IM injection<br><br>**ULU** | Rapid tranquilisation for agitation/aggression | NICE ESUOM March 2014 - A Cochrane review (2009, 4 RCTs, n=1117) has limited evidence that IM haloperidol plus promethazine is effective for the rapid tranquillisation of people with agitation or aggression associated with mental illness. Difficult to draw any firm conclusions because the results are heterogeneous. The results were not relevant to UK clinical practice. Safety analyses do not provide conclusive evidence that the combination is safer than other IM treatments, or that it reduces the adverse effects of antipsychotics when used for rapid tranquillisation - Link |
| Pyridoxal phosphate 50mg tablets<br><br>**ULM** | Uncontrolled epilepsy | Evidence to support use. Pyridoxine-dependent seizures & some other kinds of seizures respond to pyridoxine treatment, febrile seizures may not. (1,3) |
| Quetiapine<br><br>**ULU** | Generalised anxiety disorder (GAD) | NICE ESUOM May 2013 - some evidence that monotherapy improves the symptoms of GAD vs. placebo; limited evidence suggests that it is not more effective than antidepressants; limited evidence suggests that adding quetiapine to an antidepressant does not improve symptoms in GAD that has not responded to the antidepressant alone. People more likely to discontinue treatment because of adverse effects compared with placebo or active treatment – Link |
| Reflectant sun screen<br><br>Reflectant sun screen<br><br>**ULM** | Severe photosensitivity | Guidance sheet available from Ipswich Hospital pharmacy dept – see attached. |
| Ramipril<br><br>**ULU** | Treating symptoms of peripheral arterial disease e.g. intermittent claudication (IC) | NICE ESUOM July 2015 - Three small RCTs (total n=285) found that, compared with placebo, over 24 weeks, ramipril 10 mg daily improved maximum and pain-free walking times and distances in people with stable IC. Improvements in physical quality of life and distance, speed and stair-climbing scores were also seen across the studies. These differences were statistically significant, but the clinical importance of many of the results is unclear. The adverse effects most often reported were dizziness and cough, which led to discontinuation in some cases. The studies have many limitations. Ramipril has not been compared directly with other treatments for IC. Higher quality evidence on the efficacy and safety of ramipril is needed to determine its place in therapy - Link. |

| Drug | Indication | Evidence for use / Other info |
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| Rifaximin tablets<br><br>**ULU** | Pouchitis | NICE ESUOM March 2014 - One small RCT and 2 small non-comparative observational studies provide limited evidence that rifaximin alone or in combination with ciprofloxacin can improve symptoms or induce remission in people with pouchitis that is refractory to other antibiotics. One small non-comparative observational study provides limited evidence that rifaximin monotherapy can help maintain remission in people with chronic pouchitis that has responded to other antibiotics - Link |
| Risedronate | Early breast cancer (preventing recurrence and improving survival) | See "bisphosphonates" |
| Rituximab IV infusion<br><br>**ULU** | Autoimmune haemolytic anaemia (AHA) | NICE ESUOM Feb 2015 – Limited high-quality evidence. One RCT suggested that after 12 months, prednisolone plus rituximab was more effective than prednisolone monotherapy for inducing a complete response to treatment in adults with newly diagnosed and previously untreated warm AHA. Other uncontrolled studies suggested some effectiveness of rituximab in warm and cold AHA, but limitations of these studies make it difficult to draw any firm conclusions – Link |
| <br><br>**ULU** | Minimal change disease (MCD) and focal segmental glomerulosclerosis (FSGS) in adults | NICE ES Nov 2016 – Most of the evidence for using rituximab in adults with MCD and FSGS comes from uncontrolled and non-randomised observational studies performed outside the UK with small sample sizes. The populations in the included studies varied, as did the dose of rituximab used, adjuvant treatment, and follow-up time. The studies in people with MCD and FSGS in their native kidneys reported that treatment with rituximab reduced disease relapse rates, or achieved complete or partial remission. The study in renal transplant recipients with MCD and FSGS did not report any significant difference in treatment outcomes for those treated with rituximab compared to those receiving other immunosuppressants. It is difficult to draw firm conclusions on the efficacy and safety of rituximab for treating adults with MCD or FSGS – Link |
| | Skin involvement in systemic sclerosis or ebulized scleroderma | NICE ES7 March 2017 – 7 studies investigated rituximab (usually 375 mg/m2 weekly for 4 weeks at 0 and 6 months, or 1,000 mg at 0 and 2 weeks) for treating skin involvement in systemic sclerosis (mainly diffuse). In 6 of the 7 studies, compared with baseline, statistically significant improvements were seen with rituximab at follow-ups of 6 months to 4 years in: skin thickening, functional impairment, and disease activity and severity.<br>Although the studies included in this evidence summary suggest that rituximab may be effective for treating skin involvement in some people with diffuse systemic sclerosis, the evidence is of low |

| Drug | Indication | Evidence for use / Other info |
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| ULU | | quality and has many limitations. Most were open-label observational studies without a comparator, and included only small numbers of participants (total n=177). In the majority, there was no blinding of treatment or outcome assessment. Also, participants in many studies were receiving concomitant immunosuppressants and it cannot be excluded that these contributed to any improvement. Study populations varied and it is unclear which people might benefit most from treatment. Specialists involved in producing this evidence summary considered that rituximab should be used only for treating skin involvement in diffuse systemic sclerosis that is refractory to standard treatments, after all other options (such as autologous stem cell transplantation), have been explored, and taking into account the risk of serious adverse effects. (Link) |
| Sildenafil<br>ULU | Digital ulcers | NICE ESUOM March 2015 – Data limited. Individual RCTs have not shown a statistically significant treatment effect of sildenafil on digital ulcers. However, a small observational study has shown some benefit for sildenafil on ulcer healing and a meta-analysis has shown benefit for phosphodiesterase type 5 inhibitors as a drug class for ulcer healing and improvement. Larger RCTs, particularly with other comparative treatments, are needed to clarify efficacy and safety of using sildenafil for managing digital ulcers – Link |
| ULU | Persistent pulmonary hypertension in neonates (PPHN) | NICE ESUOM March 2016 – There is evidence from small, short-term RCTs in resource-limited settings where nitric oxide is not available that oral sildenafil reduces mortality and improves physiological parameters of oxygenation compared with placebo in term or near-term neonates with PPHN. However, there is very little evidence of sildenafil use for PPHN in settings such as the UK where inhaled nitric oxide is available. In a small RCT in premature neonates at risk of bronchopulmonary dysplasia (BPD) sildenafil was not beneficial, and it remains unclear if sildenafil leads to improved outcomes in premature neonates with BPD-associated pulmonary hypertension. The long-term safety of sildenafil in neonates with PPHN is not known – Link |
| Sodium benzoate 500mg tablets, 500g in 5ml liquid and 2g in 10ml IV<br>ULM | Rare metabolic disorder | Used as part of the treatment of hyperammonaemia that occurs in inborn errors of the urea cycle. (1, 3) Effective in reducing plasma-glycine concentrations in nonketotic hyperglycinaemia, may not be effective in preventing mental retardation. (1)<br><br>Available from specials manufacturers or specialist importers. |
| Sodium chloride 30% oral liquid (5mmol in 1ml) | Sodium supplementation, sodium replacement and chronic renal loss in babies | Use in children based on best practice guidelines and advice from a network of clinical experts. (8) |

| Drug | Indication | Evidence for use / Other info |
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| ULM | | Available from specials manufacturers. |
| Sodium chloride 5% eye ointment<br>ULM | Recurrent corneal erosions | Standard treatment listed in Moorfields Eye Hospital formulary. (5) |
| Sodium phenylbutyrate injection 2g in 10ml, 250mg in 1ml, 500mg tablets<br>ULM | Adjunctive treatment of hyperammonaemia in paediatric patients with urea cycle disorders | Effective, evidence to support use. (1, 3)<br><br>Injection available from specials manufacturers or specialist importers. |
| Sodium phosphate oral solution (0.5mmol/ml phosphate)<br>ULM | Hypophosphataemia, including hypophosphataemic rickets and osteomalacia in babies | Use in children based on best practice guidelines and advice from a network of clinical experts. (8)<br><br>Available from specials manufacturers. |
| Sodium valproate tablets and liquid<br>ULU | Neuropathic pain | Evidence favours efficacy, can be used for trigeminal neuralgia in carbamazepine-intolerant patients. Also useful in painful diabetic neuropathy, postherpetic neuralgia and neuroapthic cancer pain. (1, 3) |
| Spironolactone 25mg/5ml suspension & 50mg/5ml suspension (sugar free)<br>ULM | Oedema & ascites in liver cirrhosis, malignant ascites, nephrotic syndrome, CHF, primary hyperaldosteronism | Recognised effective treatment for heart failure & oedema,doubts have been expressed over its safety during long-term administration. (1, 3)<br><br>Available from specials manufacturers. |
| Tacrolimus in Orabase<br>ULM | Pyoderma gangrenosum | Evidence favours efficacy. Small study found topical tacrolimus 0.3% in carmellose sodium paste (Orabase) to be more effective than clobetasol propionate 0.05% for peristomal pyoderma gangrenosum. (1, 3) |
| Tamsulosin<br>ULU | Relieving lower urinary tract symptoms in women | Use in women is not a caution or contraindication in the SPC. There is little information on its use, 2 small studies have shown that it is effective and safe for the treatment of lower urinary tract symptoms and renal stones in women. (12) |
| Timolol eye drops – topical use<br>ULU | Infantile haemangioma | NICE ESUOM Aug 2015 – Limited evidence from 2 small RCTs and several observational studies suggests that topical timolol reduces the redness of superficial haemangiomas and may reduce their size or volume, but the clinical significance of these changes is unclear. The number of adverse events seen in the studies was low. Systemic absorption has been shown with timolol used topically to treat infantile haemangiomas and larger studies would be useful to provide more safety data – Link |
| Tobramycin Nebules | Non-cystic fibrosis bronchiectasis | NICE ES12 April 2017 – includes 3 randomised controlled trials that investigated the efficacy of ebulized tobramycin, 300 mg twice daily compared with placebo for treating infective exacerbations caused by *P aeruginosa* in people with non-cystic fibrosis bronchiectasis.<br>Compared with placebo, statistically significant reductions were seen with 4 weeks to 6 months treatment with ebulized tobramycin in: sputum P aeruginosa density; number of hospital admissions |

| Drug | Indication | Evidence for use / Other info |
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| ULU | | and days in hospital. Compared with placebo, no statistically significant improvements were seen in: pulmonary function (FEV1 and FVC); quality of life. 1 study found no statistically significant reduction in the number of exacerbations per person over 6 months treatment, and 1 study found a statistically significant reduction in the number of exacerbations over 3 months of treatment. One study found that more participants in the tobramycin group were classified by the investigators as having improved medical condition compared with placebo; this finding was limited as it was based on a subjective assessment that did not use a validated tool.<br>All studies included small numbers of participants (n=30 to 74) in the US or Spain; study populations varied and it is unclear which patients might benefit most from treatment and for how long to treat. In current practice, when ebulized treatment is indicated in people with non-CF bronchiectasis, inhaled tobramycin is considered when treatment with other commonly used ebulized therapies is not tolerated, if the condition is deteriorating while on other ebulized antibiotics, or if cultures are sensitive to tobramycin. (Link) |
| Topiramate tablets<br>ULU | Neuropathic pain | Effective for trigeminal neuralgia, evidence inconclusive for treatment of diabetic peripheral neuropathy. May be of benefit for postherpetic neuralgia, phantom limb pain and neuropathic pain in cancer patients. (1, 3) |
| Ubiquinone 30mg tablets & liquid<br>(also known as co-enzyme Q10)<br>ULM | Co-enzyme deficiency | Evidence favours efficacy for heart failure & MELAS (mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes); evidence inconclusive for angina, diabetes, drug related alopecia, hypercholesterolaemia, hypertension, male infertility, migraine prophylaxis, Parkinsons disease, periodontal disease, pulmonary fibrosis and ventricular arrhythmia. Insufficient evidence to recommend as a dietary supplement. (1, 3, 7) |
| | Mitochondrial disorders in children | NICE ES11 March 2017 – evidence is very limited (3 case reports in a total of 6 children). The symptoms of the children described were diverse and included motor/muscle symptoms, neurological symptoms, nephrotic syndrome and hypoparathyroidism. Symptoms of all 6 children were reported to improve with co-enzyme Q10 treatment. However, as uncontrolled observational studies in individual patients, these case reports are prone to bias and other methodological problems; very limited data on objective measurable outcomes. Mitochondrial disorders are a heterogeneous group of rare diseases and these case reports may not represent all types of patients seen in clinical practice.<br>The best available evidence on the use of co-enzyme Q10 in adults and young people with |

| Drug | Indication | Evidence for use / Other info |
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| ULM | | mitochondrial disorders showed no statistically significant benefit for co-enzyme Q10 compared with placebo for the majority of outcomes assessed. However, the studies had a number of important methodological limitations, were of short duration and included only small numbers of participants. There is currently no established treatment for mitochondrial disorders and the clinical management is largely supportive. The studies included in this summary provide insufficient evidence to evaluate the place in therapy of co-enzyme Q10 for treatment of this condition. (Link) |
| Valproate ULU | Management of aggression, agitation and behavioural disturbances in dementia: valproate preparations | NICE ESUOM, March 2015 – Evidence from RCTs suggests that valproate preparations (including sodium valproate and valproate semisodium) are no more effective than placebo for treating agitation or behavioural disturbances in people with dementia. Adverse effects such as falls, sedation, gait disturbances, tremor, muscular weakness, thrombocytopenia, gastrointestinal disorders and urinary tract infections were more common in people taking valproate preparations than placebo – Link |
| Venlafaxine tablets or capsules ULU | Neuropathic pain | Evidence inconclusive, but may be of benefit for painful diabetic neuropathy and fibromyalgia. (1, 3) |
| Vitamin E capsules ULM | Treatment and prevention of vitamin E deficiency | Evidence of efficacy for treating vitamin E deficiency. Has also been tried in many other disorders, the evidence of value is lacking. (1, 3) |
| Zoledronic acid | Early breast cancer (preventing recurrence and improving survival) | See “bisphosphonates” |

NICE ESUOM**:** National Institute for Health and Care Excellence Evidence summaries: unlicensed/off-label medicines
NICE ES: National Institute for Health and Care Excellence Evidence summary

**Guidance sheets**
Copies of guidance sheets are embedded in this document or can be obtained from the Trusts pharmacy departments –
Ipswich hospital: 01473 704431, eastanglia.mis@ipswichhospital.nhs.uk
West Suffolk hospital: 01284 713109, druginfo@wsh.nhs.uk

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