NHS Lincolnshire

Prescribing and Clinical Effectiveness Bulletin

Volume 6; Number 5 **March 2012**

What's new this month?

- **Indapamide 1.5mg sustained release tablets (Natrilix SR) are designated RED-RED as they offer no advantage over indapamide 2.5mg tablets and are over three times the price (see page 2).**
- **The use of hypnotics in Lincolnshire is reviewed and updated guidance is given (see page 3).**
- **Midazolam 5mg in 1ml oromucosal solution (Buccolam) is approved for use in the treatment of prolonged acute convulsive seizures. Designation: AMBER without shared care (see page 4).**
- **Olopatadine (Opatanol) 0.1% eye drops for the treatment of the ocular signs and symptoms of seasonal allergic conjunctivitis are designated RED-RED (see page 6).**
- **Sitagliptin (Januvia/Janumet) is now licensed at reduced dose for the treatment of type 2 diabetes mellitus in patients with moderate to severe renal impairment (see page 7).**
- **Updated guidance on the treatment of commonly occurring infections is provided (see pages 8 to 12).**

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This bulletin has been created specifically to convey details of decisions taken at the Prescribing and Clinical Effectiveness Forum (PACEF) to all stakeholders across the Lincolnshire Healthcare Community in both primary and secondary care. Back issues of the *PACE Bulletin* and other PACEF publications are available through the NHS Lincolnshire website (www.lincolnshire.nhs.uk). Click on 'Commissioning' and follow the links to PACEF.

SUMMARY OF PACEF DECISIONS: FEBRUARY 2012 UPDATE

Drug	Indication(s)	Traffic Light Status
Aliskiren (Rasilez) 150mg and 300mg tablets	Treatment of essential hypertension	AMBER Should only be initiated on specialist advice; no shared care guideline required
Indapamide 1.5mg sustained release tablets (Natrilix SR)	Licensed for the treatment of hypertension	RED-RED Generic indapamide 2.5mg tablets are equivalent and less than one-third of the price.
Midazolam oromucosal solution 5mg/ml (Buccolam).	Licensed for the treatment of prolonged acute convulsive seizures in children from the age of 3 months to 18 years.	AMBER All new patients requiring liquid midazolam for this indication should be initiated on midazolam oromucosal solution 5mg/ml

		(Buccolam). 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.
Midazolam buccal liquid 10mg/ml (Epistatus)	Unlicensed product used for the emergency treatment of status epilepticus as a second line alternative to rectal diazepam.	AMBER Existing patients can continue using this therapy, although new initiations should be for licensed midazolam oromucosal solution 5mg/ml (Buccolam). 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.
Olopatadine (Opatanol) 0.1% eye drops	Licensed for the ocular signs and symptoms of seasonal allergic conjunctivitis	RED-RED

RED-RED: This signifies that a product is **not recommended** for prescribing in **either** primary or secondary care. All new products are classified as RED-RED pending assessment by PACEF.
RED: This signifies that a product has been approved for use within secondary care, tertiary care or a primary care hosted specialist service only and **should not be routinely prescribed in primary care**. RED drugs may be used within ULHT or LPFT subject to approval for use within each Trust. ULHT and LPFT reserve the right to determine whether or not RED drugs will be used within their Trusts. RED classification does not automatically signify that a drug will be available within secondary/tertiary care.
AMBER: This signifies that a drug has been approved for use in primary care **subject to specialist initiation; a shared care guideline (SCG) may also be required**. The main purpose of the SCG will be to clearly define both specialist and GP responsibilities. Not all AMBER drugs that require SCGs are currently covered by formal documents; PACEF are working to rectify this.
GREEN: This signifies a product that is **approved for initiation in either primary or secondary care.**

REPORTING INCIDENTS TO THE NATIONAL PATIENT SAFETY AGENCY (NPSA)
The NPSA are keen to encourage the anonymous reporting of patient safety errors and systems failures both from healthcare professionals and patients. The National Reporting and Learning System (NRLS) has been set up to facilitate this process. Healthcare professionals can either report patient safety incidents through their local risk management scheme or directly into the NRLS using the eForm on the NPSA website. Please access www.npsa.nhs.uk for more information. **All healthcare professionals are encouraged to report incidents, errors and systems failures; the aim is to help the NHS to learn from things that go wrong.**

REVIEW: *INDAPAMIDE 2.5MG TABLETS VS INDAPAMIDE 1.5MG SUSTAINED RELEASE (NATRILIX SR)*

In *PACE Bulletin* Volume 6 No 1 we reviewed the recent NICE Clinical Guideline on the management of hypertension in adults. For people over 55 years and black people of African or Caribbean family origin of any age, a *thiazide-like diuretic* (i.e. indapamide or chlortalidone) is indicated for patients who are not suitable for a calcium channel blocker (CCB) due to oedema or intolerance, or if there is evidence of heart failure or high risk of heart failure. Standard PACEF advice on selection of a thiazide-like diuretic is as follows:

PACEF Recommendation: *Thiazides and Thiazide-Like Diuretics*
Where a thiazide-like diuretic is indicated in new patients, indapamide (generic) 2.5mg once daily is advocated; indapamide 1.5mg sustained release (SR) tablets (Natrilix SR) present a possible alternative, but are over three times the price of the 2.5mg generic and *should not be used preferentially*.

UK Medicines Information Midlands have now completed a review of the data comparing standard indapamide 2.5mg tablets with indapamide 1.5mg sustained release tablets. Two main trials were conducted prior to the launch of Natrilix SR which compared both formulations. In these trials, the only significant difference

between the two interventions was a greater tendency towards hypokalaemia in the standard indapamide group. In terms of efficacy, both interventions were found to be equivalent with no evidence that the SR formulation improved clinical outcomes over the standard generic preparation.

PACEF Recommendation: *Indapamide Switching*
Following this review, PACEF have reached the conclusion that indapamide 2.5mg tablets and indapamide 1.5mg SR tablets are broadly equivalent. Therapeutic switching from the 1.5mg SR to the 2.5mg standard tablet is encouraged and will be supported by the Prescribing and Medicines Management Team. If all indapamide 1.5mg SR prescribing was switched to indapamide 2.5mg standard tablets, the saving across Lincolnshire primary care would be £19,250pa. Indapamide 1.5mg sustained release tablets (Natrilix SR) are designated RED-RED.

Reference: *Medicines Dispatch*, Issue 298, February 2012.

REVIEW: *USE OF HYPNOTICS IN LINCOLNSHIRE*

Risks associated with the long-term use of hypnotic drugs have been well recognised for many years. As far back as 1988, the Committee on Safety of Medicines advised that benzodiazepine (BZ) hypnotics should only be prescribed if insomnia is severe, disabling or causing the patient extreme distress. The lowest dose that controls symptoms should be used, for a maximum of four weeks and intermittently if possible. NICE published guidance on the newer hypnotics, zopliclone, zolpidem and zaleplon, in 2004 and concluded that they offered no advantages over BZs in terms of effectiveness, safety and dependence or abuse potential and should only be used second line after non-drug interventions had failed. All of these drugs, both BZ and Z, should be confined to short-term use only as defined within their licensed indications. Most recently, the MHRA in July 2011 highlighted the extent of dependence and harm associated with these drugs. A recent cohort study from the US published in *BMJ Open*, reported a small increase in absolute risk of death in patients taking hypnotics and concluded that taking hypnotics may increase mortality (*BMJ Open* 2012:2:e000850.doi:10.1136/bmjopen-2012-000850). Despite all of these warnings unfolding over nearly a quarter of a century, overall prescribing of hypnotics across the country is not declining.

In Lincolnshire, as a result of the Resources for Effective Sleep Treatment (REST) project, non-pharmacological approaches have been strongly promoted including Cognitive Behavioural Therapy for Insomnia (CBTi), sleep assessment tools, drug reduction regimes, decreased caffeine consumption, sleep diaries, sleep restriction, cognitive control and stimulus control. Despite this, we continue to spend over two-thirds of a million pounds a year on hypnotics in county; this has been steadily increasing year-on-year for the last 5 years. Use of hypnotics in Lincolnshire is significantly higher than both national and East Midlands averages (volume of hypnotic prescribing in Lincolnshire is the highest in the East Midlands).

Generic zopiclone (3.75mg and 7.5mg tablets) currently represents the hypnotic of lowest acquisition cost and is the most widely prescribed drug constituting 61% of items; generic temazepam 10mg tablets are also widely used (20.5% of items). Almost 35% of the cost of hypnotics is attributable to the various licensed and unlicensed forms of melatonin; this is usually for children and prescribed within the context of shared care. Even though all hypnotics are licensed for short-term use only, one study found that 92% of hypnotics prescribed in primary care are on repeat prescription. There is evidence that the incidence of road traffic accidents is doubled

in those taking hypnotics; there is also a link to increased incidence of falls and hip fractures.

PACEF Recommendations:
(1) Non-pharmacological methods are preferred as first line treatment for insomnia; (2) Where a hypnotic is indicated, a drug of low acquisition cost should be used (generic zopiclone tablets are preferred); (3) Always use the lowest effective dose for the shortest possible time period; anything longer than 4 weeks is beyond the licensed indications for the product; (4) Longer term users of hypnotic medication should be regularly reviewed and acquainted with the risks of continued therapy (i.e. possible dependence, increased risk of RTA, falls, fractures etc); (5) Exceptionally high cost hypnotics such as lormetazepam (500microgram tablets are nearly £2 each) should be reviewed as a matter of priority; (6) Melatonin (Circadin) has not been approved by PACEF for the treatment of insomnia and should not be prescribed for this indication; melatonin has been approved for the treatment of sleep disturbances in children with cerebral palsy, ADHD, autism and learning disability. A shared care guideline is available; a revised version is in preparation.

NEW DRUG ASSESSMENT: *MIDAZOLAM 5MG IN 1ML OROMUCOSAL SOLUTION (BUCCOLAM)*

Midazolam 5mg/ml oromucosal solution (Buccolam) is licensed for the treatment of prolonged acute convulsive seizures in children from the age of 3 months to 18 years. It is the first *licensed* midazolam liquid preparation for this indication. In February 2009, PACEF assessed the unlicensed midazolam 10mg/ml liquid formulation Epistatus and approved it for use as an AMBER drug for the emergency treatment of status epilepticus.

Supporting evidence for the efficacy of buccal midazolam comes from five studies which compared the effectiveness of buccal midazolam against rectal diazepam and in one case intravenous diazepam. Despite some identified flaws in the methodology of these trials (largely attributed to the emergency nature of the treatment) they provide clear evidence to support the effectiveness and non-inferiority of buccal midazolam compared to rectal diazepam in the management of acute seizures. All of these trials were conducted using buccally administered midazolam (Hypnovel) 10mg/2ml solution for injection rather than a specifically formulated oral liquid; nonetheless, the licensing authority has accepted Hypnovel as the reference medicinal product and these studies have been deemed to be sufficient to grant a paediatric use marketing authorisation to Buccolam.

Midazolam is implicated in a number of drug interactions. It is metabolised by the CYP3A4 enzyme and therefore those drugs that either potentiate or antagonise its effect will have the potential to either decrease or increase midazolam plasma concentrations. As expected, midazolam needs to be co-administered with caution in those already receiving treatment with other medicines which either cause enhanced sedation or respiratory depression. Adverse effects associated with midazolam are those commonly associated with benzodiazepine use; respiratory depression is the most significant adverse effect and is of particular concern in the management of acute seizures where respiratory function may already be compromised. Due to the high risk of respiratory depression, Buccolam can only be used in the youngest age group of between 3 to 6 months of age in a hospital setting under supervision where the appropriate resuscitation equipment is available.

Buccolam is a 5mg/ml midazolam solution packaged in pre-filled syringes which are available in four different doses (2.5mg/0.5ml (yellow label); 5mg/ml (blue label); 7.5mg/1.5ml (purple label); 10mg/2ml (orange label). Previously, the midazolam solution most widely used within Lincolnshire for buccal administration was the unlicensed product Epistatus which contains 10mg/ml of midazolam. The MHRA has highlighted the potential risk of confusion between the differing strengths of the licensed and unlicensed preparations in the October 2011 issue of the *Drug Safety Update* (see *PACE Bulletin*, Vol 6 No 2 (January 2012)). Parents and carers are used to administering doses of midazolam solution by volume, rather than by dose and may not be fully aware of the dose their child normally receives. Children currently receiving 10mg of midazolam will require a 2ml dose of the 5mg/ml solution rather than 1ml of the 10mg/ml solution; there is a risk of under-dosing if the normal volume of solution is administered. The risk of confusion could be further compounded by the fact that many children prescribed midazolam buccal solution will have multiple supplies as it is common practice to keep a stock at the different locations routinely visited by the child (e.g. home, school, respite care provider etc).

Standard advice from the MHRA is that prescribers should prescribe a licensed medicine where one exists in preference to an unlicensed product. However there are clinical situations when the use of unlicensed medicines or use of medicines outside the terms of their license (i.e. 'off-label') may be judged by the prescriber to be in the best interest of the patient. Guidance on the use of unlicensed medicines issued by the Royal Pharmaceutical Society advises that a licensed medicine should be supplied in preference to an unlicensed medicine unless the use of the unlicensed formulation is clinically justified.

A cost comparison reveals little difference in cost between licensed midazolam 5mg/ml oromucosal solution (Buccolam) and unlicensed midazolam solution 10mg/ml (Epistatus).

PACEF Recommendation:
PACEF recognize that the launch of a *licensed* midazolam oromucosal solution represents a preferred option in infants, children and adolescents at risk of acute convulsive seizures in epilepsy. As a result of this, midazolam 5mg/ml oromucosal solution (Buccolam) is designated AMBER for this indication. Nonetheless, serious concerns remain regarding the risk of confusion identified by the MHRA relating to the different strengths of established unlicensed formulations, such as midazolam buccal solution (Epistatus)(10mg/ml) and the licensed formulation, midazolam 5mg/ml oromucosal solution (Buccolam). To minimise this confusion, it is recommended that existing patients should remain on unlicensed midazolam 10mg/ml buccal solution (Epistatus) 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.

Stop Press: Midazolam 10mg/1ml buccal solution (Epistatus)
Special Products Ltd carried out several modifications to this unlicensed product in December 2011. The changes made were: (1) Removal of the luer tip; (2) Extension of the markings on the plunger from 1.0ml to 1.5ml; (3)

Repositioning of the plunger stop to allow delivery of 1.5ml (the previous pipette stopped at 1.0ml). This affects two batches: B/N 25658 Exp Oct 2013 first distributed 5/12/11 and B/N 27229 Exp Nov 2013 first distributed 20/01/12. There is a potential for overdose if users rely on the syringe stop rather than using the graduations and are unaware that their potential dose has increased from 1.0 to 1.5 ml. Please ensure that all patients are informed that they should use the pipette graduations and not rely on the plunger stop irrespective of the batch number(s) they have available. Special Products Ltd plan to revert to the previous syringe with a potential maximum dose of 1.0ml at the earliest opportunity. This is expected to be available from around mid April 2012. A class 4 Drug Alert highlighting the risk of potential overdose has been circulated to all Healthcare Professionals

RAPID DRUG ASSESSMENT: *OLOPATADINE 0.1% EYE DROPS (OPATANOL)*

Olopatadine (Opatanol) is a combined histamine antagonist and mast-cell stabilising agent licensed as a 0.1% eye drop for the treatment of the ocular signs and symptoms of seasonal allergic conjunctivitis. It is a potent selective antihistamine that exerts its effect both through histamine antagonism and the prevention of histamine-induced inflammatory cytokine production by human conjunctival epithelial cells.

Using a Conjunctival Allergen Challenge (CAC) method, olopatadine has been shown to be significantly more effective than placebo and superior to the active comparators, nedocromil, ketotifen and levocabastine for defined periods. Using the CAC method, patients with a history of seasonal allergic conjunctivitis are given a predetermined topical ocular dose of allergen to provoke an allergic reaction. The provoked action can then be used to evaluate an anti-allergy topical ocular product with the patient acting as his or her own control. Further clinical studies have recruited patients during the allergy season and evaluated olopatadine against sodium cromoglicate and levocarbastine. Olopatadine emerges from these studies as non-inferior to these two comparators.

Olapatadine eye drops are used twice daily in comparison to sodium cromoglicate 2% eye drops (up to four times a day) and nedocromil 2% eye drops (twice to four times daily). A cost comparison reveals the following:

Product	Dose	Price
Olopatadine 0.1% eye drops (Opatanol)	**One drop twice daily**	**5ml £3.91**
Nedocromil 2% eye drops (Rapitil)	One drop twice daily increased if necessary to four times daily	5ml £2.86
Sodium cromoglicate 2% eye drops (generic)	One or two drops up to four times daily	13.5ml £2.08
Sodium cromoglicate 2% eye drops (Hay-Crom)	One or two drops up to four times daily	13.5ml £2.30
Sodium cromoglicate 2% eye drops (Opticrom)	One or two drops up to four times daily	13.5ml £8.03
Sodium cromoglicate 2% eye drops (Vividrin)	One or two drops up to four times daily	13.5ml £8.70

PACEF Recommendation:

PACEF were not convinced that olopatadine 0.1% eye drops (Opatanol) offered significant additional benefit over existing mast cell stabiliser eye drop formulations such as nedocromil 2% eye drops (Rapitil) and sodium cromoglicate 2% eye drops. The product is also significantly more expensive than established alternatives. As a result, olopatadine 0.1% eye drops (Opatanol) are designated RED-RED. When prescribing sodium cromoglicate 2% eye drops, prescribers are reminded that all prescribing should be generic

or for the Hay-Crom brand; both Opticrom and Vividrin are prohibitively expensive and should not be prescribed.

LICENCE EXTENSION: *SITAGLIPTIN TABLETS (JANUVIA)*

Previously, sitagliptin (Januvia) could only be used in patients with type 2 diabetes mellitus who had normal renal function or, at worst, mild renal impairment (creatinine clearance (CrCl) ≥50ml/min); clinical experience in patients with moderate to severe renal impairment was limited and use within this patient group was not recommended. Following a recent license extension, sitagliptin can now be used in all stages of renal impairment subject to dose reduction:

- For patients with moderate renal impairment (CrCl ≥30 to <50ml/min) the recommended dose of sitagliptin is 50mg daily.
- For patients with severe renal impairment (CrCl <30ml/min) or with end stage renal disease (ESRD) requiring haemodialysis or peritoneal dialysis, the dose of sitagliptin is 25mg daily.

Clinical evidence to support the use of sitagliptin in patients with varying degrees of renal impairment comes from one published pharmacokinetic study and one published clinical study. These studies confirm that these reduced doses of sitagliptin in renal impairment provide glycaemic efficacy in terms of meaningful reduction in HbA1c similar to that reported in other patient populations.

PACEF Recommendation:

PACEF have recently completed a review of the DPP-4 inhibitors (or gliptins) (see *PACE Bulletin* Vol 6, No 3 (January 2012)) and have approved three of the four available agents for use: sitagliptin (Januvia/Janumet), saxagliptin (Onglyza) and linagliptin (Trajenta). The table below provides an updated version of advice on use in renal impairment relating to each of the four available products. Only sitagliptin and linagliptin (Trajenta) emerge from this comparison as appropriate choices in all grades of renal impairment. Sitagliptin remains the DPP-4 inhibitor of first choice as it has the widest range of licensed indications of all of the agents. At present, sitagliptin is only available as 100mg tablets; lower strength tablets correspondent with the lower doses required in renal impairment will be available from April 2012. Until then, linagliptin remains the DPP-4 inhibitor of choice in patients with moderate to severe renal impairment.

DPP-4 inhibitor	Advice in renal impairment
Linagliptin (Trajenta)	No dose adjustment is required in patients with renal impairment.
Saxagliptin (Onglyza)	Licensed dose of 2.5mg once daily in moderate to severe renal impairment. Manufacturer advises caution in severe impairment as clinical experience in this patient group is very limited. Saxagliptin is contraindicated in end stage renal failure.
Sitagliptin (Januvia)	For patients with mild renal impairment (creatinine clearance >50ml/min), no dose adjustment is required. For patients with moderate renal impairment (CrCl ≥30 to >50ml/min) the recommended dose of sitagliptin is 50mg daily. For patients with severe renal impairment (CrCl <30mg/min) or with end stage renal disease (ESRD) requiring haemodialysis or peritoneal dialysis, the dose of sitagliptin is 25mg daily.
Vildagliptin (Galvus)	For patients with mild renal impairment (creatinine clearance >50ml/min), no dose adjustment is required. Use of vildagliptin is not recommended in patients with moderate or severe impairment or in haemodialysis patients with end-stage renal

	disease (ESRD). A license application is expected to expand the role of vildagliptin to include moderate or severe impairment or end stage renal disease at a dose of 50mg once daily.

EMERGING SAFETY CONCERNS AROUND THE USE OF ALISKIREN (RASILEZ)

The European Medicines Agency (EMA) has started a review of aliskiren containing medicines following termination of the ALTITUDE study. Aliskiren (Rasilez) is a direct renin inhibitor licensed for the treatment of essential hypertension. It has been evaluated by PACEF and designated as AMBER (without shared care). The ALTITUDE study was conducted in 8,606 type 2 diabetic patients at high risk of adverse heart and kidney events. Aliskiren 300 mg was given in addition to an angiotensin converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB). In most patients, blood pressure was adequately controlled before they participated in the study. The study was stopped because of a preliminary interim analysis which failed to show any additional benefit from adding in aliskiren. Furthermore, there was also a higher incidence of adverse events related to non-fatal stroke, kidney complications, high blood potassium and low blood pressure. Additional analyses from ALTITUDE are ongoing and updated advice may be issued early in 2012.

As a result of this, routine (i.e. non-urgent) review is recommended for all patients currently taking aliskiren-containing medicines:

- Doctors should not prescribe aliskiren-containing medicines to diabetic patients in combination with ACE inhibitors or ARBs. Alternative treatment options should be considered if needed.
- Doctors should review the treatment of patients taking aliskiren at a routine (non-urgent) appointment; if the patient is diabetic and also taking an ACE inhibitors or ARBs, aliskiren should be stopped and alternative treatment considered.
- Patients are advised to discuss their treatment with their doctor at their next scheduled appointment.
- Patients in clinical trials with aliskiren should contact their study site for guidance on their medication.
- Patients who have any questions or concerns about their treatment should speak to their doctor or pharmacist.
- Prescribers are reminded to report any suspected adverse reactions associated with aliskiren via the yellow care scheme.

PACEF Comment
It is estimated that there are currently about 160 patients receiving aliskiren treatment in Lincolnshire primary care. All of these patients should be reviewed according to EMA criteria at their next routine appointment. Aliskiren (Rasilez) remains AMBER (without shared care).

GUIDELINES FOR THE TREATMENT OF COMMONLY OCCURRING INFECTIONS IN LINCOLNSHIRE PRIMARY CARE: WINTER 2011/12

Recent changes to Health Protection Agency guidance on the treatment of urinary tract infections have necessitated the following minor changes to existing antibacterial prescribing guidance. A more comprehensive review of local guidelines will be undertaken in preparation for Winter 2012/13 following updated HPA guidance due later in 2012. Practices with high comparative use of cephalosporins, quinolones or co-amoxiclav will notice that none of these three antibacterial treatment options feature prominently in local guidance on the treatment of commonly occurring

infections. Prescribers are encouraged to minimise antibacterial use where appropriate and to ensure that the majority of treatment for commonly occurring infections is drawn from the attached guideline.

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Stephen Gibson
Head of Prescribing and Medicines Management
NHS Lincolnshire
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GUIDELINES FOR THE TREATMENT OF COMMONLY OCCURRING INFECTIONS IN LINCOLNSHIRE PRIMARY CARE: WINTER 2011/12

Infection	Recommended Agents	Notes
Pharyngitis / sore throat / tonsillitis Average length of illness is 1 week	**Most sore throats are viral** **Antibiotics unnecessary in many cases** as 90% resolve in 7 days **Phenoxymethylpenicillin** 500mg four times a day or 1g twice daily for 10 days depending on the severity of the infection (QDS when severe) If allergic to penicillin: **Clarithromycin** 250 – 500mg twice daily for 5 days	Consider a **'no antibiotic'** or **'delayed antibiotic strategy'** and ensure that patients know that the average length of the illness is 1 week. Patients with 3 of 4 Centor criteria (presence of tonsillar exudate, tender anterior cervical lympadenopathy or lymphadenitis, presence of fever and an absence of cough) may benefit from antibiotics.
Acute Otitis Media (AOM) Antibiotics should not be routinely prescribed for AOM Average length of illness 4 days	**Antibiotics are unnecessary in many cases; AOM resolves in 60% of patients within 24 hours**. Antibiotics do not prevent deafness. First Line **Amoxicillin** 40mg/kg/day in 3 divided doses for 5 days Maximum 1g three times a day If allergic to penicillin: **Erythromycin (5 days)** Up to 2 years: 125mg four times a day; 2-8 years: 250mg four times a day; Other: 250-500mg four times a day	Depending on severity, consider prescribing antibiotics for children < 2 years with bilateral AOM and for children with otorrhoea. Children who do not meet these criteria should not be given antibiotics. Use a **'no antibiotic'** or **'delayed antibiotic'** strategy. Reassure patients/carers that antibiotics are not needed immediately because they will make little difference to symptoms and may have side effects (e.g. diarrhoea, vomiting and rash). Use analgesia for symptom relief
Acute Rhinosinusitis Antibiotics should not be routinely prescribed for sinusitis The average duration of symptoms is 2½ weeks	**Antibiotics unnecessary in many cases as 80% resolve in 14 days.** First Line (7 days) **Amoxicillin** 500mg three times daily (1g if severe) or **doxycycline** 200mg stat followed by 100mg daily or **phenoxymethylpenicillin** 500mg four times daily **For persisitent symptoms** **If there is no improvement following treatment with a first line antibiotic, an alternative first line agent should be tried before commencing with either of the third line options.** **Co-amoxiclav** 625mg three times a day for 7 days	**Many cases of sinusitis are of viral origin.** NICE CG 69 Respiratory Tract Infections recommends using a '**no antibiotic prescribing strategy'** or '**delayed antibiotic prescribing strategy'.** Patients with acute sinusitis who are likely to be at risk of developing complications should be offered an immediate antibiotic prescription in the following situations: (1) if the patient is systemically very unwell; (2) if the patient has symptoms and signs suggestive of serious illness and/or complications (3) if the patient is at high-risk of serious complications due to pre-existing co-morbidity (e.g. significant heart, lung, renal, liver or neuromuscular disease, immunosuppression, cystic fibrosis and young children born prematurely). Use adequate analgesia. Consider a 7 day delayed or immediate antibiotic when there is a purulent nasal discharge.
Acute cough /	**In primary care antibiotics have**	**Routine antibiotic treatment of uncomplicated acute**

Infection	Recommended Agents	Notes
bronchitis Average duration of cough is 3 weeks	**marginal benefits in otherwise healthy adults.** First Line **Amoxicillin** 500mg three times a day for 5 days or **doxycycline** 200mg stat followed by 100mg daily for 5 days.	**bronchitis is not recommended regardless of duration of cough.** Antibiotics should be prescribed for patients > 65 years with acute cough and 2 or more of the following, or older than 80 years with one or more of the following: - hospitalisation in previous year - type 1 or type 2 diabetes mellitus - history of congestive heart failure - current use of oral steroids Antibiotics should be prescribed for patients who are - systemically very unwell, - have symptoms or signs suggestive of serious illness and/or complications (particularly pneumonia), - are at high risk of serious complications because of pre-existing co-morbidity. This includes patients with significant heart, lung, renal, liver or neuromuscular disease, immunosuppression, cystic fibrosis and young children born prematurely.
Community acquired pneumonia	If CRB65 =0 **Amoxicillin** 500mg three times daily for 7 days or **clarithromycin** 500mg twice daily for 7 days or **doxycycline** 200mg stat/100mg daily for 7 days If CRB65 =1 and at home **Amoxicillin** 500mg three times daily for 7-10 days and **clarithromycin** 500mg twice daily for 7 -10 days or **doxycycline** alone 200mg stat/100mg daily for 7-10 days	**Start antibiotics immediately** Use CRB-65 to assess risk. Each scores 1: confusion(AMT<8); respiratory rate >30/min; age>65; BP systolic < 90 or diastolic ≤ 60. Score 0: suitable for home treatment. Score 1-2: hospital assessment or admission. Score 3-4: urgent hospital admission. If no response in 48 hrs add clarithromycin first line, or tetracycline to cover Mycoplasma infection (rare in >65y)
Acute exacerbation of COPD	Prescribe antibiotics if increased dyspnoea and sputum is more purulent than usual. First Line **Amoxicillin** 500mg three times a day for 5 days or **doxycycline** 200mg stat followed by 100mg daily for 5 days If the patient is allergic to penicillin and a tetracycline is contraindicated, use **clarithromycin** 500mg twice daily for 5 days Second Line If there is a clinical failure to first line antibiotics use: **co-amoxiclav** 625mg three times daily for 5 days	
Uncomplicated UTI in men or women (i.e. no fever or flank pain)	**In women with > 3 symptoms of UTI (dysuria, urgency,frequency, polyuria, suprapubic tenderness, haematuria): treat** **In women with < 2 symptoms: use dipstick test to guide treatment and exclude UTI.** In men: send pre-treatment MSU or, if symptoms are mild or non-specific, use a dipstick test to exclude UTI. **First Line** **Trimethoprim** 200mg twice daily or **nitrofurantoin** MR capsules 100mg twice daily. Treatment length **3 days in women** and **7 days in men**. Second Line Dependent upon sensitivities. Amoxicillin resistance is common; only use if susceptible. Community multi-resistant Extended-spectrum Beta-lactamase *E.coli* are increasing: consider nitrofurantoin (or fosfomycin 3g stat in women plus second 3g dose in men 3 days later). Microbiologist advice must be sought.	
UTI in pregnancy	Send MSU for culture and sensitivities and start empirical antibiotics. First Line **Nitrofurantoin** MR capsules 100mg twice daily for 7 days or	

Infection	Recommended Agents	Notes
	amoxicillin 500mg three times daily for 7 days (if susceptible) Second Line **Trimethoprim** 200mg twice daily for 7 days (off label). Give folic acid if first trimester Third line **Cefalexin** 500mg twice daily for 7 days	

Updated February 2012