NHS Lincolnshire

Prescribing and Clinical Effectiveness Bulletin

Volume 6; Number 10 **July 2012**

What's new this month?

- **Two recent systematic reviews have shown that once daily aspirin may reduce cancer risk. However, two previous primary prevention trials designed to investigate this issue failed to show any reduction in colorectal cancer, total cancers or cancer mortality associated with low dose aspirin. Patients should be advised that taking aspirin is not yet proven to reduce cancer risk (see page 4).**
- **Varicella zoster virus vaccine (Zostavax) has been designated RED-RED and should not be prescribed on the NHS. However, it can be prescribed privately and GPs are able to administer the vaccine as part of their NHS work (see page 5).**
- **NICE have issued Clinical Guidelines on the diagnosis and management of epilepsy in primary and secondary care (see page 5).**
- **Following a safety alert from the NPSA, prescribers are advised to ensure that liquid midazolam preparations are always prescribed by brand and that doses are prescribed in both mg and mL to minimize the risk of wrong dose errors (see page 8).**
- **More evidence continues to emerge concerning the risks of long-term use of proton pump inhibitors. Most recently, the MHRA have published data on the risks of hypomagnesaemia and bone fracture (see page 9).**

CONTENTS

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: *MAY 2012 UPDATE*

Drug	Indication(s)	Traffic Light Status
Erbulin (Halaven) injection	Licensed for the treatment of locally advanced or metastatic breast cancer when the disease has progressed after treatment with at least two chemotherapy regimens	RED-RED

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; *doses should always be prescribed in both mg and mL to minimize the risk of wrong dose errors.*
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; *doses should always be prescribed in both mg and mL to minimize the risk of wrong dose errors.*
Omacor capsules	Hypertriglyceridaemia Secondary prevention after MI	RED-RED
Varicella zoster vaccine (Zostavax)	Licensed for the prevention of herpes zoster (or shingles) and herpes zoster-related post-herpetic neuralgia (PHN) in adults 50 years of age or older	RED-RED GPs can privately prescribe but cannot supply; patients must expect to pay for the vaccine (including an additional dispensing fee) at their local community pharmacy. GPs can administer the vaccine free of charge as part of their NHS work.

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.**

NEW TRIALS IN BRIEF

OMEGA 3 FATTY ACID SUPPLEMENTATION (OMACOR) IN THE SECONDARY PREVENTION OF CARDIOVASCULAR DISEASE

Reference:
Mi Kwak S et al. Efficacy of omega-3 fatty acid supplements in the secondary prevention of cardiovascular disease. *Arch Intern Med* doi:10.1001/archinternmed.2012.262.

This meta-analysis included data from 14 double-blind, placebo controlled randomized controlled trials (RCTs) involving 20,485 patients with a history of cardiovascular disease (CVD). Omega-3 fatty acid supplementation did not reduce the risk of overall cardiovascular events, all-cause mortality, sudden cardiac death, myocardial infarction, angina, unstable angina, congestive heart failure, transient ischaemic attack or stroke. There was a small reduction in cardiovascular death which disappeared when a study with unmatched groups was excluded.

PACEF Comment:
This meta-analysis provides further confirmatory evidence that Omacor confers no additional benefit in the secondary prevention of CVD and should not be prescribed. This is the first meta-analysis to include the more recent RCTs, particularly the OMEGA study (reviewed in *PACE Bulletin* Vol 5 No 3 (February 2011)). Omacor is an unnecessary additional treatment used in a patient group that are already expected to manage complex multi-component treatment regimes. It is designated RED-RED. All remaining patients taking Omacor for secondary prevention after MI should be reviewed as a matter of urgency with a view to discontinuing treatment wherever possible. Existing spend on Omacor is approximately £50,000pa across Lincolnshire (down from £200,000pa a year ago); this could be further reduced through the implementation of this guidance.

ANTIPSYCHOTICS IN DEMENTIA

Reference:
Huybrechts KF et al. Differential risk of death in older residents in nursing homes prescribed specific antipsychotic drugs: population based cohort study. *BMJ* 2012; 344:e977

This observational study used data from 75,445 US nursing home residents aged 65 years or older and started on an antipsychotic drug. People with cancer, schizophrenia, bipolar disorder or use of both conventional and atypical antipsychotics were excluded. Deaths within 180 days of starting treatment were evaluated and non-cancer mortality rates for each drug calculated compared to risperidone. No significant differences were found in deaths and non-cancer mortality rates in this patient group between olanzapine, aripiprazole, ziprasidone and risperidone. Haloperidol was associated with a greater relative risk of death than risperidone and quetiapine with a lower risk.

PACEF Comment:
The Banerjee report highlighted that antipsychotics are of limited benefit in patients with behavioural and psychological symptoms of dementia (BPSD) and are associated with an increased risk of stroke and death. Short-term use can sometimes be appropriate when all other options have been tried, symptoms are severe and the patient presents a serious risk to themself or others. Risperidone is the only antipsychotic drug currently licensed for use in BPSD (for up to 6 weeks to treat persistent aggression in patients with moderate to severe Alzheimer's dementia unresponsive to non-pharmacological approaches and when there is a risk of harm to self or others). This observational study suggests that haloperidol is associated with a greater relative risk of death than risperidone when used in older people while quetiapine has a lower risk. A single observational study can only prove association not causation; even though the authors adjusted for a number of possible confounders, residual confounders cannot be ruled out.
When the use of antipsychotics in BPSD is unavoidable then it is best to choose the drug with the lowest harms and best evidence of benefit. Risperidone is licensed for purpose, comparable in terms of safety to most

alternatives and significantly safer than haloperidol. Although quetiapine may be safer than risperidone, there is no good quality evidence supporting its efficacy in BPSD. A recent, large, comprehensive systematic review found no benefit from quetiapine on BPSD (*JAMA* 2011; 306(12): 1359 - 1369). Consequently this study should not be used to support the use of quetiapine in BPSD.
Review of antipsychotic use for BPSD is a national priority. Prescribers are encouraged to review their use in accordance with NICE-SCIE guidance and the NICE Quality Standard on dementia. NICE have developed an audit support tool for assessing the use of medication and non-pharmacological interventions for non-cognitive symptoms, challenging behaviour and behavioural control for people with dementia. The NPC website has a patient decision aid to assist healthcare professionals in consultations with patients (and their family/carers) for whom treatment with an antipsychotic is being considered for BPSD.

ASPIRIN AND CANCER PREVENTION

Reference:
Rothwell P et al. Short-term effects of daily aspirin on cancer incidence, mortality and non-vascular death: analysis of the time course of risks and benefits in 51 randomised controlled trials. *Lancet* 2012; 379:1602 - 1612

Using data from 51 trials of low dose daily aspirin for the prevention of CVD, researchers found that allocation to aspirin reduced deaths from cancer (562 vs. 664 deaths; odds ratio 0.85, 95% CI 0.76 – 0.96) particularly from 5 years onwards, resulting in fewer non-vascular deaths overall (1021 vs 1173; OR 0.88, 95% CI 0.78—0.96). Aspirin significantly reduced the risk of incident cancer in women and men by about 25%.

Reference:
Rothwell P et al. Effect of daily aspirin on risk of cancer metastasis: a study of incident cancers during randomised controlled trials. *Lance*t 2012; 379: 1591 – 1601.

A further systematic review from the Rothwell team used data from 5 UK RCTs comparing low dose aspirin with a control for CV prevention and data from cancer registries. During a mean trial follow up of 6.5 years, allocation to aspirin reduced the risk of cancer with distant metastasis. The Hazard Ratios for all cancers was 0.64 (0.48 – 0.84) and for adenocarcinoma 0.54 (0.38 – 0.77).

PACEF Comment:
Media coverage of these studies has understandably generated a great deal of interest in aspirin and reduction in cancer risk. Unfortunately, neither of these reviews is sufficient to demonstrate a causal link. Primary prevention trials designed to investigate this issue have failed to show an effect of low dose aspirin on colorectal cancer, total cancers or cancer mortality. Two of the largest aspirin in CV prevention studies were excluded from this analysis because aspirin was given on alternate days; neither of these trials reported a lower risk of cancer or cancer death among participants taking aspirin. Patients should be advised that taking aspirin is not yet proven to reduce cancer risk and reminded of life-style changes associated with much better evidence of cancer risk reduction. Some patients may find the 'Behind the Headlines' report on these studies useful to explain the limitations of the data (accessed from www.nhs.uk).

RAPID DRUG ASSESSMENT: *VARICELLA ZOSTER VIRUS VACCINE (ZOSTAVAX)*

Zostavax is a new varicella zoster virus vaccine licensed for the prevention of herpes zoster (shingles) and herpes zoster related post-herpetic neuralgia in patients aged 50 years of age and older. The Department of Heath has referred the product to the Joint Committee on Vaccination and Immunisation (JCVI) who have recommended that a shingles vaccination programme should be introduced for people aged 70 to 79 years, conditional on the vaccine becoming available at a cost-effective price. Such a programme is not expected to launch through the NHS until 2013. In the meantime, varicella zoster virus vaccine should not be prescribed on the NHS. GPs can privately prescribe but cannot supply; patients must expect to pay for the vaccine (including an additional dispensing fee) at their local community pharmacy. GPs can administer the vaccine free of charge as part of their NHS work.

PACEF Recommendation:
In response to the national advice detailed above, varicella zoster virus vaccine (Zostavax) is designated RED-RED. It should not be prescribed on NHS prescription, although appropriate patients can be prescribed for privately; GPs are able to administer the vaccine as part of their NHS work.

NICE TECHNOLOGY APPRAISAL 250: *ERIBULIN FOR THE TREATMENT OF LOCALLY ADVANCED OR METASTATIC BREAST CANCER* (APRIL 2012)

Key Recommendations

Eribulin is not recommended, within its licensed indication, for the treatment of locally advanced or metastatic breast cancer that has progressed after at least two chemotherapy regimens for advanced disease.

People currently receiving eribulin, within its licensed indication, should have the option to continue therapy until they and their clinicians consider it appropriate to stop.

PACEF Recommendation
Erbulin (Halaven) injection is designated RED-RED for this indication.

NICE CLINICAL GUIDELINE 137: *THE EPILEPSIES: THE DIAGNOSIS AND MANAGEMENT OF THE EPILEPSIES IN ADULTS AND CHILDREN IN PRIMARY AND SECONDARY CARE* (JANUARY 2012)

Diagnosis
All patients with a recent onset suspected seizure should be seen by a specialist within two weeks for diagnosis.

Treatment

- Treatment with an antiepileptic drug (AED) is recommended after a second epileptic seizure and a diagnosis of epilepsy is confirmed by a specialist.
- In children and young people, AED treatment should be started by a specialist.
- In adults, AED should be started on the recommendation of a specialist.

PACEF Comment:
As a result of this, all AEDs for newly diagnosed epilepsy should only be initiated on the recommendation of a specialist.

Pharmacological Treatment

- An appropriate AED should be selected on the basis of the epilepsy syndrome (see Table 2 at the end of the *Bulletin*).
- If the epilepsy syndrome is not clear, base the decision on seizure type (see Table 1 below).

Table 1: Antiepileptic drug choices by seizure type

	Seizure Type				
	Primary generalised tonic-clonic	Tonic or atonic	Absence	Myoclonic	Focal
AED					
Carbamazepine	3rd line				1st line / adjunct
Clobazam	adjunct*				adjunct*
Ethosuximide			1st line / adjunct		
Gabapentin					adjunct*
Lamotrigine	2nd line / adjunct	adjunct*	2nd line* / adjunct*		1st line / adjunct
Levetiracetam	adjunct			2nd line* / adjunct	2nd line / adjunct
Oxcarbazepine	3rd line*				2nd line / adjunct
Sodium valproate	1st line / adjunct	1st line	1st line / adjunct	1st line / adjunct	2nd line / adjunct
Topiramate	adjunct			2nd line* / adjunct*	adjunct

*Unlicensed use

- Consistent supply of a particular manufacturer's AED is recommended.

PACEF Comment:
A recent incident in Lincolnshire illustrates this point. A patient with controlled epilepsy on the Keppra brand of levetiracetam lost seizure control following supply of generic levetiracetam against a generic prescription; seizure control was regained once the Keppra brand of the product was reinstated. Care should be taken to ensure consistency of supply. Where a patient is initiated and controlled on a generic AED, generic prescribing remains appropriate. However, care should be taken to ensure that patients initiated and controlled on specific branded preparations remain on those preparations; specific branded prescribing within this context should ensure consistency of supply. The *BNF* specifically advises that different preparations of carbamazepine may vary in bioavailability resulting in the potential for reduced effect or excessive side effects if the patient's regular formulation is inadvertantly changed. NICE have also recommended that carbamazepine should usually be prescribed in a controlled release formulation (see below). Within this context, branded prescribing is also recommended to avoid inadvertant supply of an alternative brand at the dispensing stage.

- Some AEDs may worsen seizure control and should not be used in certain seizure types or epilepsy syndromes.

- With sodium valproate, be aware of the teratogenic risk.
- With carbamazepine, prescribe controlled release preparations (e.g. Carbagen SR tablets, Tegretol Prolonged Release tablets).
- With vigabatrin, be aware of irreversible effect on visual fields.
- Topiramate has a less favourable side effect profile than levetiracetam and sodium valproate.

Monotherapy

- Treatment with a single AED is preferred
- If treatment with the initial AED is unsuccessful, try an alternative 1st line or a 2nd line option: increase to maximum effective/tolerated dose and then slowly taper off the first AED.
- If treatment with the 2nd drug is unsuccessful, taper either the 1st or 2nd drug depending on efficacy, side effects and tolerability before starting another drug.

Combination therapy

- Only consider if monotherapy has not resulted in seizure freedom.
- If trials of combination therapy do not improve seizure control, revert to drug(s) most accepted by the patient.

Review

All epileptic patients should be given an annual, structured review. This should be carried out by a:

- GP or specialist in adults
- Specialist in children and young people

Continuing, withdrawing or stopping treatment

Discuss the risks and benefits of continuing or withdrawing treatment in individuals who have been seizure free for at least 2 years.

- Withdrawal of AEDs should be managed by a specialist
- Withdraw one AED at a time, over at least 2 to 3 months
- Withdraw benzodiazepines and barbituarates over at least 6 months

Referral

Consider referral to a tertiary service in the following situations:

- Epilepsy is not controlled with AEDs within 2 years
- Management is unsuccessful after 2 AEDs
- Children aged under 2 years
- Unacceptable side effects of AEDs
- Unilateral structural lesion
- Psychological / psychiatric co-morbidity
- Doubt about seizure type or syndrome

Women and girls with epilepsy

Contraception

- POPs and progesterone implants are not recommended in women taking enzyme-inducing AEDs.
- Adjust the dose of lamotrigine if using oestrogen-based contraception.

PACEF Comment:

According to guidance on drug interactions and hormonal contraception published by the Faculty of Sexual and Reproductive Healthcare, combined

hormonal contraception is not recommended in women on lamotrigine monotherapy due to the risk of reduced seizure control and the potential for lamotrigine toxicity during the pill free week.

Pregnancy

- Aim for seizure freedom before conception and during pregnancy
- Consider the risk of adverse effects of AEDs
- If possible, prescribe 5mg folic acid before conception.

Prolonged/repeated seizures – treatment in the community

- Only prescribe buccal midazolam or rectal diazepam for epileptics who have had a previous episode of prolonged or serial convulsive seizures. Use buccal midazolam first line.

PACEF Comment:
See *PACE Bulletin* Volume 6 No 5 (March 2012) for further advice on buccal midazolam (also see below).

Comparative costs of antiepileptic drugs

Anti-epileptic drug	**Usual adult daily dose**	**Cost per 28 days (Drug Tariff April 2012)**
Carbamazepine 400mg M/R	0.8-1.2g in divided doses	£10.24-£15.36
Clobazam 10mg	20-30mg	£7.03
Ethosuximide 250mg	1-1.5g in 2 divided doses	£76.46-£114.69
Gabapentin caps	0.9-3.6g in 3 divided doses	£5.51-£22.04
Lamotrigine 100mg	100-200mg in 1-2 divided doses	£1.83-£3.66
Levetiracetam 750mg	1500mg	£49.87*
Oxcarbazepine 600mg	0.6-2.4g in divided doses	£26.00-£103.98
Sodium valproate 500mg	1-2g in 1-2 divided doses	£4.99-£10.00
Topiramate 100mg	100-200mg in 2 divided doses	£1.63-£3.26
Buccal midazolam	10mg	£22.88 (as Buccolam®)
Rectal diazepam	10-20mg	£1.71-£3.42

*NICE recommends that levetiracetam is not cost-effective until cost falls below £38.36 per month.

NATIONAL PATIENT SAFETY AGENCY: *PREVENTION OF HARM WITH BUCCAL MIDAZOLAM* (FEBRUARY 2012)

Buccal midazolam can be used in varying doses to treat status epilepticus in adults and children. It is available in two strengths:

- a 5mg/mL oral liquid product recently licensed for paediatric use (Buccolam) (available in a range of prefilled oral syringes)
- an unlicensed 10mg/mL oral liquid product available from various 'specials' manufacturers in a multidose bottle and / or prefilled oral syringes.

It is administered to the buccal mucosa (between the gum and cheek).

A search of the National Reporting and Learning System (NRLS) showed that between 1st April 2008 and 22nd August 2011, 132 relevant medication incidents were reported with midazolam, eight of which resulted in either moderate or severe harm. Among the errors identified were wrong dose errors including:

- 2.5mL (25mg) prescribed when 0.25mL (2.5mg) was intended;
- 2.5mg prescribed where 2.5mL of 10mg/mL strength (25mg) was administered;
- 0.5mL prescribed where the pharmacy label stated ''give one 5mL spoonful''.

In order to minimize the risk of such errors, the NPSA have recommended that the dose of buccal midazolam should always be prescribed in both mg and mL.

Updated PACEF Recommendation:

In *PACE Bulletin* Volume 6 No 5 (March 2012), PACEF endorsed *licensed* midazolam oromucosal solution (Buccolam) as the preferred option in infants, children and adolescents at risk of acute convulsive seizures in epilepsy. Midazolam 5mg/ml oromucosal solution (Buccolam) was designated AMBER for this indication. In view of this further safety alert from the NPSA, existing advice is amended as follows:

(1) There is a risk of confusion between 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 currently taking unlicensed midazolam 10mg/ml buccal solution (Epistatus) should continue to be prescribed it until they or their clinician consider it to be appropriate to change or stop.

(2)* 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; *doses should always be prescribed in both mg and mL to minimize the risk of wrong dose errors.

MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY
***DRUG SAFETY UPDATE* VOL 5 ISSUE 9 (APRIL 2012)**

Proton pump inhibitors in long term use: reports of hypomagnesaemia

- Prolonged use of PPIs has been associated with hypomagnesaemia. Severe hypomagnesaemia has been reported infrequently with PPIs; the exact incidence is unknown.
- Some cases occurred after 3 months of PPI therapy, most after 1 year of treatment.
- Serious manifestations of hypomagnesaemia include: fatigue, tetany, delirium, convulsions, dizziness and ventricular arrhythmia.
- In most case reports, hypomagnesaemia improved after magnesium replacement and discontinuation of the PPI.
- For patients expected to be on prolonged treatment and, especially, those taking concurrent digoxin or drugs that may cause hypomagnesaemia (e.g. diuretics), healthcare professionals should consider measuring magnesium levels before starting PPI treatment and periodically during treatment.
- PPIs obtained over-the-counter should not be used for longer than 4 weeks without consulting a doctor.

Proton pump inhibitors in long-term use: recent epidemiological evidence of increased risk of bone fracture

- Observational studies on the risk of fracture associated with PPIs suggest there may be a modest increase in the risk of hip, wrist or spine fracture, especially if PPIs are used in high doses and over long durations (>1year).
- The increased risk is mainly in the elderly; other risk factors may also contribute.

- Two meta-analyses of published pharmacoepidemiology studies suggest the risk of fracture is increased by 10 to 40% above baseline.
- Patients at risk of osteoporosis should be treated according to current guidelines to ensure an adequate intake of calcium and vitamin D.
- PPIs obtained over-the-counter should not be used for longer than 4 weeks without consulting a doctor.

PACEF Comment

Nationally, PPI prescribing continues to escalate despite the accumulation of published evidence suggesting harms associated with long-term use. PACEF have previously issued guidance on increased risk of bone fracture, *Clostridium difficile* and pneumonia linked to long-term PPI use. The MHRA have now identified hypomagnesaemia as an additional risk. Standard advice is that PPIs should not be prescribed long-term or in high doses without regular review and discussion of risks and benefits with the patient. Community pharmacists should ensure that, wherever possible, PPIs purchased over-the-counter are not used for longer than 4 weeks without a medical consultation.

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July 2012

Table 2: Antiepileptic drug options by epilepsy syndrome

	Epilepsy syndrome								
	Childhood absence, juvenile absence or other absence syndromes	Juvenile myoclonic	Generalised tonic-clonic seizures only	Idiopathic generalised epilepsy	Infantile spasms **not** due to tuberous sclerosis**	Infantile spasms due to tuberous sclerosis**	Benign epilepsy with centrotemporal spikes or Panayiotopoulos syndrome**. Late-onset childhood occipital (Gastaut type)	Dravet syndrome**	Lennox-Gastaut syndrome**
AED									
Carbamazepine			2nd line				1st line* / adjunct*		
Clobazam			adjunct*				adjunct*	adjunct*	
Ethosuximide	1st line / adjunct								
Gabapentin							adjunct*		
Lamotrigine	2nd line* / adjunct*	2nd line* / adjunct*	1st line / adjunct	2nd line* / adjunct*			1st line* / adjunct*		adjunct
Levetiracetam		2nd line* / adjunct	adjunct	adjunct*			2nd line* / adjunct*		
Oxcarbazepine			2nd line*				2nd line* / adjunct*		
Prednisolone					1st line	2nd line			
Sodium valproate	1st line / adjunct	1st line / adjunct	1st line / adjunct	1st line / adjunct			2nd line / adjunct	1st line	1st line
Stiripentol								adjunct	
Tetracosactide					1st line*	2nd line*			
Topiramate		2nd line* / adjunct*	adjunct	3rd line* / adjunct*			adjunct*	1st line*	
Vigabatrin					1st line	1st line			

*Unlicensed use

**Refer to tertiary paediatric epilepsy specialist