

Product current status:	<input type="text"/>
Product proposed status:	<input type="text"/>
Date of next meeting:	<input type="text"/>
Decision:	Yes <input type="checkbox"/> No <input type="checkbox"/>
Restricted use:	<input type="text"/>

Drug name

Gabapentin 50 mg/ml oral solution

Indication

- For patients unable/unwilling to swallow gabapentin tablets or capsules
- For the treatment of epilepsy as:
 - an adjunctive therapy in the treatment of partial seizures with and without secondary generalisation in adults and children aged 6 years and above
 - a monotherapy in the treatment of partial seizures with and without secondary generalisation in adults and adolescents aged 12 years and above
- As a monotherapy for the treatment of peripheral neuropathic pain such as painful diabetic neuropathy and post-herpetic neuralgia in adults.

Dosage

- Gabapentin 50 mg/ml oral solution may be taken with or without food
- For all indications, therapy is initiated using a titration scheme
- Please refer to the Summary of Product Characteristics,¹ which can be found at www.medicines.org.uk/emc

Mode of action

- Gabapentin is an anti-epileptic agent
- Gabapentin is structurally related to the neurotransmitter GABA (gamma-aminobutyric acid), but its mechanism of action is different from that of several other active substances that interact with GABA synapses
- The binding site for gabapentin has been identified as the α_2 -delta subunit of voltage-gated calcium channels
- Gabapentin slightly reduces the release of monoamine neurotransmitters in vitro
- The relevance of the various actions of gabapentin to the anticonvulsant effects remains to be established.

Guidance recommendations

- NICE guidance reinforces the importance of patients receiving the same anti-epileptic formulation consistently²
- SIGN guidance states that anti-epileptic drugs like gabapentin, which do not induce hepatic enzymes, do not alter the efficacy of combined oral contraceptives³
- The Quality and Outcomes Framework indicators for epilepsy encourage GPs to keep a record of:⁴
 - the percentage of women under the age of 55 years who are taking anti-epileptic drugs who have a record of information and counselling about contraception, conception, and pregnancy in the preceding 15 months [EPILEPSY 9].

Evidence for use

- Almost 60% of patients aged >60 years experience some difficulty in swallowing solid-dose medications⁵
- A small study to assess the impact, if any, of gabapentin on concomitantly prescribed oral contraceptives found it was not metabolised and does not induce or inhibit hepatic enzymes⁶
 - anticonvulsant drugs that do not interact with oral contraceptives should be considered for women with epilepsy who are of child-bearing age.

Cost effectiveness

- Swallowing difficulties might be one factor that adversely affects compliance, particularly in elderly and stroke patients.

Contraindications

- Contraindications to gabapentin include hypersensitivity to the active substance or any of the excipients.

Precautions

- Women of reproductive years should be advised to consult their clinician if they are considering pregnancy
- It is not advisable to stop anti-epileptic therapy suddenly
- Please refer to the Summary of Product Characteristics¹ at www.medicines.org.uk/emc for a full list of precautions.

Common side effects

- Please refer to the Summary of Product Characteristics¹ at www.medicines.org.uk/emc.

NICE=National Institute for Health and Clinical Excellence; SIGN=Scottish Intercollegiate Guidelines Network

This formulary decision guide was developed from content provided by Rosemont Pharmaceuticals Ltd in a format developed by *Guidelines in Practice*. It has been reviewed by a member of the *Guidelines in Practice* editorial board. At all times editorial control has remained with *Guidelines in Practice*.

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Key points

- The following patients with epilepsy, who may become non-adherent, benefit from taking gabapentin oral solution:
 - patients aged >60 years and children who might have difficulty swallowing gabapentin tablets or capsules or other solid-dose medications
 - patients with transient swallowing difficulties, e.g. those who have suffered a stroke
 - women of child-bearing age who are taking combined oral contraceptives, and who might have difficulty swallowing tablets or capsules or other solid-dose medications.

References

1. Rosemont Pharmaceuticals Limited. *Gabapentin 50 mg/ml oral solution. Summary of Product Characteristics*. November 2012.
2. National Institute for Health and Clinical Excellence. *The diagnosis and management of the epilepsies in adults and children in primary and secondary care*. Clinical Guideline 137. London: NICE, 2012. Available at: guidance.nice.org.uk/CG137
3. Scottish Intercollegiate Guidelines Network. *Diagnosis and Management of Epilepsy in Adults*. SIGN 70. Edinburgh: SIGN, 2003. Available at: www.sign.ac.uk/pdf/sign70.pdf
4. NHS Employers. *Quality and Outcomes Framework for 2012/13*. London: NHS Employers/BMA, 2012. Available at: www.nhsemployers.org/Aboutus/Publications/Documents/QOF_2012-13.pdf
5. Strachan I, Greener M. Medication-related swallowing difficulties may be more common than we realise. *Pharmacy in Practice* 2005; **15** (9): 411–414.
6. Eldon M, Underwood B, Randinitis E, Sedman A. Gabapentin does not interact with a contraceptive regimen of norethindrone acetate and ethinyl estradiol. *Neurology* 1998; **50** (4): 1146–1148.

Abbreviated Prescribing Information: Gabapentin 50mg/ml Oral Solution. Consult Summary of Product Characteristics before prescribing.

Presentation: A clear colourless solution containing 50mg gabapentin per ml.

Therapeutic Indications: Adjunctive therapy in the treatment of partial seizures, monotherapy in the treatment of partial seizures and treatment of peripheral neuropathic pain. **Posology:** For oral use, Gabapentin can be given with or without food. For all indications, a titration scheme for the initiation of therapy is described in the SPC. **Paediatric population:** Please refer to SPC. **Contra-**

indications: Hypersensitivity to gabapentin or any of the excipients. **Excipient warnings:** Product contains parahydroxybenzoates which may cause allergic reactions. It also contains potassium which should be considered for patients with reduced kidney function or on controlled potassium diets and sodium, which should be taken into consideration for patients on a controlled sodium diet. **Drug interactions:** Gabapentin may interact with the following: morphine, antacids containing aluminium and magnesium, cimetidine. **Precautions for use:** Suicidal ideation and behaviour have been reported in patients treated with antiepileptic agents in several indications. Monitor patients for signs of suicidal ideation. If a patient develops acute pancreatitis under gabapentin treatment; consider discontinuation. Abrupt withdrawal of anticonvulsant agents in epileptic patients may precipitate status epilepticus. Some patients may experience an increase in seizure frequency or the onset of new types of seizures with gabapentin. Attempts to withdraw concomitant anti-epileptics in treatment refractive patients have a low success rate. Gabapentin is not considered effective against primary generalized seizures such as absences and may aggravate these seizures in some patients. Gabapentin should be used with caution in patients with mixed seizures including absences. Apart from one study, clinical investigations in the 65 plus age group do not indicate an adverse event profile different from that observed in younger patients. The benefits of prolonged therapy must be weighed against the potential risks, as the long-term effects on learning, intelligence and development in children and adolescents have not been adequately studied. Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) has been reported in patients taking gabapentin. Early manifestations of hypersensitivity, such as fever or lymphadenopathy, may be present even though rash is not evident. If such signs are present, evaluate patient immediately. Discontinue gabapentin if an alternative etiology for the signs or symptoms cannot be established. **Laboratory tests:** False positive readings may be obtained in the semi-quantitative determination of total urine protein by dipstick tests. **Pregnancy and Lactation:** The risk of birth defects is increased 2/3 times in the offspring of mothers treated with an antiepileptic. Most frequently reported are cleft lip, cardiovascular malformations and neural tube defects. Monotherapy should be practised whenever possible. Review the need for antiepileptic treatment when a woman is planning to become pregnant. Sudden discontinuation of antiepileptic therapy should not be undertaken. Developmental delay in children of mothers with epilepsy has been rarely observed. **Risk related to gabapentin:** Studies in animals have shown reproductive toxicity. Gabapentin should be used during pregnancy and in breastfeeding only if the potential benefit to the mother clearly outweighs the potential risk to the foetus. Gabapentin is excreted in human milk. Exercise caution when gabapentin is administered to a breast-feeding mother. **Effects on Ability to Drive and Use Machines:** Minor or moderate influences on ability to drive and use machines. Gabapentin acts on the CNS and may cause drowsiness, dizziness or other related symptoms- this is potentially dangerous in patients driving or operating machinery. **Undesirable Effects:** *Very common:* viral infection, somnolence, dizziness, ataxia, fatigue, fever. *Common:* pneumonia, respiratory infection, urinary tract infection, infection, otitis media, leucopenia, anorexia, increased appetite, hostility, confusion, emotional lability, depression, anxiety, nervousness, thinking abnormal, convulsions, hyperkinesias, dysarthria, amnesia, tremor, insomnia, headache, sensations such as paresthesia, hypaesthesia, coordination abnormal, nystagmus, increased, decreased or absent reflexes, visual disturbances, vertigo, hypertension, vasodilatation, dyspnoea, bronchitis, pharyngitis, cough, rhinitis, vomiting, nausea, dental abnormalities, gingivitis, diarrhoea, abdominal pain, dyspepsia, constipation, dry mouth or throat, flatulence, facial oedema, purpura, rash, pruritus, acne, arthralgia, myalgia, back pain, twitching, impotence, peripheral oedema, abnormal gait, asthenia, pain, malaise, flu syndrome, WBC count decreased, weight gain, elevated liver function tests, accidental injury, fracture, abrasion. *Uncommon:* allergic reactions, hypokinesia, palpitations, generalised oedema, elevated bilirubin. *Unknown:* thrombocytopenia, hypersensitivity syndrome, hallucinations, movement disorders, tinnitus, pancreatitis, hepatitis, jaundice, Stevens-Johnson syndrome, angioedema, erythema multiforme, alopecia, drug rash with eosinophilia and systemic symptoms, myoclonus, acute renal failure, incontinence, breast hypertrophy, gynaecomastia, withdrawal reactions, chest pain, sudden unexplained deaths, blood glucose fluctuations in patients with diabetes. In patients on haemodialysis, myopathy with elevated CK levels has been reported. **Overdose:** Toxicity has not been observed with gabapentin overdoses of up to 49g. Symptoms may include dizziness, double vision, slurred speech, drowsiness, lethargy and mild diarrhoea. All patients recovered fully with supportive care. Gabapentin overdoses with other CNS depressants may result in coma. Haemodialysis is not usually required. However, in patients with severe renal impairment, it may be indicated. **Shelf Life and storage:** 1 year unopened, 1 month opened, do not store above 25 degC, do not refrigerate or freeze. **Legal Category:** POM **Pack Size and NHS Price:** 50mg/ml, 150ml - £57.50. **Marketing Authorisation Holder:** Rosemont Pharmaceuticals Ltd, Rosemont House, Yorkdale Industrial Park, Braithwaite Street, Leeds, LS11 9XE, UK. **Date of Preparation:** Sept 2012.

Adverse events should be reported.

Reporting forms and information can be found at
yellowcard.mhra.gov.uk.

Adverse events should also be reported to Rosemont
Pharmaceuticals Ltd on 0113 244 1400.