Formulary decision guide: Perizam™ (clobazam) 1 mg/ml and 2 mg/ml oral suspension

Guidelines in practice

Key points

- If a liquid formulation of clobazam is indicated, it is preferable that a licensed product, which has been produced in line with good manufacturing practice is used, rather than an unlicensed special
- Perizam:
  - is a licensed liquid formulation of clobazam
  - may be used as an adjunctive therapy for certain epilepsies if standard treatment with one or more anticonvulsants has failed
- A licensed liquid formulation of clobazam:
  - provides an effective option for patients with swallowing difficulties and paediatric patients
  - may aid adherence and reduce wastage
  - will aid accurate dosing where precise doses are required (e.g. in paediatric patients).

Drug name

Clobazam (Perizam™) 1 mg/ml and 2 mg/ml oral suspension

Indication

- Perizam is indicated:[1,2]
  - in adults for the short-term symptomatic treatment (2–4 weeks) only of anxiety that is severe, disabling, or subjecting the individual to unacceptable distress
  - in adults for the treatment of anxiety states associated with affective disorders, clobazam must only be used in conjunction with adequate treatments for the underlying disorder
  - in adults with schizophrenic or other psychotic illnesses, use of benzodiazepines is recommended only for short-term symptomatic management of hyperarousal and agitation; benzodiazepines do not possess antipsychotic properties
  - in adults or children aged over 2 years with epilepsy as an adjunctive therapy, if standard treatment with one or more anticonvulsants has failed: treatment of simple or complex partial epilepsy with or without secondary generalisation and treatment of all types of generalised epilepsy (tonic/clonic, myoclonic, absence seizures).

Dosage

- Anxiety:[1,2]
  - adults—20–30 mg daily, up to maximum of 60 mg daily in severe anxiety
  - elderly—10–20 mg daily
- Epilepsy:[1,2]
  - adults—starting dose of 20–30 mg/day, increasing as necessary up to maximum of 60 mg daily
  - elderly—treatment requires low initial doses and gradual dose increments under careful observation
  - paediatric population (over 2 years)—normally started at 5 mg daily, maintenance dose of 0.3–1.0 mg/kg body weight is usually sufficient.

Mode of action

- Clobazam is a 1,5-benzodiazepine and classified as an anxiolytic[1,2]
- In single doses up to 20 mg or in divided doses up to 30 mg, clobazam does not affect psychomotor function, skilled performance, memory, or higher mental functions.[1,2]

Guidance recommendations

- NICE recommends that clobazam is offered as an adjunctive therapy in patients with with generalised tonic-clonic seizures if first-line treatments are ineffective or not tolerated[3]
- NICE guidance emphasises the importance of patients receiving a consistent supply of a particular antiepileptic formulation throughout their treatment.[3]

Clinical considerations

- If a liquid formulation of clobazam is indicated, it is recommended that a licensed product, which has been produced in line with good manufacturing practice is used, rather than an unlicensed special
- Perizam is a licensed liquid formulation of clobazam, which is sucrose-, lactose-, and gluten-free and is suitable for use in people with diabetes[1,2]
- Almost 60% of patients aged >60 years, experience some difficulty in swallowing solid-dose medications[4]
- The dosing flexibility that is associated with liquid medicines can help when titrating doses during treatment
- An oral solution of clobazam might be appropriate for patients who are unable or unwilling to swallow tablets.

Cost implications

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

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.

DTM055

Date of preparation: December 2016

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Contraindications

- Perizam is contraindicated under the following conditions:
  - hypersensitivity to benzodiazepines or any of the excipients of Perizam
  - drug or alcohol dependence
  - myasthenia gravis
  - severe respiratory insufficiency
  - sleep apnoea syndrome
  - severe hepatic insufficiencies
  - during the first trimester of pregnancy
  - a breastfeeding woman
  - acute intoxication with alcohol and central nervous system-active substances
  - must not be used in children between 6 months and 2 years old, other than in exceptional cases for anticonvulsant treatment
- Please refer to the summary of product characteristics (SPC), which can be found at: **www.medicines.org.uk/emc**

Precautions

- In patients with anxiety associated with depression, Perizam must be only used in conjunction with adequate concomitant treatment, as use of Perizam alone can precipitate suicide in such patients[1,2]
- Caution must be taken when switching between clobazam products; the mean C_{max} on single dose administration of the oral suspension is higher than that for the tablet formulation; this may increase risk of respiratory depression and sedation on switching to Perizam from tablets[1,2]
- The following may occur with clobazam and therefore caution is advised: amnesia, muscle weakness, dependence, and withdrawal symptoms upon abrupt termination; respiratory depression in patients with respiratory insufficiency; development of tolerance, psychiatric, and paradoxical reactions; suicidal ideation and behaviour[1,2]
- Dose reduction may be necessary in patients with renal or hepatic impairment and in elderly patients[1,2]
- Please refer to the SPC, which can be found at **www.medicines.org.uk/emc**

Common side-effects

- Please refer to the SPC, which can be found at **www.medicines.org.uk/emc**

References

1. Rosemont Pharmaceuticals Limited. *Perizam 1mg/ml oral suspension—summary of product characteristics*. February 2016. www.medicines.org.uk/emc/medicine/30522
2. Rosemont Pharmaceuticals Limited. *Perizam 2mg/ml oral suspension—summary of product characteristics*. February 2016. www.medicines.org.uk/emc/medicine/30521
3. NICE. *Epilepsies: diagnosis and management*. Clinical Guideline 137. NICE, 2012. Available at: www.nice.org.uk/cg137
4. Strachen I, Greener M. Medication-related swallowing difficulties may be more common than we realise. *Pharmacy in Practice* 2005; **15** (9): 411–414.

Perizam 1mg/ml Oral Suspension & Perizam 2mg/ml Oral Suspension

Abbreviated Prescribing Information: Perizam 1mg/ml and 2mg/ml Oral Suspensions **Consult Summary of Product Characteristics before prescribing. Presentation:** Off-white suspension containing 1mg and 2mg of clobazam per ml respectively. **Therapeutic Indications:** Anxiety that is severe, disabling or subjecting individual to unacceptable distress. Short term symptomatic management of hyperarousal & agitation in Schizophrenia. Adjunctive therapy in epilepsy in adults or children >2 Yrs. **Posology:** Anxiety: 20-30mg daily in adults, up to maximum of 60mg daily in severe anxiety. In elderly, doses of 10-20mg daily may be used. Epilepsy: Starting dose of 20-30mg/day, increasing as necessary up to maximum of 60mg daily. Low initial doses and gradual dose increments under careful observation. **Paediatric population:** Epilepsy: Normally started at 5mg daily, maintenance dose of 0.3-1 mg/kg body weight is usually sufficient. **Contra-indications:** Hypersensitivity to benzodiazepines or any of the excipients of Perizam. Drug or alcohol dependence. Myasthenia gravis. Severe respiratory insufficiency. Sleep apnoea syndrome. Severe hepatic insufficiencies. During first trimester of pregnancy. Breast-feeding women. Acute intoxication with alcohol and CNS-active substances. Must not be used in children between 6 months and 2 years old, other than in exceptional cases for anticonvulsant treatment. **Excipient warnings:** The product contains sodium. Patients with rare hereditary problems of fructose intolerance should not take this medicine. The product contains parahydroxybenzoates which may cause an allergic reaction. **Precautions for use**: In patients with anxiety associated with depression, Perizam must be only used in conjunction with adequate concomitant treatment, as use of Perizam alone can precipitate suicide in such patients. Caution must be taken when switching between clobazam products; the mean C_{max} on single dose administration is higher than that for the tablet formulation. This may increase risk of respiratory depression and sedation on switching to Perizam from tablets. The following may occur with Perizam and therefore caution is advised: amnesia, muscle weakness, dependence and withdrawal symptoms upon abrupt termination, respiratory depression in patients with respiratory insufficiency, development of tolerance, psychiatric and paradoxical reactions, suicidal ideation and behaviour. Dose reduction may be necessary in patients with renal or hepatic impairment and in elderly patients. **Drug interactions:** Alcohol. Central nervous system depressant drugs including antipsychotics, neuroleptics, hypnotics, anxiolytics/sedatives, antidepressant agents, narcotic analgesics, anticonvulsants, anaesthetics and sedative antihistamines. MAOIs. Narcotic analgesics. Muscle relaxants. CYP 2C19 inhibitors and CYP 2D6 substrates. **Pregnancy and Lactation:** Perizam must not be used in the first trimester of pregnancy. Use should be discontinued in women intending to become pregnant or suspect they are pregnant. Use before or during childbirth can result in respiratory depression and symptoms of "floppy infant syndrome". Should only be used if there are compelling indications in later stages of pregnancy, however, the infant may develop dependence and withdrawal symptoms in the post natal period. Perizam must not be given to breast feeding mothers. **Effects on Ability to Drive and Use Machines:** This product has major influence on the ability to drive and use machines, as it can impair cognitive function. Do not drive until you know how the medicine affects you. **Undesirable Effects:** Uncommon (<1/100): sedation, fatigue, drowsiness and sleepiness, slowing of reaction time, dizziness, headache, ataxia, and confusion. Rare (<1/1000): restlessness and muscle weakness. Very rare (<1/10,000): impairment of consciousness, respiratory disorders (particularly in elderly). Frequency not known: dryness of mouth, constipation, loss of appetite, nausea, fine tremor, slowed/distinct speech, unsteadiness of gait, visual disorders, weight gain, loss of libido, unmasking of pre-existing depression, respiratory depression, anterograde amnesia, inappropriate behaviour, tolerance and dependence, paradoxical reactions, cutaneous reactions, Stevens-Johnson syndrome, Toxic Epidermal Necrosis. **Overdose:** Should not present a threat to life unless combined with other CNS depressants. Management includes inducement of vomiting if the patient is conscious, or gastric lavage with the airway protected if the patient is unconscious. Activated charcoal may be given to reduce absorption. Consideration should be given to the use of flumazenil as a benzodiazepine antagonist. **Shelf Life and storage:** Unopened: 3 years. Once opened: Use within 28 days. Do not store above 25°C. **Legal Category:** POM. **Pack Size and NHS Price:** 1mg/ml,150ml - £90.00, 2mg/ml 150ml - £95.00. **Marketing Authorisation Holder:** Rosemont Pharmaceuticals Ltd, Rosemont House, Yorkdale Industrial Park, Braithwaite Street, Leeds, LS11 9XE, UK. **Date of Preparation**: April 2016.

Information about adverse event reporting can be found at https://yellowcard.mhra.gov.uk/

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