Rosemont Excipients Handbook

Paediatric Liquid Medicines

Rosemont®

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LEADERS IN LIQUID MEDICINES

At Rosemont, our mission is to improve the health, quality of life and well-being of people through the development, manufacture and supply of high-quality liquid medicines.

With more than 50 years' experience and a range of over 130 products, you can rely on Rosemont - we are the specialists in liquid medicines. Rosemont leads the market with an unrivalled 70 licensed products, manufacturing in excess of 4 million bottles a year. All of our medicines, both licensed and 'Specials' are developed in accordance with the European Commission and Evaluations of the Joint FAO/WHO Expert Committee on Food Additives (JECFA) safety guidelines and are produced to good manufacturing practice (GMP standards).

We listen to our customers and respond to their needs through a continual programme of new product development and to ensure that we create formulations that patients find palatable as well as effective, we run rigorous taste trials for all new products.

We are committed to the pursuit of excellence in everything we do and invest heavily in research and development. At our advanced laboratories in Leeds (UK) our extensive team of scientists investigate ways to make our liquid medicines even better.

The oral route of administration is commonly used for dosing medicinal products to paediatric patients across a wide age range, but a major concern is at what age children can safely swallow solid oral dosage forms[1].

Solid dose medications can present significant problems for young children and adolescents who have difficulty swallowing. The age at which children can swallow intact tablets or capsules, is highly dependent on the individual and the training and support that they receive from healthcare professionals and caregivers[1].

Liquid formulations are most appropriate for younger paediatric patients (birth to 8 years) who are unable to swallow capsules or tablets. In particular within the pre-school population, liquids are the dosage form of choice[1].

For paediatric patients, palatability is of even greater significance than with adults, and key in aiding compliance[2].

We use flavourings to mask the taste of drug substances. These are specifically selected dependent on the properties of the drug substance in order to ensure better palatability.

Colourings were historically added to products for reasons such as differentiation between strengths. We no longer add colourings when developing new products as we aim to remove unnecessary excipients of no therapeutic value.

Another key objective is to formulate our medicines to be sugar free. Sugar content within liquid medicines is a concern often voiced by parents and healthcare professionals[3]. For many children, sugar in continuously administered liquid medicines is a factor in dental caries, gingivitis and periodontal disease[4].

We use excipients in our liquid medicines to optimise the formulation, to ensure palatability, improve shelf-life and/or aid the manufacturing processes.

All of the excipients used in our medicines are carefully chosen to ensure they are appropriate for the age group and to minimise the risk of adverse events.

The roles of excipients

The excipients we use in our medicines can be divided into functional classes dependent on their composition and the role they play in the final formulation. We conduct extensive studies to choose the optimal excipients for our liquid medicines.

A diluent	most commonly purified water
Solubility	pH control - surfactants, solvents
Stability	pH control – buffers, anti-oxidants, chelating agents
Physical stability	suspending agents
Acceptability	flavours, thickening agents, sweeteners
Preservation	anti-microbial, anti-fungals (sometimes products are self-preserving)

Table 1

Certain excipients such as propylene glycol, benzyl alcohol, surfactants and ethanol can be undesirable in medicines for children of certain ages[5].

However, appropriate substitutes for these excipients are yet to be identified and approved for use in paediatric medicines[5]. Therefore, we only use such excipients at the lowest possible levels, when absolutely necessary and when no acceptable alternative is available.

All of our medicines are age-indicated and all excipients are clearly labelled to comply with European Commission guidelines and labelling requirements[6].

Some healthcare professionals and parents may be concerned about excipients found in some liquid medicine preparations. These include methyl, ethyl or propyl parahydroxybenzoate (parabens), propylene glycol and ethanol. We ensure that our use of such excipients is kept to a minimum and proplyene glycol is completely avoided wherever possible. When any one of these excipients is used, it is always within the European Medicines Agency (EMA) recommended levels[7].

Table 2 opposite shows excipients which commonly feature in liquid medicines and their related function within the formulation.

EXCIPIENT	FUNCTION	PUBLISHED SAFE LEVEL	OTHER COMMENTS
Methyl, ethyl, propyl parahydroxybenzoates	Anti-microbial preservatives	Daily intake up to: methyl, ethyl – 10mg/kg body weight[8] propyl – 2mg/kg body weight[9]	May cause allergic reactions[6]. Short chain parahydroxybenzoates are perceived to be safer therefore we try to use these over the longer chain molecules
Benzoic acid	Anti-microbial preservative	Daily intake up to 5mg/kg body weight[8]	Benzoic acid is not commonly used within our products. A warning is required for use in newborns[6]
Ethanol	Solvent and/or anti-microbial preservative	15mg/kg body weight per dose[6]	We avoid ethanol for any new formulations. Inclusion must be justified especially in paediatric/geriatric use. Where the level of Ethanol is less than 15mg/kg body weight per dose, a statement in the SPC/ Leaflet is added to provide reassurance to parents for use[6]
Propylene glycol	Solvent/ preservative	Daily intake up to 25mg/kg body weight[8]	Safety warnings are dependent on age group[6]. We aim to avoid the use of this in any new formulation
Glucose	Sweetener	Regarded as safe for use[8]	Not suitable for patients with a sugar or fructose intolerance[6]
Saccharin	Artificial sweetener	Daily intake up to 5mg/kg body weight[8]	
Sorbitol	Bulk sweetener	Regarded as safe for use[8]	Not suitable for patients with a fructose intolerance[6]
Liquid maltitol	Bulk sweetener/ stabiliser	Regarded as safe for use[8]	Not suitable for patients with a fructose intolerance[6]
Sucralose	Artificial sweetener	Daily intake up to 0-15mg/kg body weight[8]	

Table 2

Moving forward, our approach is to avoid excipients of concern wherever possible, to ensure that our products are suitable for the widest range of patient groups.

The following pages detail just some of our commonly used liquid medicines licensed for use within the paediatric population. For full details on our product portfolio, please visit

www.rosemontpharma.com

Please refer to the full Summary of Product Characteristics (SmPC) before prescribing.

Anti-epileptic

Perizam 1mg/ml and 2mg/ml, Clobazam

PRODUCT DESCRIPTION

Perizam Oral Suspension, Clobazam

STRENGTH

1mg/ml and 2mg/ml

PACK SIZE

150ml

AGE RANGE INDICATIONS

Children over 2 years old

INDICATIONS FOR PAEDIATRICS

Perizam may be used as adjunctive therapy in epilepsy in children over 2 years, 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).

EXCIPIENTS

- Aluminium magnesium silicate
- Citric acid monohydrate
- Disodium hydrogen phosphate dihydrate
- Simethicone emulsion (including benzoic acid†)
- Sucralose
- Polysorbate 80
- Masking flavour (contains propylene glycol*)
- Raspberry flavour (contains propylene glycol*)
- Xanthan gum
- Sodium methyl parahydroxybenzoate
- Sodium propyl parahydroxybenzoate
- Liquid maltitol
- Purified water

† Low levels of benzoic acid. Total level 0.001mg/ml.

* Low levels of propylene glycol found in flavouring. Total level 6.21mg/ml.

Prescribing Information appears on page 14.

Anti-epileptic

Gabapentin Rosemont 50mg/ml

PRODUCT DESCRIPTION

Gabapentin Rosemont Oral Solution

STRENGTH

50mg/ml

PACK SIZE

150ml

AGE RANGE INDICATIONS

Adjunctive therapy: Children aged 6 years and above.

Monotherapy: Adolescents aged 12 years and above.

INDICATIONS FOR PAEDIATRICS

Gabapentin is indicated as adjunctive therapy in the treatment of partial seizures with and without secondary generalization in children aged 6 years and above.

Gabapentin is indicated as monotherapy in the treatment of partial seizures with and without secondary generalization in adolescents aged 12 years and above.

EXCIPIENTS

- Acesulfame potassium
- Saccharin sodium
- Propylene glycol*
- Methyl parahydroxybenzoate
- Ethyl parahydroxybenzoate
- Carmellose sodium
- Aniseed flavour (containing flavouring preparations, isopropyl alcohol and water)
- Purified water

* Propylene glycol guidance requires warnings on products indicated for children 5 years and below[7]. This product is indicated for use in 6 years and above. Total level 35mg/ml.

Prescribing Information appears on page 14.

Anti-epileptic

Topiramate Rosemont 10mg/ml and 20mg/ml

PRODUCT DESCRIPTION

Topiramate Rosemont Oral Suspension

STRENGTH

10mg/ml and 20mg/ml

PACK SIZE

10mg available in 150ml

20mg available in 280ml

AGE RANGE INDICATIONS

Monotherapy: 6 years and above

Adjunctive therapy: 2 years and above

INDICATIONS FOR PAEDIATRICS

Monotherapy in children over 6 years of age with partial seizures with or without secondary generalised seizures, and primary generalised tonic-clonic seizures.

Adjunctive therapy in children aged 2 years and above with partial onset seizures with or without secondary generalisation or primary generalised tonic-clonic seizures and for the treatment of seizures associated with Lennox-Gastaut syndrome.

EXCIPIENTS

- Citric acid monohydrate
- Disodium hydrogen phosphate dihydrate
- Simethicone emulsion (including benzoic acid*)
- Sucralose
- Blackcurrant flavour
- Sodium methyl parahydroxybenzoate
- Sodium ethyl parahydroxybenzoate
- Dilute hydrochloric acid
- Xanthan gum
- Glycerol
- Purified water

* Low levels of benzoic acid. Total level 0.001mg/ml.

Prescribing Information appears on page 15.

Corticosteroid

Dexsol 2mg/5ml, Dexamethasone

PRODUCT DESCRIPTION

Dexsol Oral Solution, Dexamethasone

STRENGTH

2mg/5ml

PACK SIZE

75ml and 150ml

AGE RANGE INDICATIONS

Suitable for use in the paediatric population

INDICATIONS FOR PAEDIATRICS

Dexamethasone is a corticosteroid. It is designed for use in certain endocrine and non-endocrine disorders, in certain cases of cerebral oedema and for diagnostic testing of adrenocortical hyperfunction.

Childhood Croup: Heterogeneous group of illnesses affecting the larynx, trachea and bronchi. Laryngotracheitis, laryngotracheobronchitis, laryngotracheobronchopneumonitis and spasmodic croup are included in the croup syndrome

Children: Dosage should be limited to a single dose on alternate days.

Childhood Croup: A single dose is recommended.

EXCIPIENTS

- Benzoic acid†
- Propylene glycol*
- Citric acid monohydrate
- Liquid maltitol
- Garden mint flavour (containing isopropanol and propylene glycol*)
- Sorbitol solution 70%
- Sodium citrate
- Purified water

† Total Level of benzoic acid 5mg/5ml.

* Dosing on alternate days limits exposure to propylene glycol. Total level 450.6mg/5ml.

Prescribing Information appears on page 16.

Cytotoxic

Methotrexate 2mg/ml

PRODUCT DESCRIPTION

Methotrexate Oral Solution

STRENGTH

2mg/ml

PACK SIZE

35ml and 65ml

AGE RANGE INDICATIONS

Oncological indications: Methotrexate should be used with caution in children.

Non oncological indications: Polyarthritic forms of juvenile idiopathic arthritis (JIA) in children over 3 years.

INDICATIONS FOR PAEDIATRICS

Oncological:- the maintenance treatment of Acute Lymphocytic Leukemia (ALL) in children and treatment of malignant trophoblastic tumours.

Other:- Polyarthritic forms of active, severe JIA in adolescents and children aged 3 years and over when the response to non-steroidal anti-inflammatory drugs (NSAIDS) has been inadequate.

EXCIPIENTS

- Sodium methyl parahydroxybenzoate
- Sodium ethyl parahydroxybenzoate
- Disodium hydrogen phosphate dihydrate
- Citric acid monohydrate
- Sucralose
- Raspberry flavour (containing propylene glycol* and sulphites)
- Purified water

* Low level of propylene glycol found in flavouring. Total level 1.93mg/ml.

Prescribing Information appears on page 18.

Anticholinergic

Glycopyrronium Oral Solution 1mg/5ml

PRODUCT DESCRIPTION

Glycopyrronium Oral Solution

STRENGTH

1mg/5ml

PACK SIZE

150ml

INDICATIONS

Symptomatic treatment of severe sialorrhea (chronic pathological drooling) in children and adolescents aged 3 years and older with chronic neurological disorders

EXCIPIENTS

- Citric acid monohydrate (E330)
- Sodium citrate (E331)
- Sodium benzoate (E211)
- Strawberry flavour
- Liquid sorbitol (E420)
- Glycerol (E422)
- Purified water

Prescribing Information appears on page 19.

Proton Pump Inhibitor

Omeprazole, Powder for Oral Suspension

1mg/ml, 2mg/ml and 4mg/ml

PRODUCT DESCRIPTION

Omeprazole, Powder for Oral Suspension

STRENGTH

1mg/ml, 2mg/ml and 4mg/ml

PACK SIZE

Each bottle contains 90ml of oral suspension of which at least 75ml is intended for dosing

INDICATIONS FOR PAEDIATRICS

1mg/ml indicated for infants 1-12 months

- Treatment of reflux oesophagitis
- Symptomatic treatment of heartburn and acid regurgitation in gastro-oesophageal reflux disease

2mg/ml and 4mg/ml indicated for infants over 1 month of age

- Treatment of reflux oesophagitis
- Symptomatic treatment of heartburn and acid regurgitation in gastro-oesophageal reflux disease

2mg/ml and 4mg/ml for children over 4 years of age and adolescents

- In combination with antibiotics in treatment of duodenal ulcer caused by *H-pylori*

Omeprazole 2mg/ml Oral Suspension is suitable for doses of ≤15mg. For doses of 20mg or greater, Omeprazole 4mg/ml Oral Suspension is suitable

The only range of liquid omeprazole products, licensed from one month

EXCIPIENTS

- Sodium hydrogen carbonate (E500)
- Potassium hydrogen carbonate (E501)
- Sodium alginate (E401)
- Maltitol (E965)
- Mannitol (E421)
- Sucralose (E955)
- Xanthan gum (E415)
- Natural Mint Flavouring containing Gum Arabic / Acacia Gum (E414), pulegone
- Titanium dioxide (E171)
- Sodium benzoate (E211)
- Sodium methyl parahydroxybenzoate (E219)
- 2mg/ml also contains Natural Vanilla Flavouring containing Maltodextrin (Maize), silicon dioxide (E551) and vegetable oil fats to aid palatability for infants.
- 1mg/ml contains Natural Strawberry Flavouring containing Maltodextrin (Maize), Starch Modified Corn (E1450) and Acetic Acid (E260)

Prescribing Information appears on page 20.

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:** Short-term symptomatic treatment of anxiety that is severe, disabling or subjecting the individual to unacceptable distress. Short term symptomatic management of hyperarousal & agitation in Schizophrenia. Adjunctive therapy in epilepsy in adults or children >2 Yrs. Posology and Method of Administration: 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 Adults: Starting dose of 20-30mg/day, increasing as necessary up to maximum of 60mg daily. Elderly: Low initial doses and gradual dose increments under careful observation. Hepatic and renal failure: low initial doses and gradual dose increments under careful observation, regardless of the age group. **Paediatric population:** Epilepsy: Normally started at 5mg daily or 0.1 mg/kg/day for younger patients and increased by step of 0.1 to 0.2 mg/kg/day at 7 days intervals, maintenance dose of 0.3-1 mg/kg body weight is usually sufficient. Oral use. Perizam can be taken with or without food. Shake the bottle thoroughly before use. **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. 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. **Special Warnings and Precautions for use:** In patients with anxiety associated with depression, Perizam must be only used in conjunction with adequate concomitant treatment. Caution must be taken when switching between clobazam products. The duration of treatment should be as short as possible. The following may occur with Perizam and therefore caution is advised: amnesia, psychiatric and 'paradoxical' reactions, serious skin reactions, respiratory depression in patients with respiratory insufficiency, muscle weakness, depression and personality disorder, dependence and withdrawal symptoms upon abrupt termination, development of tolerance, psychiatric and paradoxical reactions, suicidal ideation, and behaviour. Dose reduction may be necessary in patients with renal, hepatic impairment, elderly patients and in patients who are poor metabolisers of CYP2C19. Patient should abstain from drinking alcohol. **Excipient warnings:** Sodium Methyl parahydroxybenzoate, Sodium Propyl parahydroxybenzoate, Liquid Maltitol and Propylene Glycol. **Any warning from the MC, CHM CSM or MHRA. Black Triangle notice:** Not applicable. **Legal Category:** Prescription only medicine. **Undesirable Effects:** *Very common:* somnolence, fatigue. *Common:* decreased appetite, irritability, aggression, restlessness, depression, drug tolerance, agitation, sedation, dizziness, disturbance in attention, slow speech/dysarthria/speech disorder, headache, tremor, ataxia, dry mouth, nausea, constipation. *Uncommon:* abnormal behaviour, confusional state, anxiety, delusion, nightmare, loss of libido, emotional poverty, amnesia, memory impairment, anterograde amnesia, diplopia, rash, weight increased, fall. *Not known:* dependence, initial insomnia, anger, hallucination, psychotic disorder, poor sleep quality, suicidal ideation, cognitive disorder, altered state of consciousness, nystagmus, gait disturbance, respiratory depression, respiratory failure, photosensitivity reaction, urticaria, Stevens-Johnson syndrome, toxic epidermal necrolysis, muscle spasms, muscle weakness, slow response to stimuli, hypothermia. **Pack Size and NHS Price:** 1mg/ml - 150ml - £90.00, 2mg/ml – 150ml - £95.00. **Marketing Authorisation Number:** 1mg/ml PL00427/0227 and 2mg/ml PL00427/0228. **Marketing Authorisation Holder:** Rosemont Pharmaceuticals Ltd, Rosemont House, Yorkdale Industrial Park, Braithwaite Street, Leeds, LS11 9XE, UK. **Date of Preparation:** December 2022.

Adverse events should be reported.
Reporting forms and information can be found at www.mhra.gov.uk/yellowcard
Adverse events should also be reported to Rosemont Pharmaceuticals Ltd on 0113 244 1400.

Abbreviated Prescribing Information: Gabapentin Rosemont 50mg/mL Oral Solution Consult Summary of Product Characteristics before prescribing. Presentation: A clear, colourless oral solution. Each 1 mL containing 50 mg Gabapentin. **Therapeutic Indications:** Gabapentin is indicated as adjunctive therapy in the treatment of partial seizures with and without secondary generalization in adults and children aged 6 years and above. Gabapentin is also indicated for treatment of peripheral neuropathic pain such as painful diabetic neuropathy and post-herpetic neuralgia in adults. **Posology and Method of Administration:** For epilepsy: Adults and young people over 12 years old the usual starting dose is between 300mg and 900mg a day (6 to 18mL). Based on individual patient response and tolerability the dose can be further increased. The maximum dose is 3,600mg a day (72 mL). The medicine can be taken in three separate doses and the maximum time interval between the doses should not exceed 12 hours to prevent breakthrough convulsions. For children aged 6 years old and above, the effective dose of gabapentin is 25 to 35 mg/kg/day. It is usually given in three separate doses and the maximum time interval between doses should not exceed 12 hours. Gabapentin is not recommended for use in children under 6 years old. For peripheral neuropathic pain in adults, the usual starting dose is between 300mg and 900mg a day (6 to 18 mL) and the maximum recommended dose in a day is 3,600 mg (72 mL). The medicine is taken in three separate doses: once in the morning, once in the afternoon and once in the evening. A different dosing schedule and/or dose may be prescribed by doctor for elderly patients and patients with kidney related problems or patients undergoing haemodialysis. **Paediatric population:** Gabapentin is not recommended for use in children under 6 years old. **Contra-indications:** Hypersensitivity to the active substance or to any of the excipients. **Special Warnings and Precautions for use:** Severe, life-threatening, systemic hypersensitivity reactions such as Drug rash with eosinophilia and systemic symptoms (DRESS) have been reported in patients taking antiepileptic drugs including gabapentin. Gabapentin should be discontinued if an alternative etiology for the signs or symptoms cannot be established. **Anaphylaxis:** Gabapentin can cause anaphylaxis. Signs and symptoms in reported cases have included difficulty breathing, swelling of the lips, throat and tongue, and hypotension requiring emergency treatment. Patients should be instructed to discontinue gabapentin and seek immediate medical care should they experience signs or symptoms of anaphylaxis. **Suicidal ideation and behaviour:** Cases of

suicidal ideation and behaviour have been observed in patients treated with gabapentin in the post-marketing experience. Discontinuation of gabapentin treatment should be considered in case of suicidal ideation and behaviour. **Acute pancreatitis:** If a patient develops acute pancreatitis under treatment with gabapentin, discontinuation of gabapentin should be considered. **Seizures:** Although there is no evidence of rebound seizures with gabapentin, abrupt withdrawal of anticonvulsant agents in epileptic patients may precipitate status epilepticus. Gabapentin treatment has been associated with dizziness and somnolence, which could increase the occurrence of accidental injury (fall). **Concomitant use with opioids:** Caution is advised when prescribing gabapentin concomitantly with opioids due to risk of CNS depression. **Respiratory depression:** Gabapentin has been associated with severe respiratory depression. Caution should be exercised when gabapentin is used in elderly patients, as somnolence, peripheral oedema, and asthenia occurred in higher percentage in patients aged 65 years or above with neuropathic pain, than in younger patients. **Abuse and Dependence:** Cases of abuse and dependence have been reported in the post-marketing database. **Any warning from the MC, CHM CSM or MHRA. Black Triangle notice:** Not applicable. **Legal Category:** POM. **Undesirable Effects: Very common and Common reactions are presented below and refer the SmPC for details of other adverse reactions:** Viral infection, Pneumonia, respiratory infection, urinary tract infection, infection, otitis media, leucopenia, anorexia, increased appetite, hostility, confusion and emotional lability, depression, anxiety, nervousness, thinking abnormal, somnolence, dizziness, ataxia, convulsions, hyperkinesias, dysarthria, amnesia, tremor, insomnia, headache, sensations such as paresthesia, hypaesthesia, coordination abnormal, nystagmus, increased, decreased, or absent reflexes, Visual disturbances such as amblyopia, diplopia, 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 most often described as bruises resulting from physical trauma, rash, pruritus, acne, arthralgia, myalgia, back pain, twitching, impotence, fatigue, fever, peripheral oedema, abnormal gait, asthenia, pain, malaise, flu syndrome, WBC (white blood cell count) decreased, weight gain, accidental injury, fracture and abrasion. **Pack Size and NHS Price:** 150 mL - £67.29. **Marketing Authorisation Number: UK:** PL 00427/0155 **and Ireland:** PA23081/010/001. **Marketing Authorisation Holder:** Rosemont Pharmaceuticals Ltd. (UK) and TAW PHARMA (IRELAND) LTD. **Date of Preparation:** November 2023.

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Reporting forms and information can be found at www.mhra.gov.uk/yellowcard
Adverse events should also be reported to Rosemont Pharmaceuticals Ltd on 0113 244 1400.

Abbreviated Prescribing Information: Topiramate Rosemont 10mg/ml and 20mg/ml Oral Suspension Consult Summary of Product Characteristics before prescribing. Presentation: Colourless or off-white suspension. Each 1ml contains 10mg of topiramate for the 10mg/ml strength and 20 mg for the 20mg/ml strength. **Therapeutic Indications:** Topiramate is indicated to treat seizures in adults and children over age 6 and to prevent migraine headaches in adults. Topiramate can also be used with other medicines to treat seizures in adults and children aged 2 years and above. **Posology and Method of Administration:** It is recommended that therapy be initiated at a low dose followed by titration to an effective dose. Dose and titration rate should be guided by clinical response. If low doses are required, the 10mg/ml strength product is the most suitable presentation. If high doses are required, the 20mg/ml strength product is the most suitable presentation. For Adults: Titration should begin at 25 mg nightly for 1 week. The dosage should then be increased at 1- or 2-week intervals by increments of 25 or 50 mg/day, administered in two divided doses. If the patient is unable to tolerate the titration regimen, smaller increments or longer intervals between increments can be used. **Paediatric population:** Dose and titration rate in children should be guided by clinical outcome. Treatment of children over 6 years of age should begin at 0.5 to 1 mg/kg nightly for the first week. The dosage should then be increased at 1 or 2 week intervals by increments of 0.5 to 1 mg/kg/day, administered in two divided doses. If the child is unable to tolerate the titration regimen, smaller increments or longer intervals between dose increments can be used. *For children aged 2 years and above:* The recommended total daily dose of topiramate as adjunctive therapy is approximately 5 to 9 mg/kg/day in two divided doses. Titration should begin at 25 mg (or less, based on a range of 1 to 3 mg/kg/day) nightly for the first week. The dosage should then be increased at 1- or 2-week intervals by increments of 1 to 3 mg/kg/day (administered in two divided doses), to achieve optimal clinical response. **Contra-indications:** Hypersensitivity to the active substance or to any of the excipients listed. Migraine prophylaxis in pregnancy and in women of childbearing potential if not using a highly effective method of contraception. **Special Warnings and Precautions for use:** Topiramate may cause fetal harm and fetal growth restriction (small for gestational age and low birth weight) when administered to a pregnant woman. Before the initiation of treatment with topiramate in a woman of childbearing potential, pregnancy testing should be performed, and a highly effective contraceptive method advised and the patient should be fully informed of the risks related to the use of topiramate during pregnancy. Decreased sweating and hyperthermia (rise in body temperature) may occur especially in young children exposed to high ambient temperature. An increased incidence of mood disturbances and depression has been observed during topiramate treatment. Suicidal ideation and behaviour have been reported in patients treated with antiepileptic agents in several indications. Patients therefore should be monitored for signs of suicidal ideation and behaviour and appropriate treatment should be considered. Serious skin reactions (Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN)) have been reported in patients receiving topiramate. It is recommended that patients be informed about the signs of serious skin reactions and use of topiramate should be discontinued. In patients with impaired renal function (CLCR ≤70mL/min) topiramate should be administered with caution as the plasma and renal clearance of topiramate are decreased. In hepatically impaired patients, topiramate should be administered with caution as the clearance of topiramate may be decreased. A syndrome consisting of acute myopia associated with secondary angle closure glaucoma has been reported in patients receiving topiramate. Treatment includes discontinuation of topiramate,

as rapidly as possible in the judgment of the treating physician, and appropriate measures to reduce intraocular pressure. Visual field defects have been reported in patients receiving topiramate independent of elevated intraocular pressure. If visual field defects occur at any time during topiramate treatment, consideration should be given to discontinuing the drug.Hyperchloremic, non-anion gap, metabolic acidosis is associated with topiramate treatment. Chronic metabolic acidosis increases the risk of renal stone formation and may potentially lead to osteopenia. Topiramate should be used with caution in patients with conditions or treatments that represent a risk factor for the appearance of metabolic acidosis. There have been reports in the literature of impairment of cognitive function in adults on topiramate therapy which required reduction in dosage or discontinuation of treatment. Hyperammonemia with or without encephalopathy has been reported with topiramate treatment. The risk for hyperammonemia with topiramate appears dose related. Hyperammonemia has been reported more frequently when topiramate is used concomitantly with valproic acid. Some patients may experience weight loss whilst on treatment with topiramate. It is recommended that patients on topiramate treatment should be monitored for weight loss. **Any warning from the MC, CHM CSM or MHRA. Black Triangle notice:** Not applicable. **Legal Category:** Prescription only medicine. **Undesirable effects:** Very common and common reactions are presented below and refer the SmPC for details of other adverse reactions: Nasopharyngitis, Depression, Paraesthesia, Somnolence, Dizziness, Nausea, Diarrhoea, Fatigue, Weight decreased, Anaemia, Hypersensitivity, Anorexia, decreased appetite, Bradyphrenia, Insomnia, Expressive language disorder, Anxiety, Confusional state, Disorientation, Aggression, Mood altered, Agitation, Mood swings, Depressed mood, Anger, Abnormal behaviour, Disturbance in attention, Memory impairment, Amnesia, Cognitive disorder, Mental impairment, Psychomotor skills impaired, Convulsion, Coordination abnormal, Tremor, lethargy, Hypoaesthesia, Nystagmus, Dysgeusia, Balance disorder, Dysarthria, Intention tremor, SLedation, Vision blurred, Diplopia, Visual disturbance, Vertigo, Tinnitus, Ear pain, Dyspnoea, Epistaxis, Nasal congestion, Rhinorrhoea, Cough*, Vomiting, Constipation, Abdominal pain upper, Dyspepsia, Abdominal pain, Dry mouth, Stomach discomfort, Paraesthesia oral, Gastritis, Abdominal discomfort, Alopecia, Rash, Pruritus, Arthralgia, Muscle spasms, Myalgia, Muscle twitching, Muscular weakness, Musculoskeletal chest pain, Nephrolithiasis, Pollakiuria, Dysuria, Nephrocalcinosis, Pyrexia, Asthenia, Irritability, Gait disturbance, Feeling abnormal, Malaise, and Weight increased. **Pack Size and NHS Price:** 150ml 10mg/ml £228.96 or 280ml 20mg/ml £330.72. **Marketing Authorisation Number:** PL 00427/0245 and PL 00427/0246. **Marketing Authorisation Holder:** Rosemont Pharmaceuticals Ltd, Rosemont House, Yorkdale Industrial Park, Braithwaite Street, Leeds, LS11 9XE, UK. **Date of Preparation:** January-2023.

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Reporting forms and information can be found at www.mhra.gov.uk/yellowcard
Adverse events should also be reported to Rosemont Pharmaceuticals Ltd on 0113 244 1400.

Abbreviated Prescribing Information: DEXSOL 2mg/5ml Oral Solution. Consult Summary of Product Characteristics before prescribing. Presentation: A colourless to faint yellow solution with an odour of mint containing 2mg Dexamethasone as dexamethasone sodium phosphate in each 5ml. **Therapeutic Indications:** Dexamethasone is a corticosteroid. It is designed for use in certain cases of cerebral oedema and certain endocrine and non-endocrine disorders; Allergy and anaphylaxis; Arteritis collagenosis; Haemotological disorders; Gastroenterological disorders; Muscular disorders; Neurological disorders; Ocular disorders; Renal disorders; Pulmonary disorders; Rheumatic disorders; Skin disorders; Oncological disorders; Intense allergic reactions; as immunosuppressant in organ transplantation; as an adjuvant in the prevention of nausea and vomiting and in the treatment of cancer with oncolytics that have a serious emetic effect; Heterogeneous group of illnesses affecting the larynx, trachea and bronchi, and Covid-19: in adult and adolescent patients who require supplemental oxygen therapy. **Posology and Method of Administration:** Adults: The dosage should be titrated to the individual response and the nature of the disease. The lowest effective possible dosage should be used. The initial dosage varies from 0.5 – 9mg a day. In more severe diseases, doses higher than 9mg may be required. If satisfactory response does not occur after a reasonable time, discontinue treatment and transfer the patient to another therapy. Chronic dosage should preferably not exceed 1.5mg daily. If the drug is to be stopped after more than a few days of treatment, it should be withdrawn gradually. If a dose less then 5ml is required, an oral dosing device should be employed. **Paediatric:** Dosage should be limited to a single dose on alternate days. **Childhood Croup:** A single dose of 0.15mg/kg is recommended. A second dose may be administered after 12 hours, if considered necessary by the treating physician. However, no more than a maximum of 10mg is recommended. Elderly: Care should be taken. For the treatment of Covid-19, 6 mg orally, once a day for up to 10 days are recommended for adults and paediatric patients (adolescents aged 12 years and older with body weight at least 40kg). Oral use, suitable for administration via nasogastric (NG) or percutaneous endoscopic gastrostomy tubes (PEG). **Contraindications**: Hypersensitivity to dexamethasone or any of the excipients. Systemic infection unless specific anti-infective therapy is employed. Systemic fungal infections. Stomach or duodenal ulcer. Infection with tropical worms. Avoid live vaccines in patients receiving immuno suppressive doses. In general, no contraindications apply in conditions where the use of glucocorticoids may be lifesaving. **Special Warnings and Precautions for use:** Corticosteroids should only be used in systemic fungal infections to control drug reactions due to amphotericin. Suppression of the inflammatory response and immune function increases the susceptibility to infections and their severity. The clinical presentation may be atypical. Appropriate anti-microbial therapy should accompany glucocorticoid therapy when necessary. There may be decreased resistance and inability to localise infection in patients on corticosteroids. Treatment of acute respiratory distress syndrome with corticosteroids should be initiated within the first two weeks of onset. Chickenpox and measles are of particular concern. Exposed patients should be advised to seek medical advice without delay. Corticosteroids may activate latent infections or exacerbate active disease due to pathogen. Should not be used in cerebral malaria. Prolonged use may produce

subcapsular cataracts, glaucoma with possible damage to the optic nerves, and may enhance the establishment of secondary ocular infections due to fungi or viruses. Salt restriction and potassium supplementation may be necessary. Calcium excretion will be increased. Adrenal cortical atrophy develops during prolonged therapy. Withdrawal after prolonged therapy must always be gradual. During prolonged therapy, any intercurrent illness, trauma, stress or surgical procedure will require a temporary increase in dosage; if corticosteroids have been stopped following prolonged therapy they may need to be temporarily re-introduced. Patients under stress may require increased doses prior, during and after the period of stressful situation. Stopping corticosteroids after prolonged therapy may cause withdrawal symptoms including fever, myalgia, arthralgia and malaise. There is an enhanced effect in patients with hypothyroidism and in those with cirrhosis. Particular care is required with the following conditions: renal insufficiency, hypertension or congestive heart failure, diabetes mellitus (or a family history of diabetes), osteoporosis, previous corticosteroid-induced myopathy, glaucoma (or family history of glaucoma), myasthenia gravis, non-specific ulcerative colitis, diverticulitis or fresh intestinal anastomosis, peptic ulceration, existing or previous history of severe affective disorders (especially previous steroid psychosis), liver failure, epilepsy, migraine, history of allergy to corticosteroids, tuberculosis, herpes simplex, psychiatric disorders. Fat embolism has been reported as a possible complication of hypercortisonism. Large doses may mask the symptoms of gastro-intestinal perforation. Use with great caution after recent myocardial infarction. Decrease or withdrawal could reveal underlying diseases that are accompanied by eosinophilia in patients with asthma. Potentially severe psychiatric adverse reactions may occur. Seek medical advice if worrying psychological symptoms develop. Particular care is required in patients with or having close relatives with existing history of severe affective disorders. Children on prolonged therapy should be carefully monitored for growth retardation. Preterm neonates: Evidence of long-term neurodevelopmental adverse events after early treatment (<96 hours) in chronic lung disease. Tumour lysis syndrome (TLS) has been reported in patients with haematological malignancies. Corticosteroids should only be administered to patients with suspected or identified pheochromocytoma after an appropriate risk/benefit evaluation. Visual disturbance may be reported with systemic and topical corticosteroid use. **Any warning from the MC, CHM CSM or MHRA:** No. **Black Triangle notice:** Not applicable. **Legal Category:** POM. **The reported adverse reactions are:** Increased susceptibility and severity of infections with suppression of clinical symptoms and signs, opportunistic infections, recurrence of dormant tuberculosis, Decreased resistance to infection, Decreased responsiveness to vaccination and skin tests, Leucocytosis, Hypersensitivity including anaphylaxis, Menstrual irregularities and amenorrhoea, Suppression of the hypothalamic-pituitary-adrenal axis, Premature epiphyseal closure, Development of Cushingoid state, Hirsutism, Secondary adrenocortical and pituitary unresponsiveness, Negative protein and calcium balance, Sodium retention, Fluid retention, Potassium loss, Hypokalaemic alkalosis, Increased calcium excretion, Increased appetite, Impaired carbohydrate tolerance with increased requirement for anti-diabetic therapy, Convulsions and aggravation of epilepsy, Vertigo, Headache, Increased intra-cranial pressure with papilloedema in children (Pseudotumour cerebri), usually after treatment withdrawal, Psychological dependence, Depression, Insomnia, Aggravation of schizophrenia and psychic disturbances, Affective disorders, Psychotic reactions, Behavioural disturbances, Irritability, Anxiety, Sleep disturbances and cognitive dysfunction including confusion and amnesia, Posterior subcapsular cataracts, Increased intra-ocular pressure, Glaucoma, Papilloedema, Corneal or scleral thinning, Exacerbation of ophthalmic viral or fungal diseases, Exophthalmos, Vision blurred, Chorioretinopathy, Congestive heart failure in susceptible patients, Myocardial rupture following recent myocardial infarction, Thromboembolism, Hypertension. Dyspepsia, Peptic ulceration with perforation and haemorrhage, Acute pancreatitis, Candidiasis, Abdominal distension and vomiting, Ulcerative oesophagitis, Perforation of the small and large bowel, Nausea, Hiccups, Impaired wound healing, Thin fragile skin, Petechiae and ecchymoses, Erythema, Striae, Telangiectasia, Acne, Increased sweating, Suppressed reaction to skin tests, Allergic dermatitis, Urticaria, Angioneurotic oedema, Thinning scalp hair, Osteoporosis, Vertebral and long bone fractures, Avascular necrosis, Tendon rupture, Proximal myopathy, Muscle weakness, Aseptic necrosis of femoral and humeral heads, Loss of muscle mass, Growth suppression in infants, Children and adolescents, Malaise, Abnormal fat deposits, Increased or decreased motility and spermatozoa, and Weight gain. **Pack Size and NHS Price:** 75ml - £21.15 and 150ml - £42.30. **Marketing Authorisation Number:** UK: PL 00427/0137 and IE: PA23081/006/001. **Marketing Authorisation Holder:** Rosemont Pharmaceuticals Ltd, Rosemont House, Yorkdale Industrial Park, Braithwaite Street, Leeds, LS11 9XE. **Date of Preparation:** April 2023.

Adverse events should be reported.
Reporting forms and information can be found at www.mhra.gov.uk/yellowcard
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Abbreviated Prescribing Information: Methotrexate 2mg/ml Oral Solution Consult Summary of Product Characteristics before prescribing. Presentation: A clear yellow oral solution, each ml of oral solution contains 2.19mg Methotrexate disodium equivalent to 2mg Methotrexate. **Therapeutic Indications:** Methotrexate 2mg/ml Oral Solution is indicated in the following oncological indications: The maintenance treatment of Acute Lymphocytic Leukaemia (ALL) in children and adults. The treatment of malignant trophoblastic tumours; The treatment of severe active rheumatoid arthritis in adults; Polyarthritic forms of active, severe juvenile idiopathic arthritis (JIA) in adolescents and children aged 3 years and over when the response to non-steroidal anti-inflammatory drugs (NSAIDs) has been inadequate. The treatment of severe forms of psoriasis vulgaris including chronic plaque psoriasis, erythrodermic psoriasis, psoriatic arthritis and pustular psoriasis which are not responsive to other conventional therapies such as phototherapy, PUVA and retinoids. **Posology and Method of Administration:** *Dosage in adult patients with rheumatoid arthritis:* The usual dose is 7.5 – 15mg (3.75ml – 7.5ml) once weekly. The schedule may be adjusted gradually, depending on the individual activity of the disease and tolerability by the patient to achieve an optimal response but should not exceed

a total weekly dose of 20mg (10ml). Thereafter the dose should be reduced to the lowest possible effective dose which in most cases is achieved within 6 weeks. ***Dosage in children with and adolescents with polyarthritic forms of juvenile idiopathic arthritis:*** Patents with JIA should always be referred to a rheumatology unit specialising in the treatment of children/adolescents. The recommended dose is 10 – 15mg (5 – 7.5ml)/m^2 body surface area (BSA)/week. In therapy-refractory cases the weekly dosage may be increased to 20mg (10ml)/m^2 BSA/week. However, increased monitoring frequency is indicated if the dosage is increased. The treating physician will decide how long the patient should be treated. Treatment of severe active rheumatoid arthritis and severe JIA represents a long-term treatment. ***Dosage in oncological indications* (low dose therapy: single dose < 100mg/m^2)** Doses are usually based on the patient's body surface area (BSA). Doses in excess of 100mg are usually given parenterally, when an injectable preparation should be used. ***Malignant Trophoblastic Tumours:*** 15mg/m^2, Day 1 to Day 5. Usually, such courses may be repeated 3 to 5 times as required, with rest periods of one or more weeks interposed between courses, until any manifesting toxic symptoms subside. ***Acute Lymphocytic Leukaemia:*** Low-dose methotrexate is used in the maintenance treatment of acute lymphocytic leukaemia in children and adults within complex protocols in combination with other cytostatic medicinal products for maintenance treatment. Common accepted single doses lie in the range of 20 - 40mg/m^2 body surface area. If methotrexate is administered in combination chemotherapy regimens, the dosage should be reduced, taking into consideration any overlapping toxicity of the other drug components. ***Dosage for psoriasis:*** Before starting treatment, it is advisable to give the patient a test dose of 2.5 – 5.0mg to exclude unexpected toxic effects. If, one week later, appropriate laboratory tests are normal, treatment may be initiated. The usual dose is 10mg – 25mg (5ml – 12.5ml) taken once weekly. As necessary, the total weekly dose can be increased up to 25mg. Thereafter the dose should be reduced to the lowest effective dose according to therapeutic response which is most cases is achieved within 4 to 8 weeks. ***Elderly:*** Methotrexate should be used with extreme caution in elderly patients, a reduction in dosage should be considered due to reduced liver and kidney function as well as lower folate reserves which occurs with increased age. ***Patients with renal impairment:*** Since methotrexate is predominantly eliminated renally, in patients with impaired creatinine clearance, delayed elimination is to be expected, which can lead to severe side effects. In patients with impaired renal function, the dose regimens must be adjusted according to the creatinine clearance and serum methotrexate concentrations. **Paediatric population:** ***Oncological indications:*** Methotrexate should be used with caution in children. ***Non-oncological indications:*** Polyarthritic forms of juvenile idiopathic arthritis: Use in children under 3 years of age is not recommended. **Contra-indications:** Hypersensitivity to the active substance or to any of the excipients; severe renal impairment (creatinine clearance less than 30ml/min, see section 4.2); significant hepatic impairment; alcoholism; active infectious disease; overt or laboratory evidence of immunodeficiency syndrome(s); pre-existing blood dyscrasias, such as bone marrow hypoplasia, leucopenia, or thrombocytopenia or serious anaemia; severe, acute or chronic infections such as tuberculosis and HIV; stomatitis, ulcers of the oral cavity and known active gastrointestinal ulcers; breast-feeding; during methotrexate therapy concurrent vaccination with live vaccines must not be carried out; Pregnancy. **Special Warnings and Precautions for use:** The oral solution contains 2mg of methotrexate in each ml of solution; the scaling of the dosing syringe is in ml and not mg; care should be taken that the correct dosing volume is prescribed. **Patients with rheumatological or dermatological diseases must be informed unequivocally that treatment is to be taken just once a week and not daily. Incorrect use of methotrexate can result in severe and even fatal adverse reactions. Medical staff and patients must be clearly instructed. Warnings regarding non-oncological indications:** The prescriber should specify the day of intake on the prescription. The prescriber should make sure patients understand that methotrexate should only be taken once a week. Patients should be instructed on the importance of adhering to the once-weekly intakes as incorrect intake of methotrexate can lead to severe, including potentially lethal, side effects, especially in elderly patients. Due to the risk of severe potentially life-threatening adverse reactions, methotrexate should only be used in patients with severe active rheumatoid arthritis or severe forms of psoriasis vulgaris including chronic plaque psoriasis, erythrodermic psoriasis, psoriatic arthritis and pustular psoriasis which are not responsive to other conventional therapies. **Warnings regarding all indications:** Patients undergoing methotrexate therapy should be closely monitored to prevent intoxication and to ensure fast identification of toxic side effects. Especially strict monitoring of the patient is indicated following prior radiotherapy (especially of the pelvis), functional impairment of the haematopoietic system (e.g., following prior radio- or chemotherapy), impaired general condition as well as advanced age and in very young children. Patients should be fully informed by the physician about risks and benefits of the therapy, of the need to inform the physician immediately if toxic signs occur and about necessary examinations and safety measures during treatment. Discontinuation of methotrexate therapy did not always result in a complete recovery from toxic effects. **Precautions** Before administration of methotrexate, the following check-up examinations and safety precautions are recommended: renal and hepatic function tests; a complete blood picture; urinalysis should be performed as part of the prior and follow-up examinations; chest x-ray; hepatitis A, B, C serology; tuberculosis diagnostics. Liver biopsies may also be required. **Respiratory:** Strict monitoring is necessary in patients with pulmonary dysfunction, smokers and/or patients with certain bronchopulmonary diseases, particularly bronchiectasis or fibrosis. **Hepatic**: Hepatic toxicity has been observed, usually associated with chronic hepatic disease. The administration of low doses of methotrexate for prolonged periods may give rise, in particular, to hepatic toxicity. Liver function should be closely monitored. **Gastrointestinal:** Care and possible cessation of treatment are indicated if stomatitis or GI toxicity occurs as haemorrhagic enteritis due to the danger of potentially fatal intestinal perforation. **Renal:** Renal lesions may develop if the urinary flow is impeded and urinary pH is low, especially if large doses have been administered. Renal function should be closely monitored before, during and after treatment. **Blood, Infection, and Immunosuppression:** Haematopoietic suppression caused by methotrexate may occur abruptly and with apparently safe dosages. Full blood counts should be closely monitored before, during and after treatment. The

immunosuppressive effect of methotrexate should be taken into account when immune responses of patients are important or essential. Special attention should be paid in cases of inactive chronic infections (e.g., herpes zoster, tuberculosis, hepatitis B or C) because of their potential activation. Progressive multifocal leukoencephalopathy (PML): Cases of progressive multifocal leukoencephalopathy (PML) have been reported in patients receiving methotrexate, mostly in combination with other immunosuppressive medication. Malignancy: Malignant lymphomas may occur in patients receiving low dose methotrexate, in which case therapy must be discontinued. Fertility: Methotrexate has been reported to cause impairment of fertility in both males and females. Teratogenicity – Reproductive risk: Methotrexate causes embryotoxicity, abortion and foetal malformations in humans. Skin toxicity: Severe, occasionally fatal, dermatologic reactions, including toxic epidermal necrolysis (Lyell's Syndrome) or Stevens-Johnson syndrome have been reported after single or multiple doses of methotrexate. Folic acid supplementation: If acute methotrexate toxicity occurs, patients may require treatment with folinic acid. It is recommended to check levels of vitamin B12 prior to initiating folic acid supplementation, particularly in adults aged over 50 years, as folic acid intake may mask a vitamin B12 deficiency. Methotrexate given concomitantly with radiotherapy may increase the risk of soft tissue necrosis and osteonecrosis. Exposure to intense sunlight or to UV rays should be avoided, as photosensitivity manifested by an exaggerated sunburn reaction has been observed in some individuals taking methotrexate. **Any warning from the MC, CHM CSM or MHRA. Black Triangle notice:** Not applicable. **Legal Category:** POM. **Some of the common and serious undesirable effects include:** Loss of appetite, nausea, vomiting, abdominal pain, inflammation and ulceration of mucosa of mouth and throat, stomatitis, dyspepsia, increase in liver-related enzymes (ALAT [GPT], ASAT [GOT], alkaline phosphatase and bilirubin), infections, leucopenia, thrombocytopenia, anaemia, headache, dizziness, fatigue, drowsiness, pneumonitis, interstitial pneumonitis (can be fatal), anorexia, diarrhoea, erythema, exanthema, pruritus, lymphoma, bone marrow suppression, anaphylaxis, depression, convulsions, leukoencephalopathy, cerebral oedema, pericarditis, pericardial effusion, pneumonitis, pulmonary fibrosis, gastrointestinal ulcer, gastrointestinal haemorrhage, pancreatitis, severe skin reactions, osteoporosis, haematemesis, haematorrhoea, toxic megacolon, liver failure, and sepsis (for full details of undesirable effects see SPC). **Pack Size and NHS Price:** 35ml - £95.00, 65ml - £125.00. **Marketing Authorisation Number:** PL 00427/0233. **Marketing Authorisation Holder:** Rosemont Pharmaceuticals Ltd, Rosemont House, Yorkdale Industrial Park, Braithwaite Street, Leeds, LS11 9XE, UK. **Date of Preparation:** October 2023.

Adverse events should be reported.
Reporting forms and information can be found at www.mhra.gov.uk/yellowcard
Adverse events should also be reported to Rosemont Pharmaceuticals Ltd on 0113 244 1400.

Abbreviated Prescribing Information: Glycopyrronium Bromide 1mg/5ml oral solution. Summary of Product Characteristics before prescribing. Presentation: A clear colourless to straw-yellow solution containing 1 mg of glycopyrronium bromide per 5ml. **Therapeutic Indications:** Symptomatic treatment of severe sialorrhoea in children and adolescents aged 3 years and older with chronic neurological disorders. **Posology and Method of Administration:** Not recommended for use in children younger than 3 years. It is indicated for the paediatric population only. Clinical studies have not been conducted in patients with hepatic impairment. Hepatic impairment is not thought to result in a clinically relevant increase in systemic exposure. Elimination of glycopyrrolate is severely impaired in patients with renal failure. Glycopyrronium is contraindicated in those with severe renal failure. For patients with Mild to moderate renal impairment (eGFR <90 - ≥30 ml/min/1.73m2) doses should be reduced by 30%. Other licensed Glycopyrronium products are not all interchangeable on a milligram-for-milligram basis. **Contra-indications:** Hypersensitivity to the active substance or to any of the excipients, pregnancy and breast-feeding, glaucoma, urinary retention, severe renal impairment, history of intestinal obstruction, ulcerative colitis paralytic ileus, pyloric stenosis and myasthenia gravis, concomitant treatment with potassium chloride solid oral dose products and anticholinergic medicines. **Special Warnings and Precautions for use:** Anticholinergic effects may be dose dependent and difficult to assess in a disabled child. Monitoring is required. Treatment should be stopped in the event of constipation, urinary retention, pneumonia, allergic reaction, pyrexia, very hot weather, changes in behaviour. The prescriber should evaluate and decide if treatment should continue at a lower dose. Total treatment duration should be kept as short as possible. If continuous treatment is needed or the treatment is repeated intermittently benefits and risks should be carefully considered. Glycopyrronium should not be given to children with mild to moderate sialorrhoea, should be used with caution in acute myocardial infarction, hypertension, coronary artery disease, cardiac arrhythmias and conditions characterised by tachycardia. Very fast or very slow heart rate should be reported to the prescriber. Glycopyrronium should be used with caution in patients with gastro-oesophageal reflux disease, pre-existing constipation and diarrhoea. It is important that patients receive adequate daily dental hygiene and regular dental health checks. Glycopyrronium can cause thickening of secretions, which may increase the risk of respiratory infection and pneumonia. Glycopyrronium should be discontinued if pneumonia is present. Increased central nervous system effects have been reported. Behavioural changes should be monitored. Caution should be exercised in children with compromised blood brain barrier. The effects of Glycopyrronium on the reproductive system have not been investigated. Whilst clinical studies do not report any short or long-term effect of Glycopyrronium on neurodevelopment or growth, no studies have been conducted to specifically address these issues. **Any warning from the MC, CHM CSM or MHRA. Black Triangle notice:** Not applicable. **Legal Category:** POM. A list of very common and common reactions are presented below and refer the SmPC for other reactions: Very common: irritability, flushing, nasal congestion, reduced bronchial secretions, dry mouth, constipation, diarrhoea, vomiting, urinary retention. Common - upper respiratory tract infection, pneumonia, urinary tract infection, agitation, drowsiness, epistaxis, rash, and pyrexia. **Pack Size and NHS Price:** 150ml - £91.00. **Marketing Authorisation Number:** PL 00427/0252 **Marketing Authorisation**

Holder: Rosemont Pharmaceuticals Ltd, Rosemont House, Yorkdale Industrial Park, Braithwaite Street, Leeds, LS11 9XE, UK. **Date of Preparation:** December 2022.

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

Abbreviated Prescribing Information: Omeprazole 1 mg/ml, Powder for Oral Suspension. Consult Summary of Product Characteristics before prescribing. Presentation: White/off-white/slightly yellow powder; each ml of reconstituted suspension contains 1 mg of omeprazole. **Therapeutic Indications:** Omeprazole Oral Suspension is indicated for treatment of reflux esophagitis; Symptomatic treatment of heartburn and acid regurgitation in gastro-esophageal reflux disease in children aged 1 – 12 months of age. **Posology and Method of Administration:** Omeprazole Oral Suspension should be taken on an empty stomach following reconstitution, at least 30 minutes before a meal. The oral suspension should not be mixed or administered with any drinks or foods other than milk. Omeprazole can be administered via nasogastric (NG) or percutaneous endoscopic gastrostomy (PEG) tubes. **Paediatric population aged 1 month to 12 months:** Omeprazole 1 mg/ml oral suspension should be used for patients weighing ≥ 2 kg to ≤ 5 kg. 1 mg/kg body weight once daily is recommended. Individual dose measurements ≤ 2 ml are not indicated. The treatment time is 4-8 weeks for reflux esophagitis and 2–4 weeks for heartburn and acid regurgitation in gastro-esophageal reflux disease. Dose adjustment is not needed in patients with impaired renal function. **Contraindications:** Hypersensitivity to the active substance, substituted benzimidazoles or to any of the excipients listed and concomitant use with nelfinavir. **Special Warnings and Precautions for use:** Caution should be exercised when used as Omeprazole may alleviate symptoms of malignancy and delay diagnosis. Concomitant use with atazanavir is not recommended. Omeprazole may reduce the absorption of vitamin B12 and the potential for interactions with drugs metabolised through CYP2C19 should be considered. Severe hypomagnesaemia has been reported in patients treated with proton pump inhibitors (PPIs) like omeprazole for at least three months, and in most cases for a year. Increased risk of hip, wrist and spine fracture in high doses and over long durations (>1 year) should be considered. Severe cutaneous adverse reactions are reported in association with omeprazole treatment. Treatment should be discontinued in case of suspected acute tubulointerstitial nephritis and subacute cutaneous lupus erythematosus. Omeprazole treatment should be stopped for at least 5 days before Increased Chromogranin measurements. Slightly increased risk of gastrointestinal infections such as Salmonella and Campylobacter are associated with proton pump inhibitors. Care should be exercised in patients with reduced kidney function or patients on a controlled potassium diet as this medicine contains 54.3 mg (1.39 mmol) potassium per ml or 271.5 mg (6.95 mmol) of potassium per 5 ml dose. Allergic reactions may be caused by the excipient sodium methyl para hydroxybenzoate. Risk for neonatal jaundice should be considered and patients with fructose intolerance should not take this medicine as it contains maltitol. **Any warning from the MC, CHM CSM or MHRA.** No. **Black Triangle notice (if relevant):** N/A. **Legal Category:** POM. **The reported adverse reactions are:** Leukopenia, thrombocytopenia, Agranulocytosis, pancytopenia, Hypersensitivity reactions e.g. fever, angioedema and anaphylactic reaction/shock, Hyponatraemia, Hypomagnesaemia; hypocalcaemia, hypokalaemia, Insomnia, Agitation, confusion, depression, Aggression, hallucinations, Headache, Dizziness, paraesthesia, somnolence, Taste disturbance, Blurred vision, Vertigo, Bronchospasm, Abdominal pain, constipation, diarrhoea, flatulence, nausea/vomiting, fundic gland polyps (benign), Dry mouth, stomatitis, gastrointestinal candidiasis, Microscopic colitis, Increased liver enzymes, Hepatitis with or without jaundice, Hepatic failure, encephalopathy in patients with pre-existing liver disease, Dermatitis, pruritus, rash, urticaria, Alopecia, photosensitivity, acute generalized exanthematous pustulosis (AGEP), drug reaction with eosinophilia and systemic symptoms (DRESS), Erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (TEN), Subacute cutaneous lupus erythematosus, Fracture of the hip, wrist or spine, Arthralgia, myalgia, Muscular weakness, Tubulointerstitial nephritis (with possible progression to renal failure), Gynaecomastia, Malaise, peripheral oedema, Increased sweating. **Pack Size and NHS Price:** Each bottle contains 90ml of oral suspension of which at least 75ml is intended for dosing- £111.00. **Marketing Authorisation Number:** PL 34111/0005. **Marketing Authorisation Holder:** Xeolas Pharmaceuticals Limited, Hamilton Building, DCU, Glasnevin, Dublin 9, Ireland. **Date of Preparation:** July 2023.

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Abbreviated Prescribing Information: Omeprazole 2mg/ml and 4mg/ml, Powder for Oral Suspension. Consult Summary of Product Characteristics before prescribing. Presentation: The reconstituted suspension will be a white / off-white / brownish suspension containing 2mg/ml or 4mg/ml omeprazole. **Therapeutic Indications:** Adults: Treatment of duodenal ulcers, gastric ulcers, NSAID-associated gastric and duodenal ulcers, reflux esophagitis, symptomatic gastro-esophageal reflux disease, prevention of relapse of duodenal ulcers, gastric ulcers, in combination with appropriate antibiotics, Helicobacter pylori (H. pylori) eradication in peptic ulcer disease, long-term management of patients with healed reflux esophagitis. Paediatric use: Children over 1 month of age: treatment of reflux esophagitis, symptomatic treatment of heartburn and acid regurgitation in gastroesophageal reflux disease. Children over 4 years of age and adolescents: In combination with antibiotics in treatment of duodenal ulcer caused by H. pylori. **Posology and Method of Administration:** Adults: Treatment and prevention of relapse of duodenal ulcers, gastric ulcers: 10 – 40mg once daily. H. pylori eradication 20 – 40mg once or twice daily + suitable antibiotic for one week, which may be repeated. Treatment and prevention of NSAID-associated gastric and duodenal ulcers: 20mg once daily, for 4 weeks, which may be repeated. Treatment of reflux esophagitis: 20mg once daily for 4 weeks, which

may be repeated. Severe esophagitis 40mg once daily for 8 weeks. Long-term management of patients with healed reflux esophagitis: 10 – 40mg once daily. Treatment of symptomatic gastro-esophageal reflux disease: 10-20mg daily. **Paediatric population:** 1 month to 1 year: 1mg/kg once daily. 1 year 10 – 20mg once daily. 2 years of age 20 – 40mg once daily. Reflux esophagitis: Treatment 4 – 8 weeks. Symptomatic treatment of heartburn and acid regurgitation in gastro-esophageal reflux disease: Treatment 2 – 4 weeks. Children over 4 years of age and adolescents: Treatment of duodenal ulcer caused by H. pylori: 10 – 20mg depending on weight + suitable antibiotic twice daily for one week. Special populations: Dose adjustment is not needed in patients with impaired renal function. In patients with impaired hepatic function a daily dose of 10 – 20mg may be sufficient. Dose adjustment is not needed in the elderly. Method of administration: Oral suspension should be taken on an empty stomach, at least 30 minutes before a meal. Omeprazole can be administered via nasogastric (NG) or percutaneous endoscopic gastrostomy (PEG) tubes. **Contraindications:** Hypersensitivity to the active substance, substituted benzimidazoles or to any of the excipients. Omeprazole must not be used with nelfinavir. **Special Warnings and Precautions for use:** Caution should be exercised when used as Omeprazole may alleviate symptoms of malignancy and delay diagnosis. Concomitant use with atazanavir is not recommended. Omeprazole may reduce the absorption of vitamin B12 and the potential for interactions with drugs metabolised through CYP2C19 should be considered. Severe hypomagnesaemia has been reported in patients treated with proton pump inhibitors (PPIs) like omeprazole for at least three months, and in most cases for a year. Increased risk of hip, wrist and spine fracture in high doses and over long durations (>1 year) should be considered. Severe cutaneous adverse reactions are reported in association with omeprazole treatment. Treatment should be discontinued in case of suspected acute tubulointerstitial nephritis and subacute cutaneous lupus erythematosus. Omeprazole treatment should be stopped for at least 5 days before Increased Chromogranin measurements. Slightly increased risk of gastrointestinal infections such as Salmonella and Campylobacter are associated with proton pump inhibitors. Care should be exercised in patients with reduced kidney function or patients on a controlled potassium diet as this medicine contains 54.3 mg (1.39 mmol) potassium per ml or 271.5 mg (6.95 mmol) of potassium per 5 ml dose. Allergic reactions may be caused by the excipient sodium methyl para hydroxybenzoate. Patients with fructose intolerance should not take this medicine as it contains maltitol. **Any warning from the MC, CHM CSM or MHRA.** No. **Black Triangle notice:** Not applicable. **Legal Category:** Prescription only medicine. **The reported adverse reactions are:** Leukopenia, thrombocytopenia, Agranulocytosis, Pancytopenia, Hypersensitivity reactions e.g. fever, angioedema and anaphylactic reaction/shock, Hyponatraemia, Hypomagnesaemia, Hypocalcaemia, Hypokalaemia, Insomnia, Agitation, Confusion, Depression, Aggression, Hallucinations, Headache, Dizziness, Paraesthesia, Somnolence, Taste disturbance, Blurred vision, Vertigo, Bronchospasm, Abdominal pain, Constipation, Diarrhoea, Flatulence, Nausea/Vomiting, Fundic gland polyps (benign), Dry mouth, Stomatitis, Gastrointestinal candidiasis, Microscopic colitis, Increased liver enzymes, Hepatitis with or without jaundice, Hepatic failure, Encephalopathy in patients with pre-existing liver disease, Dermatitis, Pruritus, Rash, Urticaria, Alopecia, Photosensitivity, Erythema multiforme, Stevens-Johnson syndrome, Toxic epidermal necrolysis, Subacute cutaneous lupus erythematosus, Fracture of the hip, wrist or spine, Arthralgia, Myalgia, Muscular weakness, Tubulointerstitial nephritis (with possible progression to renal failure), Gynaecomastia, Malaise, Peripheral oedema, and Increased sweating. **Pack Size and NHS Price:** Each bottle contains 90ml of oral suspension of which at least 75ml is intended for dosing. 2mg/ml x 90 ml - £124.00 4mg/ml x 90 ml - £234.00. **Marketing Authorisation Number:** 2mg/ml –PL 34111/0002, 4mg/ml – PL 34111/0003. **Marketing Authorisation Holder:** Xeolas Pharmaceuticals Limited, Hamilton Building, DCU, Glasnevin, Dublin 9, IRELAND. **Date of Preparation:** July 2023.

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