

Package leaflet: Information for the patient

Rybrila 160 micrograms/ml Oral solution glycopyrronium

Read all of this leaflet carefully before your child starts taking this medicine because it contains important information for them.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for your child only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as your child's.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Rybrila is and what it is used for
2. What you need to know before you give Rybrila
3. How to use Rybrila
4. Possible side effects
5. How to store Rybrila
6. Contents of the pack and other information

1. What Rybrila is and what it is used for

Rybrila contains the active substance glycopyrronium and belongs to a group of medicines called synthetic anticholinergics, quaternary ammonium compounds.

Rybrila is used to treat excessive production of saliva (sialorrhoea) in children and adolescents aged 3 years and older. Sialorrhoea (drooling or excessive salivation) is a common symptom of many diseases of the muscles or nerves. It is mainly caused by poor control of muscles in the face. Acute sialorrhoea may be associated with inflammation, dental or mouth infections. Rybrila acts on the salivary glands to reduce production of saliva.

2. What you need to know before you give Rybrila

Do not give Rybrila if the child:

- is **allergic** (hypersensitive) to glycopyrronium or any of the other ingredients of this medicine (listed in section 6)
- has **glaucoma** (increased pressure in the eye)
- has a condition called **myasthenia gravis** which leads to muscle weakness and fatigue
- has an **obstruction of the stomach** (pyloric stenosis) **or bowel** causing vomiting, abdominal pain and swelling (paralytic ileus)
- is unable to completely **empty the bladder** (urinary retention)
- suffers from **chronic end stage kidney disease** and require dialysis
- is taking **potassium chloride** solid dose products
- is taking **anticholinergic medicines**

Warnings and precautions

Talk to a doctor or pharmacist before giving Rybrila if the child:

- has **gastric reflux** (a condition in which the liquid stomach contents backs up into the gullet)

- has **ulcerative colitis** (a chronic inflammation of the large intestine (colon) which can cause abdominal pain, diarrhoea and bleeding from the back passage)
- has just had a **heart attack** or are suffering from **heart disease, irregular heartbeats** or **high blood pressure**, because this medicine can cause a change to their normal heart rate
- has a condition characterised by a **faster heartbeat** than normal (this can be caused by conditions such as an **overactive thyroid gland, heart failure** or **heart surgery**)
- is due to have **surgery** (including at the dentist) during which they will be 'put to sleep' using **inhalation anaesthesia**. This is because this medicine may cause a change in their normal heart rhythm
- has **diarrhoea**, especially if they have had an **ileostomy** or **colostomy**
- has a **high temperature** (fever) or the environmental temperature is high, as this medicine will reduce the amount they sweat, making it harder for their body to cool down
- has **kidney disease**, because this medicine's dose may need to be decreased
- has **compromised blood brain barrier**
- has been told by their doctor that they have an **intolerance to some sugars**, because this medicine contains sorbitol

In addition, stop treatment and talk to their doctor if the child is suffering with the following:

- seem unwell with a very fast or very slow heart rate
- constipation
- pneumonia
- changes in behaviour

The doctor will decide if treatment should continue and if there should be a dose reduction, after evaluating any of these events.

If you are not sure any of the above applies to your child, talk to a doctor or pharmacist before giving Rybrila.

Rybrila reduces salivation which can increase the risk of dental disease, therefore teeth should be brushed daily and have regular dental checks.

Children under 3 years

This medicine is **not recommended for children younger than 3 years**. Talk to a doctor or pharmacist before taking this medicine or if this medicine has been prescribed for a child less than 3 years.

Other medicines and Rybrila

Tell the doctor or pharmacist if your child is taking, have recently taken, or might take any other medicines. This includes medicines you have bought without a prescription.

- If their doctor tells you to give both this medicine and one or more **similar medicines** such as **oxybutynin**, then they may need to take less than the usual dose of this medicine. This is because of an **increased risk** of other **side effects** such as dry mouth, retention of urine and constipation when glycopyrronium and **similar medicines** are taken together.

Please **tell the doctor** if your child is taking or have recently taken:

- **Antidepressants** such as amitriptyline, clomipramine, lofepramine or imipramine (known as tricyclic antidepressants) or **monoamine oxidase inhibitors (MAOIs)** such as phenelzine, moclobemide, rasagiline, selegiline or tranylcypromine
- **Phenothiazines** such as chlorpromazine, fluphenazine, prochlorperazine or trifluoperazine, used to treat **mental problems** or **nausea, vomiting** or **vertigo**
- **Antihistamines** such as promethazine, used to treat **allergies**
- **Parasympathomimetics** such as carbachol, neostigmine or physostigmine which affect the transmission of nerve impulses to muscles
- **Corticosteroids** such as prednisolone, used to treat various conditions including **asthma** and **inflammation**
- **Inhaled anaesthetics**, given before surgery (including at the dentist)

- **Clozapine** or **haloperidol**, used to treat **schizophrenia**
- **Nefopam**, used to treat **acute and chronic pain**
- **Domperidone** or **metoclopramide**, used to treat **nausea** and **vomiting**
- **Amantadine** or **levodopa**, used to treat **Parkinson's disease**
- **Memantine**, used to treat **Alzheimer's disease**
- Slow-dissolving **digoxin** tablets, **disopyramide** or **atenolol**, used to treat **heart problems**
- **Metformin**, used to treat **type 2 diabetes**
- **Glyceryl trinitrate** tablets, used to treat **angina**. These may not dissolve under the tongue as well as usual because this medicine can cause a dry mouth
- **Topiramate** or **zonisamide**, used to treat **epilepsy** and to prevent **migraines**
- **Potassium chloride** containing solid dose products (see section 2 "Do not give Rybrila if")
- **Anticholinergic medicines**. (see section 2, "Do not give Rybrila if")

Long term use efficacy and safety of Rybrila has not been studied beyond recommended 24 weeks of use. Continued use should be discussed with child's doctor every 3 months to check that Rybrila is still right for the child.

Rybrila with food and drink

The effect of Rybrila may be reduced when taken with high fat foods. For this reason, this medicine should be given at least one hour before or two hours after meals. Speak to the child's doctor if administration with a meal is required.

Pregnancy and breastfeeding

Glycopyrronium is not recommended in pregnancy or breastfeeding. If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.

Driving and using machines

Rybrila may make the patient **feel drowsy** or cause their **eyesight** to become **blurred** and this could interfere with their ability to drive or operate machinery safely. Do not drive or operate machinery until these effects have fully cleared. If there is any doubt, ask your doctor for advice.

Rybrila contains E420 (sorbitol), E217 and E219

- This medicine contains 250 mg of **sorbitol (E420)** in each ml. Sorbitol is a source of fructose. If you have been told by the doctor that your child has an **intolerance to some sugars**, or if your child has been diagnosed with **hereditary fructose intolerance (HFI)**, a rare genetic disorder in which a person cannot break down fructose, talk to the doctor before giving this medicinal product.
- This medicine contains **sodium propyl parahydroxybenzoate (E217)** and **sodium methyl parahydroxybenzoate (E219)**. These may cause **allergic reactions** (possibly delayed) and exceptionally, bronchospasms (a narrowing of the airways).
- This medicinal product contains less than 1 mmol sodium (23 mg) per maximum dose, that is to say essentially 'sodium free'.

3. How to use Rybrila

Always give this medicine exactly as the doctor has told you. Check with your doctor or pharmacist if you are not sure.

There are other oral solutions with glycopyrronium, but each one can have a different method of administration. Read carefully how to use this medicinal product and check with your doctor or pharmacist if you are not sure. Use only the oral syringe included in the container of this product.

Use in children and adolescents aged 3 years and older

Give the dose prescribed by your doctor to the child three times each day, at least **one hour before or two hours after** a meal.

The initial dose will be calculated based on the weight of the child, and will be decided by the doctor using the table below as a guide. The dose will depend on both the effect of Rybrila and any side effects the patient is experiencing. Section 4 includes possible side effects related to the use of Rybrila. These should be discussed with the child's doctor, including those for dose increases and decreases, and at any other time should you be concerned. The child should be monitored at regular intervals to check that Rybrila is still the right treatment for them.

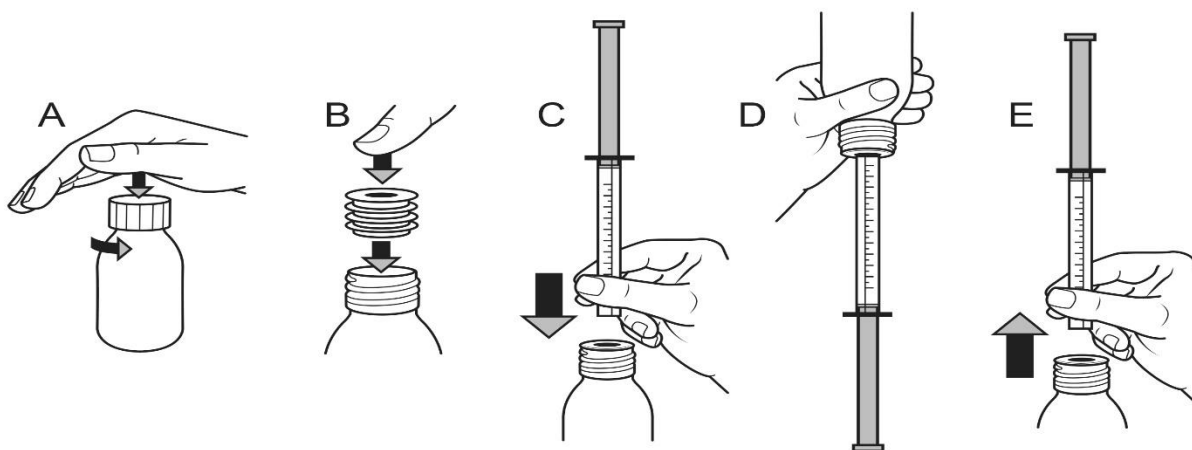
| Weight (Kg) | Dose Level 1 (ml) | Dose Level 2 (ml) | Dose Level 3 (ml) | Dose Level 4 (ml) | Dose Level 5 (ml) |
|-------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| 13-17 | 1.5 | 3 | 4.5 | 6 | 7.5 |
| 18-22 | 2 | 4 | 6 | 8 | 10 |
| 23-27 | 2.5 | 5 | 7.5 | 10 | 12.5 |
| 28-32 | 3 | 6 | 9 | 12 | 15 |
| 33-37 | 3.5 | 7 | 10.5 | 14 | 15 |
| 38-42 | 4 | 8 | 12 | 15 | 15 |
| 43-47 | 4.5 | 9 | 13.5 | 15 | 15 |
| ≥48 | 5 | 10 | 15 | 15 | 15 |

Route and method of administration

For oral use and use with nasogastric and or PEG tubes only.

A 15 ml graduated oral syringe and a "Press-In" Bottle Adapter (PIBA) are provided with the product.

1. Open the bottle and at first use insert the PIBA (see pictures A-B). *Note: this may have been done already by the pharmacist.*
2. Insert the syringe into the PIBA and draw out the required volume from the inverted bottle (see pictures C-D). *Note: check you have correct level. Maximum dose of the highest dose level is 15 ml.*
3. Remove the filled syringe from the bottle in the upright position (see picture E).
4. Discharge the syringe contents into the child's mouth.
5. Replace the cap on the bottle, the PIBA remains in place.
6. Rinse the syringe with warm water and allow to dry after each use.



If your child is given the medicine through a feeding tube, flush the tube with 20 ml of water after you have given the medicine.

If you give more Rybrila than you should

If you give more of this medicine to the child than prescribed, they are more likely to experience side effects. Consult the doctor or **get medical advice immediately**. If possible, show the bottle and this leaflet to the medical staff.

If you forget to give Rybrila

- If you forget to give a dose, give it as soon as possible. Then give the next dose at the correct time, in accordance with the instructions given to you by the doctor. However, if the next dose is due, do not give the dose missed; just give the next dose as normal.
- **Do not give a double dose to make up for the forgotten one.**

If you have any further questions on the use of this medicine, ask the doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

If any of the following serious side effects occur, **stop giving the medicine and seek medical advice immediately**:

- Severe allergic reaction (swelling of the tongue, lips, face or throat) - unknown
- Constipation (difficulty in passing stools) – very common
- Urinary retention (unable to completely empty the bladder) – common
- Pneumonia (severe chest infection) – common
- Allergic reaction (hives, difficulty breathing or swallowing, itching) – uncommon
- Fever (pyrexia) – common
- Changes in behaviour such as mood changes, irritability – very common

Other side effects:

Very common side effects (may affect more than 1 in 10 people)

- Dry mouth
- Diarrhoea
- Being sick (vomiting)
- Flushing
- Nasal congestion
- Reduced secretions in the chest
- Reduced secretions in the airways

Common side effects (may affect up to 1 in 10 people)

- Upper respiratory tract infection (chest infection)
- Urinary tract infection
- Drowsiness (sleepiness)
- Agitation
- Rash

Uncommon side effects (may affect up to 1 in 100 people)

- Allergy
- Headache
- Involuntary eye movement (nystagmus)
- Bad breath (halitosis)
- Rash (Hives)
- Nose bleeds (epistaxis)
- Fungal infection (thrush) of the throat (oesophageal candidiasis)

- Widening of the pupil of the eye (mydriasis)
- Dehydration
- Thirst
- Urgent need to urinate
- Insomnia (difficulty in sleeping)
- Abnormal contractions of digestive tract when food is ingested (gastrointestinal motility disorder)
- A disorder of the muscles and nerves in the intestine which causes an obstruction or blockage (pseudo-obstruction)

Unknown side effects (frequency cannot be estimated from the available data)

- Nausea
- Angle-closure glaucoma (increased pressure in the eye)
- Photophobia
- Dry eyes
- Angioedema
- Decrease in heart rate (transient bradycardia)
- Sinus infection (sinusitis)
- Skin dryness
- Sweat inhibition

Reporting of side effects

If you notice any side effects, talk to your doctor, pharmacist or nurse. **This includes any possible side effects not listed in this leaflet.** You can also report side effects directly via HPRA

Pharmacovigilance Website: www.hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Rybrila

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and bottle after EXP. The expiry date refers to the last day of that month.

This medicine should be stored below 25°C in its original bottle.

Keep the bottle in the original carton in order to protect from light.

Once the bottle has been opened this medicine should be used within 28 days.

Do not throw away any medicines via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Rybrila contains

- The active substance is glycopyrronium. Each ml contains 200 micrograms glycopyrronium bromide equivalent to 160 micrograms of glycopyrronium.
- The other ingredients are:
 - o Glycerol
 - o Sorbitol (E420) (see section 2)
 - o Sodium methyl parahydroxybenzoate (E219) (see section 2)
 - o Sodium propyl parahydroxybenzoate (E217) (see section 2)
 - o Citric acid monohydrate (E330)

- Trisodium citrate dihydrate (E331)
- Purified water
- Strawberry flavour:
 - Flavouring substance
 - Maltodextrin (maize)
 - Acacia (E414)
 - Triacetin (E1518)

What Rybrila looks like and contents of the pack

Rybrila is a clear, colourless, strawberry flavoured liquid supplied in a 150 ml amber glass bottle with a tamper evident child resistant HDPE/PP screw cap. Each pack contains a carton with one 150 ml bottle, a 15 ml graduated LDPE oral syringe and a PE syringe adaptor.

Multiple packs of 2 x 150 ml, 3 x 150 ml, 4 x 150 ml, and 5 x 150 ml cartons are available, but not all packs may be marketed.

Marketing Authorisation Holder

Clinigen Healthcare B.V.
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Manufacturer

Labialfarma - Laboratório de Produtos Farmacêuticos e Nutracêuticos, S.A.
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This medicine is authorised in the Member States of the European Economic Area under the following names: Rybrila

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