Package leaflet: Information for the user

AMGLIDIA 0.6 mg/mL oral suspension

Glibenclamide

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- 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 those of your child.
- 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 AMGLIDIA is and what it is used for
2. What you need to know before you give AMGLIDIA
3. How to give AMGLIDIA
4. Possible side effects
5. How to store AMGLIDIA
6. Contents of the pack and other information

1. What AMGLIDIA is and what it is used for

AMGLIDIA contains the active substance called glibenclamide which belongs to a group of medicines called sulphonylureas used for lowering blood sugar (blood-glucose).

AMGLIDIA is used in newborns, infants and children to treat diabetes that occurs at birth (known as neonatal diabetes mellitus). Neonatal diabetes is a disease where the child's body does not release enough insulin to control the level of blood sugar; AMGLIDIA is used only in patients who still have some ability to make insulin.

Sulphonylureas like glibenclamide have been shown to be effective in certain genetic mutations responsible for the genesis of neonatal diabetes.

This medicine is an oral suspension, to be taken by mouth, which is a more convenient treatment for newborns and young children compared to regular injections of insulin.

You must talk to a doctor if your child does not feel better or if he/she feels worse after a few days.

2. What you need to know before you give AMGLIDIA

Do not give AMGLIDIA
- if your child is allergic to glibenclamide or any of the other ingredients of this medicine (listed in section 6).
- if your child has ketoacidosis (high blood levels of acid substances called ketones).
- if your child suffers from porphyria (inability to break down body chemicals called porphyrins).
- if your child is treated with bosentan, e.g. a medicine used to treat problems of blood circulation.
- if your child suffers from severe renal dysfunction.
- if your child suffers from severe liver dysfunction.

Warnings and precautions
Talk to your doctor before your child is given AMGLIDIA.

Your child's blood sugar levels may become too low (hypoglycaemia) after taking AMGLIDIA. Tell the doctor if your child is pale, sweating, has irregular heart rhythm or seems disoriented, confused or unresponsive.

Ask your doctor to determine at which frequency capillary blood sugar should be checked.

G6PD is an enzyme evolved in sugar metabolism. If your child carries a G6PD enzyme deficiency, he/she may experiment an abnormal breakdown of red blood cells (acute haemolytic anaemia) after taking AMGLIDIA.

Tell the doctor if you know that your child is affected by G6PD deficiency and contact him/her if you notice that your child is pale as compared to usually.

Tell your doctor if your child suffers from renal or liver disorders.

Children and adolescents
AMGLIDIA is to be used for newborns, infants and children. Adolescents are not in need of this oral suspension formulation.

Other medicines and AMGLIDIA
Tell your child's doctor or pharmacist if your child is taking, has recently taken or might take any other medicines.

Interactions of AMGLIDIA with other medicines are presented in the table below:

Medicines	Potential effects
ACE inhibitors (used to treat hypertension) (such as captopril and enalapril)	Blood sugar levels too low
Acetazolamide (used to treat glaucoma)	Increased blood sugar levels
Adrenaline (epinephrine) and other sympathomimetic agents (used to treat serious allergic reaction, cardiovascular arrest, asthma)	Increased blood sugar levels
Alcohol (Alcohol present in medicines)	Blood sugar levels too low
	Increased blood sugar levels
	Incorrect control of plasma sugar
Anabolic steroids and male sex hormones (such as testosterone enanthate) (used to treat testosterone deficiency)	Blood sugar levels too low
Barbiturates (such as phenobarbital used to treat epilepsy)	Increased blood sugar levels
Beta-receptor blockers (such as propranolol used to treat high blood pressure, control irregular or fast heart beats, help prevent additional heart attack)	Blood sugar levels too low
	Incorrect control of plasma sugar low blood sugar levels may be hidden
Biguanides (such as metformin) used to treat diabetes mellitus	Blood sugar levels too low
Bosentan used to treat high blood pressure in the blood vessels between the heart and the lungs	Incorrect control of plasma sugar (see section 2 "Do not give AMGLIDIA")
Calcium channel blockers (such as nifedipine used to treat high blood pressure)	Increased blood sugar levels
Chloramphenicol (in case of oral route) is an antibiotic used to treat infections	Blood sugar levels too low
Ciclosporin used to prevent rejection of the transplanted organ	Increased toxicity of ciclosporin
Cimetidine used to relieve the symptoms of stomach and duodenal ulcers, oesophageal reflux disease and the Zollinger-Ellison syndrome	Increased blood sugar levels
Clarithromycin is an antibiotic used to treat certain infections	Blood sugar levels too low
Clonidine used to treat arterial hypertension	Blood sugar levels too low
	Incorrect control of plasma sugar
	Increased blood sugar levels
Colesevelam used to lower cholesterol	Incorrect control of plasma sugar
Corticosteroids (such as prednisone, prednisolone) used in various indications such as inflammation and asthma	Increased blood sugar levels
Coumarin derivatives (such as dicoumarol, acenocoumarol) used to decrease the clotting ability of the blood	Blood sugar levels too low
	Incorrect dosage of coumarin derivatives administered
Cyclophosphamides used to treat different types of cancer	Blood sugar levels too low
Diazoxide used for low blood sugar	Increased blood sugar levels
Disopyramide used to treat an irregularity in the heartbeat	Blood sugar levels too low
Diuretics (such as furosemide, hydrochlorothiazide) used to treat arterial hypertension	Increased blood sugar levels
Fibrates (such as bezafibrate, fenofibrate, gemfibrozil used to lower the level of fats)	Blood sugar levels too low
Fluoxetine used to treat depression and anxiety disorders	Blood sugar levels too low
Glucagon used to treat high blood-glucose level	Increased blood sugar levels
Guanethidine used to treat high blood pressure	Blood sugar levels too low
	Incorrect control of plasma sugar
H2-receptor antagonists used for reducing stomach acid (such as ranitidine) to relieve the symptoms of stomach and duodenal ulcers, oesophageal reflux disease and the Zollinger-Ellison syndrome	Incorrect control of plasma sugar
Heparin used to decrease the clotting ability of the blood	Blood sugar levels too low
Ifosfamide used to treat different types of cancers	Blood sugar levels too low
Insulin used to lower blood sugar level	Blood sugar levels too low
Isoniazid used to treat tuberculosis	Increased blood sugar levels
Large doses of laxatives (such as macrogol)	Increased blood sugar levels
MAO inhibitors (such as iproniazide) used to treat depression	Blood sugar levels too low
Miconazole used to treat fungal infection	Blood sugar levels too low
Nicotinic acid (in high doses) used to decrease high levels of cholesterol and triglycerides which are fat-like substances in the blood	Increased blood sugar levels
Oestrogens (such as 17-beta oestradiol) used for hormonal treatment	Increased blood sugar levels
Other oral antidiabetics (such as metformin) used to lower blood-glucose level	Blood sugar levels too low
Oxypentifylline used to improve peripheral blood flow	Blood sugar levels too low
Phenothiazine derivatives (such as chlorpromazine) used to treat schizophrenia and other psychoses	Increased blood sugar levels
Phenytoin used to treat epilepsy	Increased blood sugar levels
Probenecid used to treat gout, gouty arthritis	Blood sugar levels too low
Progestogens (such as desogestrel, dydrogesterone) used for hormonal treatment	Increased blood sugar levels
Quinolone antibiotics (such as nalidixic acid and ciprofloxacine) used to treat infections	Blood sugar levels too low
Rifampicin used to treat infections including tuberculosis	Increased blood sugar levels
Sulfamethoxazole with trimethoprim (Co-trimoxazole) used to treat infections	Blood sugar levels too low
Thyroid hormones (such as L-thyroxin) used for hormonal treatment	Increased blood sugar levels
Salicylates (such as aminosalicylic acid, para-aminosalicylic acid used for tuberculosis)	Blood sugar levels too low
Tetracycline antibiotics (such as doxycycline and minocycline) used to treat infections	Blood sugar levels too low

Tell your doctor or pharmacist if your child is taking, has recently taken or might take any other medicines.

AMGLIDIA with alcohol
Both acute and chronic alcohol intake may attenuate the hypoglycaemic effect of glibenclamide or dangerously potentiate it by delaying its metabolic inactivation. Nausea, vomiting, flushing, dizziness, headache, chest and abdominal discomfort, and general hangover-like symptoms among others have occurred following the concomitant use of alcohol and glibenclamide. Concomitant use of alcohol and glibenclamide should be avoided.

Pregnancy and breast-feeding
This medicine may only be used for the treatment of neonatal diabetes in newborns, infants and children.

This medicine is not intended to be used in pregnant women and patients planning a pregnancy should inform their doctor. It is recommended that such patients change treatment to insulin.

Breast-feeding seems to be compatible, but as a precautious measure monitoring of the fully breast-fed infant's blood sugar level is advisable.

Driving and using machines
Glibenclamide may increase the risk of low blood sugar and therefore have a moderate influence on the ability to drive, to take part in road traffic otherwise or use machines.

AMGLIDIA contains sodium and benzoate salt
This medicine contains 2.80 mg of sodium per mL. To be taken into consideration by patients on a controlled sodium diet.

This medicine contains 5 mg benzoate salt in each mL oral suspension. Benzoate salt may increase jaundice (yellowing of the skin and eyes) in newborns (up to 4 weeks old).

3. How to give AMGLIDIA

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

Dosage
Glibenclamide therapy should be started by a doctor experienced in the treatment of patients with very early onset diabetes.

The dose of AMGLIDIA depends on your child's body weight, and will be calculated by the doctor as an amount (volume) in mL oral suspension to be measured with the oral syringe (either an 1 mL or a 5 mL syringe) supplied with the medicine. Your doctor will prescribe the specific presentation and strength including the particular syringe you should use. Do not use any other syringe to administer AMGLIDIA.

It is important you do not adjust yourself the doses of either AMGLIDIA or insulin, unless specifically directed to do so by your child's doctor.

Make sure that you use correct strength of the medicine and the appropriate oral syringe prescribed by your doctor to avoid accidental administration of too high or too low amounts.

The starting dose of AMGLIDIA is 0.2 mg of glibenclamide for each kilogram (kg) of body weight daily, divided in two doses of 0.1 mg/kg. As the dose is increased, it is usually possible to reduce and then stop the dose of insulin the patient is already receiving.

Higher doses of AMGLIDIA can be given and administered in up to four intakes per day, based on blood-glucose monitoring, as per titration recommendations given by the referring doctor.

In case of minor vomiting, an antivomiting medicine will be prescribed by your doctor and AMGLIDIA can be continued.

As generally recommended in such situations, if vomiting occurs less than 30 minutes following administration of AMGLIDIA, a new dose can be given. If vomiting occurs more than 30 minutes following administration of AMGLIDIA, no new dose should be given. Always ask your child's doctor for advice in such circumstances.

In case of major vomiting, ketonemia and ketonuria should be closely monitored by the treating doctor. The doctor may start insulin therapy again, when ketonemia or ketonuria were found to be responsible for the major vomiting. In case of inability of food or beverage intake, the child should go to the emergency department to get an insulin and glucose perfusion until vomiting stops.

Method of administration
Always give the medicine 15 minutes before feeding.

The medicine should be given at the same times each day.

In case of milk feeding, recommendation is given to administer the suspension 15 minutes before child's milk feeding.

This medicine is a ready-for-use oral suspension to be given with a marked oral syringe. Only the oral syringe included in the carton should be used.

The 1 mL syringe is thin and small and graduated in steps of 0.05 mL. The 5 mL syringe is thick and long and graduated in steps of 0.1 mL.

Instructions for use
The dose is measured by drawing the plunger of the syringe back until it reaches the marking for the dose the doctor has prescribed for your child.

The dose in mL per administration and the number of administrations per day have to carefully follow the medical prescription.

While the child is awake, position the child in a half-sitting position in the hollow of your arm, with the child's head resting on your arm.

Slip about the first 1 cm of the syringe into the child's mouth and place it against the inside cheek; let the child suck.

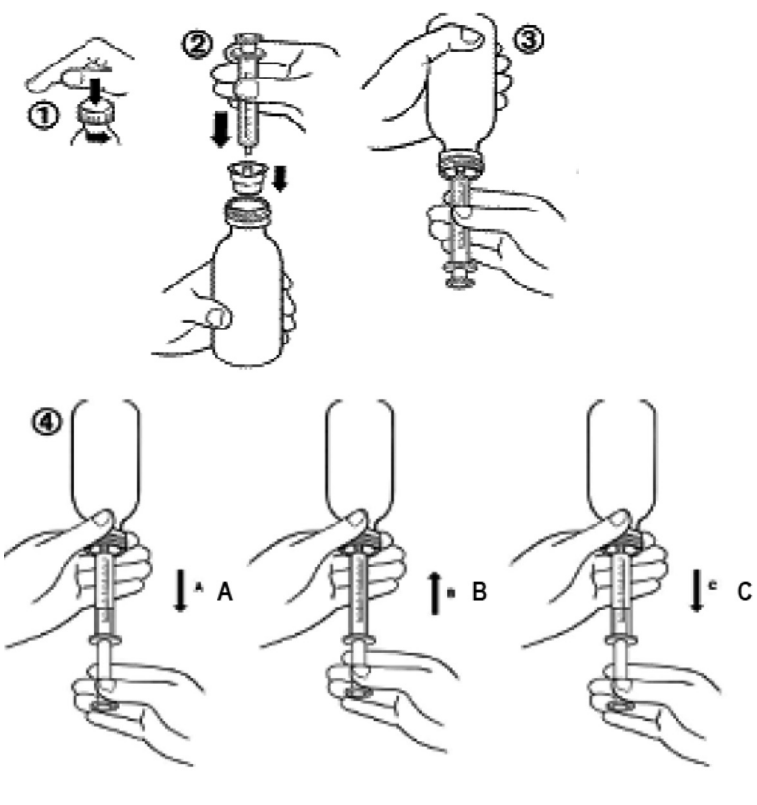
If the child does not suck, slowly press the plunger of the syringe so that the suspension trickles into the mouth.

Do not lay the child down directly after administration. It is recommended to wait until the child has swallowed the medicine before reverting back to lying position.

For first use

1. Open the bottle by unscrewing the child-resistant closure while pressing downwards.
2. Insert the adaptor firmly into the bottle while holding the bottle the right way up.
3. Replace the screw cap on the bottle with the adaptor.
4. Retighten the screw cap to push the adaptor well into the bottle.

For each administration
1. The bottle does not need to be shaken before administration. The medicine is administered as a ready-for-use oral suspension to be given using a specific marked syringe.
2. Open the bottle by unscrewing the child-resistant closure while pressing downwards (figure 1).
3. Holding the bottle the right way up, insert the syringe firmly into the adaptor fitted to the bottle (figure 2).
4. Turn the bottle with the syringe upside down (figure 3).
5. Draw back the plunger to obtain the desired volume (figure 4A). Then push the plunger to remove as many air bubbles as possible from the syringe (figure 4B). Finally, draw back the plunger until graduation corresponding to the prescribed dose in ml (figure 4C).
   Note: if air gets into the syringe, empty the syringe into the bottle and start the procedure again.
6. Turn the bottle with the syringe into its upright position.
7. Remove the syringe from the adaptor. Put the syringe into the child's mouth and push the plunger to slowly administer the medicine into the mouth.
8. Close the bottle by tightening the screw cap well on top of the adaptor. The bottle must be closed after each use and stored for a **maximum of 30 days.**
9. The syringe must be rinsed thoroughly with water, wiped dry after each use and replaced back into the medicine's carton. The oral syringe in the carton should be used only with this medicine.



If you give more AMGLIDIA to your child than you should
See your doctor, nurse or your hospital pharmacist immediately.

There is a risk of hypoglycaemia. You should check capillary blood sugar of your child and follow the instructions described in section 4.

If you forget to give AMGLIDIA
If you forget to give AMGLIDIA, there is a risk of high blood sugar.

You must check your child's blood sugar (capillary blood sugar) and give AMGLIDIA as soon as you realise you have forgotten to use it. If your child's capillary blood sugar exceeds 3 g/L (or 300 mg/dL or 16.5 mmol/L), check for the presence of ketonuria with a finger stick or urine stick tests according to your child's doctor recommendations. If ketonuria is detected, you must inject insulin immediately according to the procedure defined beforehand with your child's doctor and contact him/her or his/her team for advice.

Do not give a double dose to make up for a forgotten dose.

If you stop giving AMGLIDIA
There is a risk of high blood sugar.

You should check your child's blood sugar (capillary blood sugar). Diabetes symptoms may reappear and may lead to a serious disturbance of the body's metabolism with high blood levels of ketones (ketoacidosis), dehydration and disturbance of the balance of acids in the body.

You should therefore never stop the medicine without checking with the doctor looking after your child. Seek advice from your doctor.

You will be requested to bring back remaining AMGLIDIA oral suspension to your doctor at each consultation.

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

4. Possible side effects

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

Serious side effects

Too low blood sugar (hypoglycaemia) (very common: may affect more than 1 in 10 people)

If you take AMGLIDIA, you are at risk of getting too low blood sugar (hypoglycaemia). The signs of too low blood sugar may include:
- shaking, sweating, feeling very anxious or confused, fast heart beat
- excessive hunger, headache

If your child starts to become pale, sweating, has irregular heart rhythm or seems disoriented, confused or unresponsive, these may be signs that the child's blood sugar is too low; you should first solve the situation as explained below and you should then talk to your child's doctor to adapt AMGLIDIA's dose.

The risk of low blood sugar is increased if the medicine is not taken with a meal, is taken with alcohol, or if combined with certain medicines. Such low blood sugar should be managed by taking sugar by mouth followed by a snack or meal. If very low blood sugar occurs that affects consciousness, emergency services should be called and an intravenous glucose injection performed. After such a severe episode of hypoglycaemia, the child and family should see the child's doctor to check the appropriateness of the dose of glibenclamide suspension.

Allergic reactions
This medicine may cause allergic reactions, which may be serious in isolated cases, including difficulties to breath, low blood pressure and shock. If your child presents any of these symptoms, you should immediately go to the nearest emergency department.

Gastro intestinal disorders (very common: may affect more than 1 in 10 people):
- Diarrhoea
- Abdominal (belly) pain
- Vomiting
- Stomach ache (Dyspepsia)

Teeth problems (common: may affect up to 1 in 10 people):
- Tooth discoloration.

Abnormal blood test results (very common: may affect more than 1 in 10 people)
Laboratory blood tests may show changes in blood cells (decrease in white blood cells: leucopenia) and effects on liver function (brief increase in enzymes called transaminases).

Other side effects:
Tell your doctor or pharmacist if you notice any of the following side effects:
- Skin rash: itching, nettle rash (urticarial), allergic skin reaction, blistering of the skin, skin inflammation.
- Increase in sensitivity of the skin to sunlight
- Transient visual disturbances.
- Other laboratory blood tests changes: increased levels of the white blood cells called eosinophils (hypereosinophilia), mild to severe decrease in blood components called platelets (thrombocytopenia), which can lead to subcutaneous bleeding (purpura).

Reporting of side effects
If you notice any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme in UK Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store AMGLIDIA

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.

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

After first opening, use within 30 days. Keep the bottle tightly closed.

Do not throw away any medicines via wastewater or household waste. 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 AMGLIDIA contains
- The active substance is glibenclamide. Each mL contains 0.6 mg glibenclamide.
- The other ingredients are: xanthan gum, hydroxyethylcellulose, lactic acid, purified water, sodium citrate and sodium benzoate (E211) (see section 2 "AMGLIDIA contains sodium and benzoate").

What AMGLIDIA looks like and contents of the pack
AMGLIDIA is a white and odourless oral suspension.
Each carton contains:
- 1 bottle containing 30 mL oral suspension.
- One 1 mL oral syringe (thin and small) and **or** 5 mL oral syringe (thick and long) depending on the prescribed dose and the volume to be given. The syringe is packed in a transparent bag.
- One syringe adaptor.

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