

PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

Hemangiol Oral Solution

Active ingredient: The active ingredient is propranolol. Each mL of solution contains 3.75 mg propranolol (equivalent to 4.28 mg propranolol hydrochloride).

Inactive and allergenic ingredients: see section 6 "Further information".

Read this leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

In addition to this leaflet, Hemangiol also has an information guide for the patient's parents. This guide contains important safety information that you must know and follow before starting, and during treatment with Hemangiol. Read both the information guide for the patient's parents and the package insert before starting to use the medicine. Keep the information guide for further reference, if necessary.

This medicine has been prescribed for your child only. Do not pass it on to others. It may harm them, even if it seems to you that their ailment is similar. Hemangiol is intended for infants from 5 weeks to 5 months of age.

1. WHAT IS THE MEDICINE INTENDED FOR?

This medicine is used to treat infantile hemangioma. A hemangioma is a collection of extra blood vessels that form a lump in or under the skin. A hemangioma can be superficial or deep. It is sometimes called a 'strawberry mark' because its surface resembles the shape of a strawberry.

Hemangiol treatment is given to infants aged 5 weeks to 5 months, in the following situations:

- the hemangioma is life- or function-threatening.
- the hemangioma is ulcerated and painful, and/or does not respond to simple treatment measures.
- there is a risk of permanent scarring or disfigurement.

Therapeutic group:

Hemangiol belongs to the beta blocker group of medicines.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- your child was born prematurely and has not reached the corrected age of 5 weeks (the corrected age of a premature baby is the baby's chronological age had he been born on his expected due date).
- your child is allergic to the active ingredient propranolol or to any of the other ingredients contained in this medicine (see section 6 "Further information" in this leaflet). An allergic reaction can include a skin rash, itching or shortness of breath.
- your child has asthma or a history of breathing difficulties.
- your child has a slow heart rate for his age. Refer to the doctor if you are not sure.
- your child has a heart problem (such as heart rhythm problems or heart failure).
- your child has very low blood pressure.
- your child has a circulation problem which causes the toes and fingers to be numb and pale.
- your child is prone to low blood sugar levels.
- your child has high blood pressure caused by a tumor in the adrenal gland. This tumor is called pheochromocytoma.

Do not give this medicine to your child if you are breastfeeding and taking medicines that must not be taken together with Hemangiol (see "Drug interactions" section below).

Special warnings regarding use of the medicine

Before giving Hemangiol to your child, tell the doctor if:

- your child has liver or kidney problems. Administration of this medicine is not recommended in case of liver or kidney problems.
- your child has ever had an allergic reaction, regardless of its origin (e.g., from medicines or from a nutritional supplement, etc.). An allergic reaction can include a rash, itching or shortness of breath.
- your child has psoriasis (a skin condition in which red dry plaques or skin thickening occurs), as this medicine may worsen the symptoms of the condition.
- your child has diabetes: in this case, monitor his blood sugar level more frequently.
- your child has PHACE syndrome (a condition combining hemangioma with vascular abnormalities including cerebral blood vessels), as this medicine may increase the risk of cerebral stroke.

Important signs to pay attention to after administering Hemangiol to your child:

- Risk of low blood sugar level (hypoglycemia)

This medicine may mask the warning signs of low blood sugar levels (hypoglycemia). The medicine may also aggravate hypoglycemia in children, especially during fasting period (e.g., low food intake, inflammatory disease, vomiting) or when glucose demands are higher than usual (cold, stress, inflammation), or in case of overdose. The signs may be:

- Minor: pallor, tiredness, sweating, shaking, palpitations, anxiety, hunger, difficulty waking up.
- Major: sleeping more than usual, difficulty obtaining a response from your child, poor feeding, decrease in body temperature, convulsions, brief pauses in breathing, loss of consciousness.

The risk of hypoglycemia remains significant throughout the whole treatment period with the medicine.

To avoid risk of hypoglycemia, give Hemangiol to your child during or straight after a meal and avoid giving last dose close to night bedtime (see section 3). Your child must be fed sufficiently and regularly during treatment. If your child is not eating enough, develops another illness or is vomiting, it is recommended to skip the dose. Do not give Hemangiol to your child until he/she starts eating normally again. If your child shows any sign of hypoglycemia while taking Hemangiol, stop treatment with the medicine and contact a doctor immediately or proceed to a hospital. If the child is conscious, give him/her a drink of liquid containing sugar.

- Risk of bronchospasm

Stop treatment and contact a doctor immediately if after giving Hemangiol to your child, you observe any of the following symptoms that could be indicative of bronchospasm (breathing difficulties due to temporary narrowing of the airways in the lungs): cough, rapid breathing, difficulty breathing, or wheezing with or without bluish-colored skin.

Stop treatment with the medicine and contact a doctor immediately if your child shows cold-like symptoms associated with difficulty in breathing and/or wheezing during the course of treatment with Hemangiol.

- Risk of hypotension and low heart rate (bradycardia)

Hemangiol can decrease blood pressure and heart rate. This is why your child will be kept under close clinical and heart rate monitoring for two hours after administration of the first dose or after increasing the dosage of the medicine. Then, the doctor should regularly examine the child during treatment.

Stop treatment with the medicine and contact a doctor immediately if your child has any signs of tiredness, coldness, pallor, bluish-colored skin, or fainting while using Hemangiol.

- Risk of high potassium level in the blood (hyperkalemia)

Hemangiol may increase blood potassium levels. In case of a large ulcerated hemangioma, your child's blood potassium level should be monitored.

If your child is due to undergo general anesthesia

Tell the doctor that your child is receiving Hemangiol. This is because your child could suffer from low blood pressure if given certain anesthetics while taking this medicine (see below in "Drug interactions"). It may be necessary to stop taking Hemangiol for at least 48 hours before anesthesia.

Pregnancy, breastfeeding and fertility

If you are breastfeeding your child

- Tell your doctor before giving this medicine to your child.
- Do not give this medicine to your child if you are taking medicines that must not be used with Hemangiol (see "Drug interactions").

Tests and follow up

- If your child has diabetes, monitor his blood sugar levels more frequently (see "Special warnings regarding use of the medicine").
- Hemangiol can cause a decrease in blood pressure and heart rate. Therefore, your child must be under close clinical monitoring, with heart rate monitoring 2 hours after administration of the first dose or after a dosage increase. Then, the doctor must regularly examine the child during the course of treatment. (see "**Important signs to pay attention to after administering Hemangiol to your child**").
- Hemangiol may increase blood potassium levels. In case of a large ulcerated hemangioma, your child's blood potassium level should be measured. (see "**Important signs to pay attention to after administering Hemangiol to your child**").

Drug interactions

- **If your child is taking, or has recently taken, or is due to take, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.** This is because Hemangiol can change the way other medicines act, and some medicines can have an effect on the way Hemangiol acts.
- **If you are breastfeeding your child, it is important to tell your doctor, pharmacist or the medical staff if you are taking any medicines, as they may pass into the mother's breast milk and influence your child's treatment. Your doctor will advise you on whether you should stop breastfeeding.**

Tell the doctor or pharmacist if your child is taking or if you are breastfeeding and taking:

- Medicines to treat diabetes.
- Medicines for heart or blood vessel problems such as heart rate disturbances, chest pain or angina, high blood pressure, heart failure.
- Medicines to treat anxiety and depression as well as medicines for more serious mental health problems and epilepsy.
- Medicines to treat tuberculosis.
- Medicines to treat pain and inflammation.
- Medicines to lower blood lipid levels.
- Medicines for anesthesia.

If you have further questions, consult your doctor or pharmacist.

Use of the medicine and food

The medicine should be given immediately after or while feeding the child.

Important information about some of the ingredients of the medicine

The medicine contains less than 1 mmol (23 mg) sodium per dose (essentially sodium-free).

The medicine also contains 2.08 mg propylene glycol/kg/day. If your baby is less than 4 weeks old, consult the doctor or pharmacist before giving this medicine, especially if the baby is taking other medicines that contain propylene glycol or alcohol. (see section 6 "Further information").

3. HOW SHOULD YOU USE THE MEDICINE?

The treatment of your child is in accordance with the recommendations of a doctor who has expertise in the diagnosis and treatment of infantile hemangioma. Always use according to the doctor's instructions. Check with your doctor or pharmacist if you are not sure about the dosage and treatment regimen of the medicine.

The dosage and treatment regimen will be determined by the doctor only.

Never change the dosage given to your child on your own. Every increase or change in dosage in accordance to your baby's weight must be done by the attending doctor only.

• Dosage:

The dosage will be determined in accordance with your baby's weight, as per the following dosage regimen:

Weeks (daily dose)	Dose for oral intake	Timing of doses
First week (1 mg/kg/day)	0.5 mg/kg	• once in the morning • once in late afternoon
Second week (2 mg/kg/day)	1 mg/kg	• at an interval of at least 9 hours between the 2 doses
Third and following weeks (3 mg/kg/day)	1.5 mg/kg	

Do not exceed the recommended dose.

• How to give Hemangiol to your child: Hemangiol is for oral use.

- Give the medicine immediately after or while feeding the child.
- Always measure the dose by using the oral syringe supplied with the package and do not replace it with any other syringe. If you lost the syringe, contact the registration holder.
- Administer the medicine directly into your child's mouth using the syringe supplied with the bottle. If necessary, you may mix the medicine with a **small quantity** of baby-milk or age-suitable apple and/or orange juice, and give it to your child in a baby bottle. Do not mix the medicine with a full bottle of milk or fruit juice. For children weighing up to 5 kg, you may mix the dose with one teaspoonful (approximately 5 mL) of baby-milk. For children weighing more than 5 kg, the dose may be mixed with one tablespoonful (approximately 15 mL) of baby-milk or age-suitable apple or orange juice. Use the mixture within 2 hours of preparation.
- Feed your child regularly to avoid a prolonged fast.
- If your child does not eat sufficiently or is vomiting, skip the dose.
- If your child spits up the dose or if you are uncertain whether he got the full dose, do not give another dose; wait until the next scheduled dose.
- Feeding and administration of the medicine must be done by the same person in order to avoid the risk of low blood sugar levels (hypoglycemia) in your child. If different people are involved in treating the child, good communication between them is essential in order to ensure the safety of the child.

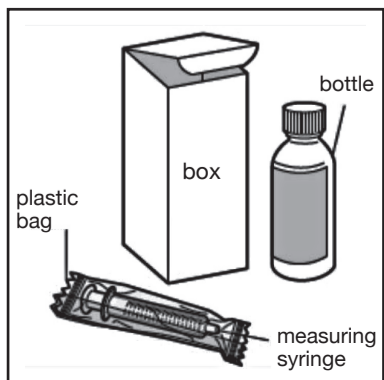
• Instructions for use:

◦ Step 1 - Remove the items from the box

The box contains the following items that you will need to administer the medicine:

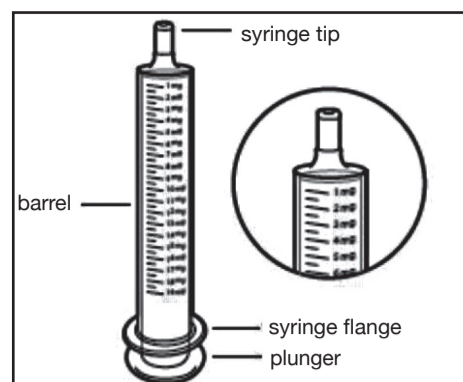
1. A glass bottle containing 120 mL Hemangiol oral solution.
2. An oral syringe, graduated in mg, provided with this medicine.

Remove the bottle from the box and the oral syringe from the plastic bag.



◦ Step 2 - Check the dose

Check the Hemangiol dose in milligrams (mg) as prescribed for your child by the doctor. Locate this number on the oral syringe.



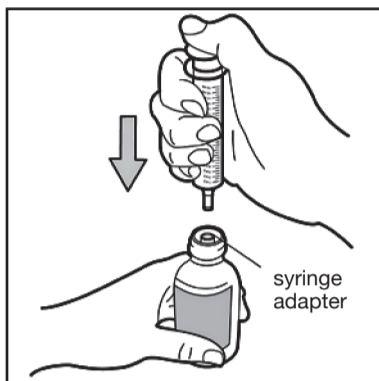
◦ Step 3 - Open the bottle

The bottle has a child-proof cap. Open the bottle as follows: push the plastic cap downwards while turning the cap counter-clockwise (to the left). Do not shake the bottle before use.



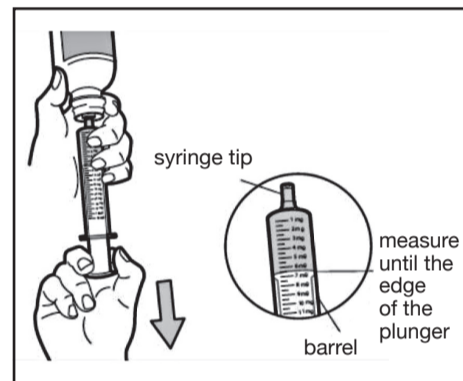
◦ Step 4 - Insert the syringe

Push the plunger of the syringe all the way down and insert the tip of the syringe into the upright bottle. Do not remove the syringe adapter from the neck of the bottle. Only use the oral syringe that is supplied with the medicine to measure and administer the dose. Do not use a spoon or any other measuring device.



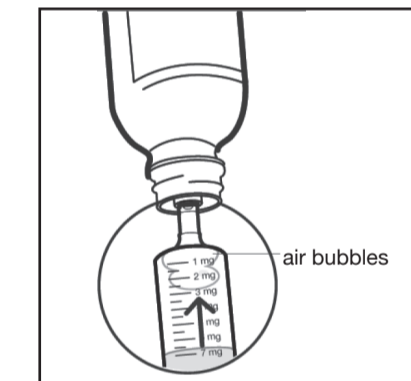
◦ Step 5 - Remove the dose

With the oral syringe in place, turn the bottle upside down. Pull the plunger of the syringe up to the number of milligrams you need.



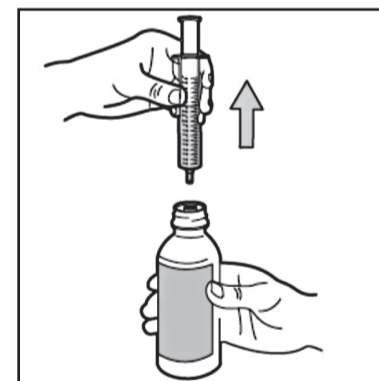
◦ Step 6 - Check for air bubbles

If there are air bubbles in the syringe, hold the syringe upright, push the plunger upwards until all the large air bubbles have been pushed out and then readjust to the dose prescribed for your child by the doctor.



◦ Step 7 - Remove the syringe

Turn the bottle upright and remove the entire syringe from the bottle. Be careful not to push the plunger in during this step.



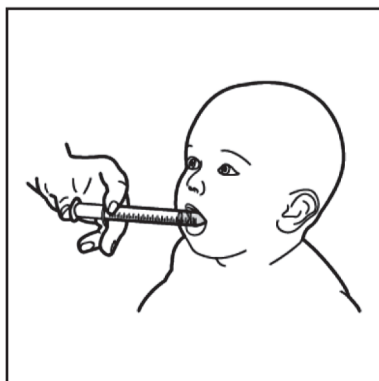
◦ Step 8 - Close the bottle

Replace the plastic cap on the bottle by turning it clockwise (to the right).



◦ Step 9 - Give Hemangiol to your child

Insert the syringe into your baby's mouth and place it against the inside of the cheek. Now you can slowly squirt Hemangiol from the syringe directly into your baby's mouth. Do not lie the child down immediately after administering the medicine.

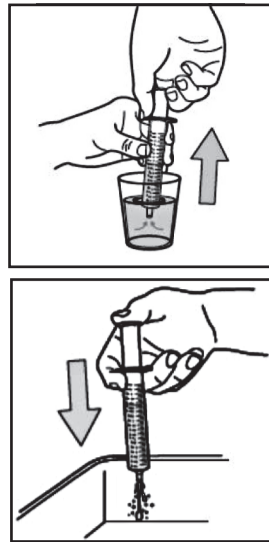


◦ Step 10 - Clean the syringe

Do not dismantle the syringe. After each use, rinse the empty syringe in a glass of clean water:

1. Take a glass of clean water
2. Pull the plunger
3. Discard the water into the sink

4. Repeat this cleaning process 3 times



Do not use any soap or alcohol-based product for cleaning. Wipe the outside dry. Do not put the syringe in a sterilizer or a dishwasher. Until the next use, store the bottle and the syringe together in the medicine package, in a safe place where your child will not be able to see or reach it. Discard the syringe once the bottle is finished.

If you accidentally give your child a higher dosage of the medicine than required, contact the doctor immediately.

If you forget to give the medicine to your child, skip the forgotten dose and do not give a double dose to make up for the forgotten dose. Continue the treatment at the usual frequency: one dose in the morning and one dose in the late afternoon. Adhere to the treatment regimen recommended by the doctor.

If you stop giving the medicine to your child

Hemangiol may be stopped at once at the end of the treatment, in accordance with the doctor's decision.

- **Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them.**

If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Hemangiol can cause side effects in some users. Do not be alarmed by reading the list of side effects. Your child may not suffer from any of them.

After administering Hemangiol, pay attention to important warning signs associated to the following side effects: low blood pressure, slow heart rate, low blood sugar level, and bronchospasm (breathing difficulties). See section 2 of this leaflet.

Very common side effects (may occur in more than 1 in 10 patients):

- Inflammation of the bronchi (bronchitis)
- Sleep disorders (insomnia, poor quality of sleep and difficulties waking up)
- Diarrhea and vomiting

Common side effects (may occur in up to 1 in 10 patients):

- Bronchospasm (breathing difficulties)
- Bronchiolitis - inflammation of the small bronchi, with breathing difficulties and wheezing in the chest, accompanied by cough and fever
- Decreased blood pressure
- Decreased appetite
- Agitation, nightmares, irritability
- Somnolence
- Cold extremities
- Constipation, abdominal pain
- Erythema - skin redness
- Diaper rash

Uncommon side effects (may occur in up to 1 in 100 patients):

- Heart problem or heart rhythm disorders (slow or uneven heart beats)
- Urticaria (allergic reaction of the skin), hair loss (alopecia)
- Decreased blood sugar level
- Reduction of the number of white blood cells

Side effects of unknown frequency (frequency cannot be estimated from the available data):

- Convulsions linked to a low blood sugar level (hypoglycemia)
- Bradycardia (abnormally slow heart rate)
- Low blood pressure
- Very low levels of white blood cells that fight infection
- Circulation problems which cause pallor and numbness in the fingers and toes
- Elevated blood potassium level

If a side effect occurs, if one of the side effects worsens or if your child suffers from a side effect not mentioned in this leaflet, consult with the doctor.

Reporting side effects

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link: <https://sideeffects.health.gov.il>

In addition, you can report to Perrigo via the following address: www.perrigo-pharma.co.il

5. HOW SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine and any other medicine should be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.
- Store below 25°C. Do not freeze. Store the bottle in the original package to protect from light.
- Between uses, store the syringe together with the bottle in the original package.
- After first opening the bottle it may be used for two months, but no later than the expiry date.
- Do not discard the medicine into the waste water or household waste. Consult the pharmacist on how to dispose of the medicine. These measures will help protect the environment.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:

Hydroxyethylcellulose, Vanilla flavour (contains Propylene glycol, Vanillin, Water, Butyric acid, Ethyl butyrate, Piperonal), Saccharin sodium, Strawberry flavour (contains Propylene glycol, Ethyl butyrate, Vanillin, Undecalactone/Gamma, Ethyl acetate, Ethyl propionate, Maltol, Hydroxy-2-5-dimethyl-3(2h)-furanone/4-, Hexyl alcohol, Hexen-1-Ol/Cis-3, Linalool, Isoamyl butyrate, Ethylhexanoate, Ethyl-2-methylbutyrate, Hexen-1-Yl acetate/Cis-3-, Decalactone/gamma-, Methylbutyric acid/2-, Hydroxyphenyl)-2-butanone/4(para-, Methyl dihydrojasmonate, Methyl cinnamate, Ethyl isovalerate, Hexenal/trans-2-, Hexanoic acid, Diacetyl natural, Isovaleric acid, Ionone/alpha, Ionone/beta, Ionone/gamma, Tocopherol/alpha), Citric acid monohydrate, Purified water. For further information, see section 2 "Important information about some of the ingredients of the medicine".

What the medicine looks like and the contents of the package:

Hemangiol is a clear, colorless to yellowish, fruit-scented oral solution. The package of the medicine contains a dark brown glass bottle containing 120 mL Hemangiol solution, which is closed with a child-proof cap. The package contains an oral measuring syringe.

Registration Holder:

Perrigo Israel Agencies Ltd., 1 Rakefet St., Shoham.

Manufacturer:

PIERRE FABRE, Boulogne, France. Revised in May 2021 according to MOH guidelines
Registration number of the medicine in the National Drug Registry of the Ministry of Health: 15968.35287