

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

The medicine is dispensed with a physician's prescription only

Malarone Tablets for Adults

250 mg/100 mg film-coated tablets

Malarone Paediatric Tablets

62.5 mg/25 mg film-coated tablets

Active ingredients and their quantities:

Malarone Tablets for Adults

Each tablet contains 250 mg atovaquone and 100 mg proguanil hydrochloride

Malarone Paediatric Tablets

Each tablet contains 62.5 mg atovaquone and 25 mg proguanil hydrochloride

Inactive and allergenic ingredients in the preparation – see section 6 “Additional information” and in section 2 “Important information about some of the ingredients of the medicine”.

Read the 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 physician or pharmacist.

This medicine has been prescribed for you/your child. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar.

1. WHAT IS THE MEDICINE INTENDED FOR?

♦ Prevention of malaria

Malarone is intended for the prevention of *Plasmodium falciparum* malaria, also in areas where chloroquine resistance has been reported.

♦ Treatment of malaria

Malarone is intended for the treatment of acute, uncomplicated *Plasmodium falciparum* malaria. Malarone has been shown to be effective in regions where the medicines chloroquine, halofantrine, mefloquine and amodiaquine may have unacceptable treatment failure rates, presumably due to drug resistance.

Therapeutic group

Malarone belongs to a group of medicines called *antimalarials*. It contains two active ingredients: atovaquone and proguanil hydrochloride.

Malaria is spread by the bite of an infected mosquito, which passes the malaria parasite (*Plasmodium falciparum*) into the bloodstream. Malarone

prevents malaria by killing the parasite. For people who are already infected with malaria, Malarone also kills these parasites.

Protect yourself/your child from catching malaria

People of any age can get malaria. It is a serious disease, but is preventable. As well as taking Malarone, it is very important that you also take steps to avoid being bitten by mosquitoes:

- **Use a mosquito repellent on exposed areas of the skin**
 - **Wear light coloured clothing that covers most of the body**, especially after sunset as at this time the mosquitoes are most active
 - **Sleep in a screened room** or under a mosquito net impregnated with insecticide
 - **Close windows and doors at sunset**, if they are not screened
 - **Consider using an insecticide** (stickers, spray, plug-ins) to clear the room from insects or to deter mosquitoes from entering the room.
- **If you need further advice**, talk to your physician or pharmacist.

It is still possible to get malaria after taking the necessary precautions. Some types of malaria infection take a long time to cause symptoms, so the illness may not start until several days, weeks or even months after returning from abroad.

- **See a physician immediately if you/your child experience/s symptoms** such as high temperature, headache, shivering and tiredness after returning home.

2. BEFORE USING THE MEDICINE

Do not use the medicine:

- **if you are/your child is sensitive (allergic) to atovaquone, proguanil hydrochloride**, or any of the additional ingredients contained in the medicine, as listed in section 6.
 - **for preventing malaria, if you/your child suffer/s from severe kidney disease.**
- **Tell your physician if either of these applies to you/your child.**

Special warnings regarding use of the medicine

Before beginning treatment with Malarone, tell the physician if:

- you/your child have/has severe kidney disease
 - your child is being treated for malaria and weighs less than 5 kg or is given Malarone Paediatric Tablets to prevent malaria and weighs less than 11 kg.
- Tell your physician or pharmacist if any of these apply to you/your child.

Drug interactions

If you are/your child is taking, or you have/your child has recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the physician or pharmacist.

Some medicines can affect the way Malarone works, or Malarone itself can strengthen or weaken the effectiveness of other medicines taken at the same time. These include:

- **metoclopramide**, used to treat nausea and vomiting
 - the antibiotics **tetracycline**, **rifampicin** and **rifabutin**
 - **efavirenz** or **certain highly active protease-inhibitors** used to treat Human Immunodeficiency Virus (HIV)
 - **warfarin** and other medicines that prevent blood clotting
 - **etoposide** used to treat cancer.
- **Tell your physician** if you are/your child is taking any of these. Your physician may decide that Malarone is not suitable for you/your child, or that you/your child will need extra check ups while taking it.
- **Remember to tell your/your child's physician** if you/he start/s taking any other medicines while taking Malarone.

Use of the medicine and food

Take/give Malarone with food or a milky drink, where possible. This will increase the amount of Malarone your body/child's body is able to absorb, and make your/his treatment more effective.

Pregnancy and breastfeeding

If you are/your child is pregnant, do not take/give Malarone unless your physician recommends it.

→ Consult with your physician or pharmacist before taking/giving Malarone.

Do not breastfeed while taking Malarone, as the ingredients that Malarone contains may pass into the breast milk and harm your baby.

Driving and using machines

If you/your child feel/s dizzy, do not drive.

Malarone makes some people feel dizzy. If this happens to you/to your child, do not drive, do not use machines or take part in activities where you/he may put yourself/himself or others at risk.

Important information about some of the ingredients of the medicine

Malarone contains sodium.

The medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium free'.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the preparation according to the physician's instructions.

Check with the physician or pharmacist if you are uncertain about the dosage and treatment regimen of the preparation.

Take/give Malarone with food or a milky drink, where possible.

The tablets should be swallowed whole.

However, for children who find them difficult to swallow, Malarone Paediatric Tablets may be crushed just before being taken and mixed with food or a milky drink.

There is no information regarding halving.

Regarding Malarone Tablets for Adults, there is no information regarding halving/crushing/chewing.

It is recommended to take Malarone at the same time each day.

If you/your child vomit/s:

For preventing malaria:

- **If you/your child vomit/s within 1 hour of taking Malarone**, take/give another dose straight away.
- **It is important to take the full course of Malarone treatment.** If you have/your child has taken extra tablets due to vomiting, you/he may need another prescription.
- **If you vomit/your child vomits**, it is especially important to use additional precautions, such as mosquito repellents and bednets. Malarone may not be as effective, as the amount absorbed will be reduced.

For treating malaria:

- **If you/your child suffer/s from vomiting and diarrhoea**, tell your/your child's physician. You/your child will need to undergo routine blood tests. Malarone will not be as effective, as the amount absorbed will be reduced. The tests will check whether the malaria parasite has been cleared from your/your child's blood.

The dosage and treatment regimen will be determined by the physician only. The usual dosage is generally:

A. To prevent malaria

◦ Adults

The usual dose for adults is 1 Malarone Tablet **for Adults** (strength for adults: 250 mg atovaquone/100 mg proguanil hydrochloride) once a day, taken as described below.

◦ Children

For children, the dose depends on their body weight:

Weight (kg)	Treatment regimen
11-20	1 Malarone Paediatric Tablet once a day
21-30	2 Malarone Paediatric Tablets (as a single dose) once a day
31-40	3 Malarone Paediatric Tablets (as a single dose) once a day
>40	1 Malarone Tablet for Adults once a day

How to use Malarone Tablets for Adults and Malarone Paediatric Tablets to prevent malaria:

- start taking/giving Malarone 1 to 2 days before travelling to an area which has malaria
- continue taking/giving it every day during your/your child's stay
- continue taking/giving it for another 7 days after your/your child's return to a malaria-free area.

For maximum protection, you/your child must complete the full course of treatment.

B. To treat malaria

- Adults

The recommended dose for adults is 4 tablets of Malarone Tablets **for Adults** (strength for adults: an overall daily dose of 1 g atovaquone/400 mg proguanil hydrochloride) once a day, for 3 consecutive days.

- Children

For children, the dose depends on their body weight:

Weight (kg)	Treatment regimen
5-8	2 Malarone Paediatric Tablets once a day for 3 consecutive days
9-10	3 Malarone Paediatric Tablets once a day for 3 consecutive days
11-20	1 Malarone Tablet for Adults once a day for 3 consecutive days
21-30	2 Malarone Tablets for Adults as a single daily dose for 3 consecutive days
31-40	3 Malarone Tablets for Adults as a single daily dose for 3 consecutive days
>40	4 Malarone Tablets for Adults as a single daily dose for 3 consecutive days

Do not exceed the recommended dosage

If you took an overdose, or if a child has accidentally swallowed the medicine, refer immediately to a physician or proceed to a hospital emergency room, and bring the package of the medicine with you.

If you forget to take/give the medicine

It is very important to take/give the full course of Malarone treatment.

If you forgot to take/give this medicine at the required time, take/give it as soon as you remember, then continue the treatment as before. **Do not take/give extra tablets to make up for the missed dose.** Just take/give the next dose at the usual time.

Adhere to the treatment regimen as recommended by the physician.

Keep taking/giving Malarone for 7 days after you return/your child returns to a malaria-free area. Take/give the full course of Malarone for maximum protection. Stopping early puts you/your child at risk of getting malaria, as it takes 7 days to ensure that any parasites that may be in your/your child's blood resulting from a bite from an infected mosquito are killed.

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 physician or pharmacist.

4. SIDE EFFECTS

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

Look out for the following severe reactions. They have occurred in a small number of people, but their exact frequency is unknown.

Severe allergic reactions – the signs include:

- rash and itching
- sudden wheezing, tightness of the chest or throat, or breathing difficulties
- swollen eyelids, face, lips, tongue or other part of the body.

→ **Contact a physician immediately** if you/your child get/s any of these symptoms. **Stop taking/giving Malarone.**

Severe skin reactions

- skin rash, which may blister and look like small targets (central dark spots, surrounded by paler area with a dark ring around the edge) (*erythema multiforme*)
- severe widespread rash with blisters and peeling skin, particularly occurring around the mouth, nose, eyes and genitals (*Stevens-Johnson syndrome*).

→ **If you notice any of these symptoms contact a physician urgently.**

Most of the other side effects reported have been mild and have not lasted very long.

Very common side effects - effects that occur in more than 1 user in 10

- headache
- nausea and vomiting
- stomach pain
- diarrhoea.

Common side effects - effects that occur in up to 1 user in 10

- dizziness
- sleeping problems (*insomnia*)
- strange dreams
- depression
- loss of appetite
- fever
- rash which may be itchy
- cough.

Common side effects, which may show up in blood tests are:

- reduced numbers of red blood cells (*anaemia*) which can cause tiredness, headaches and shortness of breath
- reduced numbers of white blood cells (*neutropenia*) which may make you more likely to catch infections
- low levels of sodium in the blood (*hyponatraemia*)
- an increase in the level of liver enzymes.

Uncommon side effects - effects that occur in up to 1 user in 100

- anxiety
- an unusual awareness of abnormal beating of the heart (*palpitations*)
- swelling and redness of the mouth
- hair loss
- itchy, bumpy rash (hives).

Uncommon side effects that may show up in blood tests:

- an increase in amylase (*an enzyme produced in the pancreas*).

Rare side effects - effects that occur in up to 1 user in 1,000

- seeing or hearing things that are not there (*hallucinations*).

Other side effects

Other side effects have occurred in a small number of people but their exact frequency is unknown.

- inflammation of the liver (*hepatitis*)
- blockage of the bile ducts (*cholestasis*)
- increase in heart rate (*tachycardia*)
- inflammation of the blood vessels (*vasculitis*) which may be visible as red or purple raised spots on the skin but can affect other parts of the body
- fits (*seizures*)
- panic attacks, crying
- nightmares
- severe mental health problem in which the person loses contact with reality and is unable to think and judge clearly
- indigestion
- mouth ulcers
- skin blisters
- peeling skin
- increased sensitivity of the skin to sunlight.

Other side effects that may show up in blood tests:

- a decrease in all types of blood cells (*pancytopenia*).

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

Reporting of side effects

Side effects may be reported to the Ministry of Health by clicking 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 following link: <https://sideeffects.health.gov.il>

5. HOW SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine, and any other medicine, should be kept in a closed 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 physician.

- 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 30°C.
- Do not throw away any medicine via waste water or household waste. Ask your pharmacist how to throw away medicines that are not in use. These measures will help protect the environment.

6. ADDITIONAL INFORMATION

- In addition to the active ingredients, the medicine also contains:
Low substituted hydroxypropyl cellulose, microcrystalline cellulose, povidone K30, sodium starch glycolate (type A), magnesium stearate, poloxamer 188, pink colour concentrate OY-SR-24972 [hypromellose, titanium dioxide, macrogol 400, red iron oxide (E172)], macrogol 400, polyethylene glycol 8000.
- What the medicine looks like and the contents of the package:
Malarone Tablets for Adults: film-coated, round, pink, biconvex tablets, with one side debossed with "GX CM3". Child-resistant blister package containing 12 or 24 tablets.
Malarone Paediatric Tablets: film-coated, round, pink, biconvex tablets, with one side debossed with "GX CG7". Child-resistant blister package containing 12 or 24 tablets.

Not all pack sizes may be marketed.

- License Holder: GlaxoSmithKline (Israel) Ltd., 25 Basel St., Petach Tikva.
- Manufacturer: Glaxo Wellcome S.A., Burgos, Spain.
- Registration number of the medicine in the National Drug Registry of the Ministry of Health:
Malarone Tablets for Adults: 128-46-30733
Malarone Paediatric Tablets: 128-45-30732

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