

# PREVENTION AND TREATMENT OF MALARIA

## Information for individuals who stay regularly or for long periods in malaria areas.

### 1 General

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Complete prevention of malaria is now no longer possible, and there is no single method for achieving this. Everything is aimed at the possibility of minimising a malaria attack as much as possible. As this risk is no longer zero, information on a correct therapy for any attack is indispensable.

The strategy to be adopted by anyone who finds him/herself in a malaria area is thus also now based on 3 principles:

- Measures for prevention of contact with the malaria mosquito (external repellents)
- In a number of cases chemoprophylaxis for prevention of a malaria attack.
- What to do in the event of an attack of malaria

### 2 External repellents for prevention of exposure

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This means the elimination or reduction of contact with the malaria mosquito. These mosquitoes bite exclusively between dusk and daybreak. It must never be assumed that there are no mosquitoes about simply because one is not aware of them (*Anopheles* mosquitoes scarcely hum at all).

Prevention of contact with the malaria mosquito is in itself already a very effective measure in the prevention of malaria and is particularly useful with young children.

The significance of these measures has increased enormously due to the increasing resistance to the conventional chemoprophylaxis.

- You should use an undamaged mosquito net that is preferably impregnated with a mosquito-repellant and mosquitocidal substance (see further). You should tuck the edges of the mosquito net under the mattress and fasten the net to posts on the 4 corners of the bed or hang it up with a rope on 4 points. The net must be regularly checked for holes. A mosquito net is also used over the baby's cot, perambulator etc..
- You should stay in a room the windows and ventilation grates of which are covered with gauze that does not let in any mosquitoes, or in a room with air-conditioning protected with gauze (if this protection is not there the air-conditioning system can just be an easy point of entry for mosquitoes).

- You can distribute a pyrethrum-based insecticide by spraying or atomization (aerosol or powder can), vaporization (by electrically heated plates: either during the daytime in a sealed room or else at night while sleeping so long as there is good ventilation), or by combustion of an anti-mosquito coil.
- When you are outside of the dwelling in the evenings you should wear clothing that covers the arms and legs as much as possible. You should apply a preferably 20 to 30% DEET-based insect repellent to the remaining parts of the skin that are exposed to mosquito bites and regularly renew this application (every 4 to 6 hours).
- If you are pregnant you are not advised against using these DEET-based repellents, as no side effects of short-term use have been reported, though the possible effects of prolonged use are not known. It is advisable to wash off any repellent residues from the skin when the protection is no longer needed. Side effects in young children have very occasionally been reported (a partial absorption through the skin is possible) and this repellent should therefore be applied to these with the necessary caution. An alternative is to apply the repellent to the clothing, though it must be added that a number of mosquitoes are repelled only from a very short distance (less than 1 cm) by the applied product. Avoid contact with the eyes and mouth. DEET-based products can attack plastic spectacle glasses. Autan-Active® and Mosegor® are good, safe products. The manufacturers advise the use of Autan-Active® for children only if they are over 2 years old.

### 3 Impregnation of the mosquito net

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You can best always treat (impregnate) the mosquito net with an insecticide such as permethrine or deltamethrine, which remain behind as a thin film on the fibres of the net. The insecticide kills or repels any mosquitoes that land on the net before they can bite, and any mosquitoes present in the room are eliminated. These insecticides are safe for humans, even for small children. If used over a baby's cot, you should make sure that the baby cannot get hold of or suck on the net. Preimpregnated mosquito nets are also available on the market.

These products remain active for many months, so long as the mosquito net is not washed.

The minimum quantity of liquid required for completely soaking a synthetic net is usually 800 cc for an individual net or 1 litre for a collective net. For a **cotton mosquito net** the required quantity of fluid is approximately 4 times greater.

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| <ul style="list-style-type: none"><li>▪ Individual net = 10 to 12 m<sup>2</sup> - absorbs 800 cc water</li><li>▪ Collective net = 13 to 15 m<sup>2</sup> - absorbs 1000 cc water</li></ul> |
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The required quantity of permethrine/deltamethrine is dissolved in and mixed well with the required quantity of water. Always wear rubber gloves (contact with the concentrated liquid must be avoided). The net is immersed in the liquid and thoroughly kneaded until all the fluid is absorbed, so that the whole net is thoroughly impregnated. The net should be dried in the shade, as ultraviolet sunlight can decompose permethrine and deltamethrine.

- **Deltamethrine** is active for 12 months (so long as the net is not washed), though the product is not available in small bottles in Belgium. In France and in many French-speaking African countries it is readily available under the name **K-Othrine®** (Roussel Uclaf Company) (2,5% = 25 mg deltamethrine per ml) for the specific purpose of impregnation of mosquito nets. A clearly understandable instruction sheet is supplied with it. A number of professional camping businesses import K-Othrine® directly into Belgium.

**1 ml** of this **2,5%** solution **per m<sup>2</sup>** of surface area of the net is mixed with the ultimately required total quantity of water (gives 25 mg/m<sup>2</sup>).

- Another product is **lambda-cyhalothrine**, which is comparable with deltamethrine, and is obtainable in Kenya under the name **Iconet®** (Zeneca Company), among others.
- Another possible solution to the problem is the use of **Permethrine**, e.g. under the name **Permas®** (Edialux Company) **100 ml** (10% = 10 g permethrine or 100 mg/ml) obtainable via the big drugstores. Permethrine remains active for 6 months (so long as the net is not washed). This product is not actually registered as impregnating fluid for synthetic mosquito nets, though as the vital importance of impregnation of mosquito nets has been recognized for years by the World Health Organization, these guidelines also apply to it, in anticipation of the appearance of commercial products on the Belgian market.

5 ml of this 10% solution per m<sup>2</sup> of surface area of the net is mixed with the ultimately required total quantity of water (gives 500 mg/m<sup>2</sup>; the concentration being 40 times higher than for deltamethrine, as deltamethrine is 40 times more active).

- **Permethrine Tropenzorg®** has also recently become available via the specialist camping and outdoor sports businesses. In other countries (including France) permethrine is available under the name **Peripel®** (Wellcome Company).

- **Permethrine** can also be used for impregnating cotton ankle- or armbands, and even **outer clothing** (such as army uniforms) (concentration: approximately 2 g/l), e.g. 10% Permas® 100 ml: dilute 1 part with 50 parts water, or 0.2% BioKill® 500 ml: use undiluted. Note: Direct contact with the skin must be avoided, the impregnated bands or articles of clothing are worn over other clothing! Impregnation of outer clothing is indicated only in very specific cases. Only the outside of the outer clothing may be treated with a spray.

## 4 Taking of tablets for prevention of malaria

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### 4.1 General

In the past prophylaxis was simple. **Chloroquine (NIVAQUINE®)** was always active everywhere against the most important and most dangerous form of malaria, namely that caused by *Plasmodium falciparum*. As resistance has increasingly occurred and steadily become more widespread, this is no longer the case. There are however gradations in this increasing resistance.

- Resistance does not mean that chloroquine is generally no longer effective. In a number of cases activity still remains (though this varies greatly with the country or the area). Symptoms might become milder or even temporarily suppressed, though unfortunately insufficient to definitively control the disease (even after a high dose of chloroquine has been taken). Nivaquine® frequently delays development of dangerous complications by keeping the number of parasites in the blood rather low.
- The fact that resistance to chloroquine is present in a certain area, does not mean that 100% of the malaria strains are less sensitive or totally insensitive. It concerns a certain percentage, which will increase in the course of the coming years. In a number of places this may have already reached 100% (especially in Southeast Asia and on the east coast of Africa).

Chloroquine thus remains partly active in areas where resistance to chloroquine is present, and continues to offer practically 100% protection against attack by the other types of malaria (see below). Chloroquine is for the moment maintaining its position as prophylactic medicine, though it nearly always has to be supplemented with another medication, namely with **proguanil (PALUDRINE®)**. Nivaquine alone is still adequate in some malaria areas (including North Africa and Central America).

**Mefloquine (LARIAM®)** is now also used as chemoprophylaxis; and if necessary Lariam®

may continue to be taken for months or even years. In exceptional cases one should take **doxycycline** for a long time as prophylactic.

Individuals who come to live for the first time in a certain malaria area should usually take prophylactic medications for the first few months and sometimes for the first few years, as malaria infections can very quickly lead to dramatic and life-threatening situations.

The guidelines in connection with the malaria prophylaxis to be adopted should in fact be according to the country and the area, the season and the living conditions. Advice on prevention of malaria will therefore often be "personalised"! See also : <http://www.itg.be/>

Prophylaxis is preferably started one week before departure to see whether the medication is tolerated sufficiently well. If you have never taken mefloquine before, you should start taking it 3 weeks before departure. You should in principle continue taking these medications for 4 weeks after returning home, as the incubation or maturation period of malaria can last for several weeks.

These antimalaria agents do not prevent a malaria infection, but act on the young parasitic forms that attack the red blood cells after they have matured in the liver. Administration of these substances thus prevents the malaria from developing into a genuine disease attack. As chloroquine and mefloquine have a rapid action, they can in selected cases also be used as treatment, though then in higher doses (see part III). Proguanil on the other hand acts very slowly and hence is only prophylactically active. It is therefore certainly not suitable for treating an attack. Doxycycline in combination with quinine is also used as treatment.

The combination Nivaquine® - Paludrine®, and for a number of selected cases Lariam®, is now considered to be the best possible chemoprophylactic when dosing for several years is necessary. The choice of these medications over all the other medications (such as Camoquine® or Flavoquine®, Daraprim®, Maloprim® and Fansidar®) is determined by the fact that they are very safe, satisfactorily effective medications. All other medications have a very small but nevertheless real risk of serious and even fatal side effects if taken for a long time.

## 4.2 Prevention of malaria with Nivaquine®-Paludrine®

For adults :

- **Chloroquine (NIVAQUINE®)** : 3 x 100 mg tablets to be taken in one dose once per week, e.g. on Sundays, or in some cases 1 x 100 mg tablet per day. This medication is best taken during or after a meal.
- **Proguanil (PALUDRINE®)** : 2 x 100 mg tablets per day in one dose (or one tablet each morning and one tablet each evening), during a meal.

- NB: **Savarine®**, 1 tablet of which contains 100 mg Chloroquine and 200 mg Paludrine®, is now available in France and in a number of French-speaking African countries. Dose: 1 tablet per day, every day.

Modified dose for children:

- **Chloroquine (NIVAQUINE®)**: 5 mg per kg bodyweight, in one dose per week.
- **Proguanil (PALUDRINE®)**: 4 mg per kg bodyweight, in one dose (or one dose in the morning and once in the evening) per day, rounded upwards.

	<b>Paludrine®</b>		<b>Nivaquine®</b>
<b>Weight</b>	<b>Daily dose in 100 mg tablets</b>	<b>Weight</b>	<b>Weekly dose in 100 mg tablets</b>
5-8 kg	0,25	5-6 kg	0,25
9-16 kg	0,5	7-10 kg	0,5
		11-14 kg	0,75
		15-18 kg	1
17-24 kg	0,75	19-24 kg	1,25
25-35 kg	1	25-35 kg	2
36-50 kg	1,5	36-50 kg	2,5
> 50 kg	2	> 50 kg	3

“International Travel and Health - Vaccination requirements and health advice”, WHO

- N.B. Chloroquine tablets should be kept out of reach of children! There have been regular reports of fatal cases of intoxication in children who have accidentally taken an overdose.
- Side effects : These medications are very safe. Both of them can cause some gastric or intestinal discomfort. Nivaquine® may also be associated with complaints of slight diminishment of visual acuity. Itching and/or skin rash occurs occasionally. These discomforts disappear after the medication has been stopped. After 5 years of use of Nivaquine® in the above-named dose an ophthalmologist should be consulted every two years in order to detect the beginning of possible irreversible damage to the eye resulting from accumulation. Generally speaking, we can however state that these two medications are very safe (certainly in comparison with others) and that any side effects can be kept in check.

- **Pregnant women** should always take malaria prophylaxis. There is no contraindication whatever for the combination Nivaquine®-Paludrine®. The normal dose has never had any detrimental effect. On the contrary, any malaria attack is much more dangerous both for the pregnant woman and for the unborn child. Lariam® is permitted in the second trimester of pregnancy.

### 4.3 Prevention of malaria with Lariam®

- **Lariam®** 1 tablet per week. You start taking this medication at least 1-2 weeks before departure, though if there is sufficient time, and certainly if you have never taken the medication before, **it is better for you to start 3 weeks before departure** (in order to detect any side effects such as dizziness, insomnia, nightmares, excitation, inexplicable anxiety, cardiac palpitations). You should continue to take the medication for 4 weeks after leaving the malaria area. If Lariam® is tolerated well, it may in selected cases be taken for **many months and even for years**.
- For children the weekly dose of **Lariam®** (4-5mg/kg) is modified as follows:

Lariam®	
Weight	Weekly dose - 5 mg/kg/week In 250 mg tablets
<5 kg	Not advised
5-12 kg	0,25
13-16 kg	0,33
17-24 kg	0,5
25-35 kg	0,75
36-50 kg	1
>50 kg	1

“International Travel and Health – Vaccination requirements and health advice”, WHO

- Lariam® is not given to pregnant women (in considered circumstances it can certainly be taken from the 4th month of pregnancy) nor to children weighing less than 5 kg. Women who take Lariam® as prophylaxis or as treatment should make sure that they continue to use effective contraception for three months after the last dose.

#### 4.4 Alternatives for prevention of malaria for (frequent) short trips

- **Malarone®** 1 tablet/day, 1 day before departure until 7 days after returning home; for a trip of at most 4 weeks (Malarone® can be used by children weighing over 11 kg; but not by pregnant women).
- **Doxycycline** 1 tablet/day, 1 day before departure until 4 weeks after returning home (not for children under 8 years old or for pregnant women. Doxycycline should be taken while sitting and with plenty of liquid or during a meal. Doxycycline can sometimes give rise to fungal infections of the mouth and genitals and phototoxic skin rash).
- The aforesaid malaria prophylaxis is especially aimed at preventing an attack of malaria by *Plasmodium falciparum*. There are other forms of malaria (caused by *Plasmodium vivax*, *ovale*, *malariae*) that may lead to severe symptoms of the disease, though these will only very exceptionally be life-threatening. These forms of malaria have hitherto always remained sensitive to chloroquine, whereas they are occasionally insensitive to proguanil. It is for this reason, among others that chloroquine still remains part of the chemoprophylaxis in a number of areas where chloroquine-resistant malaria is present. These 3 plasmodium species may be responsible for belated attacks or relapses of malaria, e.g. after return to the country of origin. The parasite can in fact remain present in dormant form in the liver (*P. vivax*, *P. ovale*) or in the blood (*P. malariae*) for many months to several years before eliciting a fresh attack. These malaria attacks are characterised by regular bouts of fever every 48 hours alternating with fever-free periods. This requires treatment (3 days with chloroquine, followed by 14 days with primaquine) in a centre equipped to carry out malaria treatment.

## 5 What to do in the event of an attack of malaria

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### 5.1 General

One can develop a certain resistance (immunity) after repeated contacts with the malaria parasite during a long stay in the tropics. However, prolonged stays in the tropics in themselves offer no guarantee of immunity, and most people who live in the tropics do not build up any noticeable immunity. This immunity is moreover never a total immunity. It does not protect against repeated infection, as one is bitten by the malaria mosquitoes just as much as before. One may perhaps get seriously ill less quickly, which gives one somewhat more time to start a correct therapy. When one stays away from a malaria area for more than 6 months, one loses most of the acquired immunity, since this is maintained by repeated malaria infections. This same problem arises in areas where malaria occurs during only a part

of the year (wet season).

Individuals who stay a long time in the tropics can often stop taking oral prophylaxis, usually without serious consequences. If after several months (or after several years) you decide to stop taking the prophylactic medication, it is of the utmost importance **(1)** to give yourself maximum protection against mosquito bites in the evenings and at night, **(2)** you should be able to recognize (or at any rate suspect) a possible malaria attack and to treat it correctly. For growing children, pregnant women and individuals who for some reason or other have been weakened, it is often too risky not to take any prophylactic medication. Tourists who stay in malaria areas only for short periods do not find themselves in the same situation as individuals who have already lived for a long time in the tropics. They find themselves in a much more vulnerable position and also continually move around from place to place, with continually varying risk of malaria. The taking of prophylactic medications is also very important for them.

**Any rise in body temperature** (above 38°C in the armpit) continuing for more than 24 hours that occurs during or within up to three months after a stay in an area where malaria occurs must be regarded as an attack of malaria until the contrary is proved, and demands swift medical action. Make sure that you always have a thermometer to hand and regularly check your body temperature whenever you feel unwell, even if you do not think that you have a fever or high temperature! Many infectious diseases in fact begin with the same symptoms (feverish feeling, with or without fever / high temperature), which means that if you have a high temperature you should also think of other infectious diseases. If at all possible medical help should therefore always be sought and a thick smear investigation and a thin blood smear should be carried out.

If **warning symptoms** are present, e.g. if the fever / high temperature persists for more than 3 days, if the urine turns a dark colour, or if jaundice, shortness of breath or diminished consciousness occurs, urgent admission to hospital is indicated.

The following **treatment schemes** have been selected as their efficacy is nearly 100%. Many other schemes are possible, but are certainly less effective.

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| <p><b>A. MALARONE®</b></p> <p><b>B. QUININE + DOXYCYCLINE</b></p> <p><b>NB. HALFAN®</b></p> <p><b>NB. QUININE + FANSIDAR®</b></p> <p><b>NB. LARIAM®</b></p> |
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The new medicine **Artemisinin and its derivatives** are now available in various countries in the Far East (including Vietnam, Thailand and Burma), as well as in several countries in Sub-

saharan Africa. These derivatives include artemether + lumefantrine = Co-artem® (manufactured in Africa) / Riamet® (manufactured in Switzerland); artesunate = Artenam® / Arinate® (manufactured in Africa, though there are many other local brand names). None of these products is as yet registered in Belgium or in Europe. This very effective medication may replace quinine in the various named combinations for treatment of resistant malaria.

- The total dose for **Riamet®** is six times 4 tablets: 4 tablets at the time of diagnosis, 4 tablets 8 hours later, and then 4 tablets every 12 hours for a further 2 days (the **Co-artem®** package insert states that 4 x 4 tablets are sufficient, though a non-immune individual is advised to take 6 x 4 tablets, as indicated for Riamet ®, which is identical to Co-artem®)
- The dose for **Artenam/Arinate®** is 200 mg the first day, followed by 100 mg per day for the next 4 days. When this medication is used alone there is a small risk of recurrence of malaria. The combination with doxycycline or even with mefloquine, such as with quinine, is therefore advised (certainly in the Far East) upon recurrence.

## 5.2 Schema A - Malarone

A new extremely active medication for uncomplicated malaria is the product **Malarone®** (contains two ingredients in one tablet: 250 mg atovaquone + 100 mg proguanil; costs approximately Euro 45. One carton contains 12 tablets, and an adult takes 4 of these tablets in one dose per day, for three consecutive days at the same time each day, with a little food. For children (above 11 kg bodyweight) a dosage modification is necessary:

- 11-20 kg: 1 tablet/day, 3 consecutive days
- 21-30 kg: 2 tablets/day in one dose, 3 consecutive days
- 31-40 kg: 3 tablets/day in one dose, 3 consecutive days.

## 5.3 Schema B - Quinine + Doxycycline

- **QUININE** (capsules of 500 mg quinine sulphate) or **QUINIMAX®** (500 mg tablets, not available in Belgium): for an **adult, 500 mg** every 8 hours for 4 days. If the high temperature drops slowly, it is then best to take the quinine for a few days longer at the rate of 1 capsule every 12 hours. In Southeast Asia and in the Amazon region quinine should be taken for 7 days.

You also start taking (if you have a tendency to vomit wait until the 3<sup>rd</sup> day):

- either **DOXYCYCLINE (VIBRAMYCINE®, VIBRATAB®, DOXYLETS®)**, 2 x 100 mg tablets (= 3,5 mg/kg bodyweight) on the 1st day, followed by 1 x 100 mg tablet (= 2 mg/kg) bodyweight per day for the next 6 days.
- or **TETRACYCLINE** 20 mg/kg bodyweight (max. 3 x 500 mg/day) for 7 days.

The dose is modified for **children** over 8 years old according to their bodyweight (quinine:

identical scheme such as for adults; 10 mg/kg bodyweight) every 8 hours.

- This combination is still 100% effective in Africa and Latin America and almost 100% effective in Asia.
- Quinine sulphate must be prepared by the pharmacist. If the capsules are contained in a properly sealed brown glass bottle with a drying capsule, they can be kept for **1 year** (this storage time is much shorter in a carton).
- If you attempt to treat a malaria attack with quinine alone (e.g. just with Quinimax®) there is a small but real risk of later recurrence of malaria, as it is not always possible to eradicate up to the last parasite with this medication.
- Tetracycline and doxycycline alone are too weak as antimalaria agents. They must therefore **always be combined with quinine**.
- If you vomit up the medication, quinine must be administered for a few days via intravenous infusion, in the same dose, every 8 hours, each time by drip over 4 hours (as quinine dihydrochloride solution). As soon as you are better, quinine is then taken orally, supplemented with tetracycline or doxycycline.
- If an infusion is not possible, quinine can be given intramuscularly (in the thigh muscle) in the same dose every 8 hours (= 3 injections per day). **(NEVER INJECT QUININE OR ALLOW IT TO BE INJECTED INTRAVENOUSLY WITH A SYRINGE: RISK OF CARDIAC ARREST OR FATAL LOWERING OF BLOOD PRESSURE)**.
- Administration of tetracycline or doxycycline can elicit cutaneous hypersensitivity reactions upon exposure to sunlight. Caution should therefore be exercised concerning exposure to sunlight.

Tetracycline and doxycycline are not permitted for **children under 8 years old** or for **pregnant women** (because of possible tooth discoloration). In case of Fansidar resistance or sulphonamide allergy and if mefloquine is not available, quinine can be given in this group for 7 to 10 days. Malarone® should not be given to pregnant women.

Quinine drops can be given to **infants** in a dose of 10 mg (= 1 drop) per kg bodyweight every 8 hours (= 3 x per day) for 7 days (the stated dose must not be exceeded).

R/	Quinine dihydrochloride	6 g	12 g	18 g
	Sodium metabisulphite	15 mg	30 mg	45 mg
	Aqua (water) ad	30 ml	60 ml	90 ml
In brown bottle with a drop counter per ml (20 drops per ml)				

## 5.4 Alternative Scheme 1 : Halofantrine

- **HALOFANTRINE (HALFAN®)**, in 250 mg tablets (6 in 1 carton) or in syrup (but not obtainable in Belgium - 100 mg per 5 ml, 45 ml). Only oral ingestion is therefore possible.
- For adults and children weighing more than 40 kg: 3 doses of 2 tablets every 6 hours fasting (on empty stomach)! It is advisable to repeat this course after 1 week.
- For children under 40 kg: see package insert.
- Must not be used by pregnant and breast-feeding women.
- Possible side effects are gastrointestinal discomfort, itching, skin rash.
- Recent reports indicate that very occasionally the administration of Halfan® is associated with fatal cardiac rhythm disturbances. **Halfan® is therefore no longer recommended as self-medication for emergency treatment of a suspected malaria attack (without supervision of a doctor)**. However, if a patient decides to use it this can only be on condition that a previously recorded electrocardiogram was normal (that is, if the so-called "Q-T interval" was normal). Halfan® is only safe as medication if no Lariam® has been taken in the previous 4 weeks and no quinine has been taken in the previous 24 hours. This also applies for a number of other medications such as medicines for cardiac rhythm disorders, antidepressants, antiallergy agents such as Triludan®, certain antibiotics such as erythromycin and diuretics such as Lasix®, etc. It is therefore best not to take Halfan® if you are also taking other medications and if you are not sure whether the combination is safe. **Halfan® should now be totally replaced by MALARONE®.**

## 5.5 Alternative Scheme 2: Quinine + Fansidar

- First few days **QUININE** or **QUINIMAX®** as in scheme B.
- You may also take **FANSIDAR®** (no longer available in Belgium), 3 tablets in one dose. (If you have a tendency to vomit you should wait until the third day).
- If the high temperature falls slowly, it is best to continue taking the quinine for a few more days after this.
- The modification of the dose of Fansidar® for **children** must take place as follows (in proportion to the bodyweight):

children under 10 kg	½ tablet
children between 10 and 20 kg	1 tablet
children between 20 and 30 kg	1½ tablet
children between 30 and 50 kg	2 tablets
children over 50 kg	3 tablets

- Fansidar® is not given to **infants** from 0 to 2 months old.

- Quinine drops (see above) can be given to these, likewise in a dose of 10 mg (= 1 drop) per kg bodyweight every 8 hours (= 3 x per day) for 7 to 10 days (the stated dose must not be exceeded).
- Fansidar® may only be taken if there is no known allergy to sulphonamides.
- If it is a case of a mild, uncomplicated malaria attack, it can be treated with Fansidar® alone. It must then of course be remembered that a further 1 to 2 days will usually pass before Fansidar® has any obvious effect. This is one reason for always combining Fansidar® with quinine, especially when symptoms are really serious.
- There are a number of areas where resistance to Fansidar® has been reported; in the Far East this resistance is frequent. This is the principal reason why Fansidar is always best in combination with quinine. If the fever does not go down after 2 days, or if the symptoms reappear again after a few weeks, resistance to Fansidar® is likely. In this case see Scheme A of B.

## 5.6 Alternative Scheme 3: Mefloquine

- **Mefloquine (LARIAM®)** (250 mg tablets) in a short course of 25 mg/kg, spread over 3 doses, one every 8 hours (12,5 - 7,5 - 5 mg/kg respectively). This means for an average **adult** respectively 3 x 250 mg tablets – 2 x 250 mg tablets – 1 x 250 mg tablet with an interval of 8 hours between each dose. The maximum total dose amounts to 1500 mg (6 x 250 mg tablets).
- The dose is adjusted for **children** in proportion to the bodyweight: 12,5 mg per kg, followed by 7,5 mg per kg, followed by 5 mg per kg with an 8 -hour interval between each dose.
- After administration of mefloquine the fever does not disappear immediately but may persist for up to a further three days. If you are seriously ill or if the risk of vomiting up of medication is too great, you are advised to treat the illness just for a few days with **QUININE** (see scheme B). In these circumstances it is in any case best to administer quinine intravenously or intramuscularly just for a few days. Administration of mefloquine is then started again 12 hours after the final quinine dose (in contrast to Fansidar® and doxycycline, which may continue to be administered together with quinine).

The World Health Organization recommends the following dose for an adult who on his own initiative is taking Lariam® as emergency treatment: 2 x 250 mg tablets, followed by 2 x 250 mg tablets after 8 hours. This dose is smaller than that stated on the package insert! This dosage adjustment is made because Lariam® frequently has unpleasant side effects (gastrointestinal upsets, dizziness, excitation, cardiac palpitations, nightmares and insomnia), which can sometimes be very pronounced and can put the already sick person into a panic. These side effects should occur less frequently with this lower dosage. In our opinion there are sufficient reasons for not taking any Lariam® at all as self-medication if no adequate medical

supervision is possible.

## 5.7 Treatment of pregnant women

- During the first three months and during the last few weeks of pregnancy: quinine 3 times per day for 7 days.
- During the second three months (trimester) of pregnancy you can be treated either with quinine alone for 7 days, or with quinine and Fansidar (Fansidar® is permitted in this period) or with quinine with clindamycin.
- NOTE: If however you decide to treat a malaria attack with chloroquine alone (e.g. if you find yourself in an area where THE CHANCE OF CHLOROQUINE RESISTANCE IS VERY SLIGHT OR NON-EXISTENT, and if you have not taken any chloroquine as prophylaxis and you have commencing symptoms of possible malaria), it is of the utmost importance to do this in a correct manner: 25 mg/kg bodyweight for 3 days, no shorter and no longer.

### NIVAQUINE®

	<b>For adults</b>	<b>For children</b>
Day 1	6 x 100 mg tablets in one dose 3 x 100 mg tablets 8 hours later	10 mg/kg
Day 2	3 x 100 mg tablets	10 mg/kg
Day 3	3 x 100 mg tablets	5 mg/kg

- If chloroquine has no effect after 24-48 hours, resistance must be assumed. If a recurrence of the symptoms occur within 3 to 4 weeks it must likewise be assumed that the original malaria parasite has not been eradicated and that a (partial) resistance to chloroquine is involved. Under the influence of the semi-active chloroquine or Fansidar® the symptoms of malaria are sometimes much less clearly recognizable (for example, only mild fever, headache, fatigue).
- In all these situations it is important not to continue treatment with chloroquine but to change over immediately to schema A or B.

## 5.8 Concluding remarks

Many conflicting opinions on malaria are going around, contradictory advice is being given by medical practitioners and malaria specialists, and well-meaning opinions are being expressed to their immediate circle of acquaintances by people who have already spent a great deal of time in the tropics. As the situation is constantly changing, there are many unanswered questions.

This also explains why the opinions have had to be repeatedly reviewed during the last 10 years, and will continue to be modified in the future.

The purpose of this information folder is to set the current practical knowledge on a correct basis and to offer a logical approach.

Discuss the content of this folder with your treating doctors, and pass this information on to others.

## 5.9 Summary: prevention and treatment of malaria

Information for individuals staying for long periods in malaria areas

### External repellents for prevention of exposure

- Between sunset and sunrise: Impregnated mosquito net – mosquito gauze – air-conditioning - covering clothing – mosquito repellent on the skin, spraying, vaporization, antimosquito coil.

### Taking of tablets

- **Chloroquine (NIVAQUINE®)**: 3 x 100 mg tablets taken in one dose, 1 x per week, e.g. on Sundays, during a meal, or in some cases 1 tablet/day.
- **Proguanil (PALUDRINE®)**: 2 x 100 mg tablets per day in one dose (or one tablet each morning and one tablet each evening), during a meal.
- **SAVARINE®** (= combination of chloroquine and proguanil): 1 tablet per day
- **Mefloquine (LARIAM®)**: 1 tablet per week, e.g. on Sundays, during a meal. You start this medication at least 1 week before departure, but if there is sufficient time, and certainly if you have never taken the medication before, it is better for you to start 3 weeks before departure to detect any side effects. You continue to take the medication for up to 4 weeks after returning home. If Lariam® is tolerated well, it can be taken for many months or even years.

**What to do if you have an attack of malaria**

- Most effective scheme at present: **MALARONE®** (4 tablets/day – 3 days)

OR

- **QUININE**, 10 mg/kg (max. 600 mg) every 8 hours. For an average adult this means an average of 3 x 500 mg quinine sulphate tablets or 3 x 7 tablets of 100 mg Quinimax® per day for 4 days.

You also start (unless you have a tendency to vomit, when you wait until the third day):

- **DOXYCYCLINE (VIBRAMYCINE®, VIBRATAB®, DOXYLETS®)** 2 x 100mg tablets (= 3,5 mg/kg) on the 1<sup>st</sup> day, followed by 1 x 100 mg tablet (= 2 mg/kg) per day for the next 6 days.
- **Not for pregnant women or children under 8 years old !**