HAUTE AUTORITÉ DE SANTÉ

The legally binding text is the original French version

TRANSPARENCY COMMITTEE

OPINION

19 March 2008

MALARONE, film-coated tablet
Box of 12 (CIP: 344 298 0)

MALARONE 62.5 mg/25 mg PAEDIATRIC, film-coated tablet
Box of 12 (CIP: 362 264 7)

Applicant : GLAXOSMITHKLINE

Atovaquone/proguanil
ATC Code: P01BB51
List I

Marketing authorisations dates:
MALARONE, film-coated tablet: 28 August 1997
MALARONE 62.5 mg/25 mg PAEDIATRIC: 16 June 2003

Reason for request:

The Committee has been asked by the Ministry for Health and Solidarity to consider:

1) the opportunity for National Health Insurance to reimburse malaria chemoprophylaxis for insured individuals not living in malaria-endemic areas of Guiana who travel once or infrequently to malaria-endemic areas and spend less than three months there.

2) The opportunity to extend the reimbursement of malaria chemoprophylaxis to include insured individuals who are residents of Mayotte.

Health Technology Assessment Division

1. CHARACTERISTICS OF THE MEDICINAL PRODUCT

1.1. Active ingredient

MALARONE, film-coated tablet
atovaquone……. 250 mg
proguanil……. 100 mg

MALARONE 62.5 mg/25 mg PAEDIATRIC, film-coated tablet
atovaquone……. 62.50 mg
proguanil……. 25.00 mg

1.2. Therapeutic indications

- MALARONE, film-coated tablet

"Treatment of simple (uncomplicated) acute malaria caused by *Plasmodium falciparum*.

Prophylaxis of malaria caused by *Plasmodium falciparum* especially among people travelling to malaria-endemic areas where strains resistant to amino-4-quinolines (e.g. chloroquine, amodiaquine) are rampant.

- MALARONE 62.5 mg/25 mg PAEDIATRIC, film-coated tablet

Prophylaxis of malaria caused by *Plasmodium falciparum* especially among people travelling to malaria-endemic areas and where strains resistant to amino-4-quinolines (chloroquine, amodiaquine, etc.) are rampant."

1.3. Dosage and method of administration

- **MALARONE, film-coated tablet**

For oral use.

The tablets should be taken with food or a milky drink to promote the absorption of atovaquone.

Curative treatment of acute malaria caused by Plasmodium falciparum:

Adults and children aged 12 and over: four tablets taken together once a day for three consecutive days, at the same time each day.

Appropriate dosages and conditions of use for curative treatment of acute malaria caused by *Plasmodium falciparum* have not been established in subjects under 12 years of age.

Prophylaxis of malaria caused by Plasmodium falciparum:

Adults and children weighing 40 kg or more: one tablet a day at the same time each day.
Treatment should start either the day before or the day of departure to the malaria-endemic area. It should continue throughout the stay and for seven days after leaving the malaria-endemic area.
Malarone treatment should not exceed three months in this indication.

Malarone 62.5 mg/25 mg is the recommended form for individuals weighing less than 40 kg.

Elderly subjects:
There are no particular precautions or dose adjustments needed for elderly subjects.

Hepatic impairment:
No dosage adjustments are needed for individuals with mild to moderate hepatic impairment. However, since no studies have been conducted on individuals with severe hepatic impairment, the efficacy and safety of this medicinal product on this type of patient have not been determined.

Renal impairment:
No dose adjustment is necessary in individuals with mild to moderate renal impairment.
The prophylactic use of Malarone is contraindicated in individuals with severe renal impairment (creatinine clearance < 30 ml/min). To treat acute malaria in individuals with severe renal impairment, it is appropriate, whenever possible, to use an alternative form of curative treatment.

- **MALARONE 62.5 mg/25 mg PAEDIATRIC, film-coated tablet**

For oral use.

The tablets should be taken with food or a milky drink to promote the absorption of atovaquone.

In children under six, the tablets must be crushed before administration due to the risk of aspiration.

Treatment should start either the day before or the day of departure to the malaria-endemic area. It should continue throughout the stay and for seven days after leaving the malaria-endemic area.

Malarone treatment shoud not exceed three months in this indication.

Prophylaxis of malaria caused by *Plasmodium falciparum*:

Children weighing 11 to 20 kg: one tablet a day at the same time each day.

Children weighing 21 to 30 kg: two tablets a day at the same time each day.

Children weighing 31 to 40 kg: three tablets a day at the same time each day.

Individuals weighing over 40 kg: four tablets a day at the same time each day.

The Malarone 250 mg/100 mg film-coated tablet formulation has a higher dose and is better suited to individuals weighing over 40 kg and children over the age of twelve.

Appropriate dosages and conditions of use for prophylactic treatment of malaria caused by *Plasmodium falciparum* have not been established in subjects weighing less than 11 kg.

Hepatic impairment:

No dosage adjustment is needed for individuals with mild or moderatehepatic impairment. However, since no studies have been conducted on individuals with severe hepatic impairment, the efficacy and safety of this medicinal product on this type of patient have not been determined.

Renal impairment:

No dosage adjustment is needed in individuals with mild to moderate renal impairment.

The prophylactic use of Malarone is contraindicated in individuals with severe renal impairment (creatinine clearance < 30 ml/min).

2 TRANSPARENCY COMMITTEE CONCLUSIONS

2.1. Actual benefit

2.1.1. Seriousness of the disease

Malaria is a serious illness since it can be life-threatening if caused by *Plasmodium falciparum*. Furthermore, resistance of this species to certain antimalarial medications occurs frequently. This parasitosis is the subject of a WHO control programme [1].
Chemoprophylaxis is mainly used when there is a risk for *Plasmodium falciparum* infection, the outcome of which can be life-threatening.

2.1.2. Efficacy/adverse effects

The combination of atovaquone and proguanil is effective in preventing and treating malaria caused by chloroquine-resistant *P.falciparum*. Its efficacy is equivalent (i.e. > 95 %) to that of the mefloquine used for chemoprophylaxis of chloroquine-resistant *P. falciparum*[2,3]. The combination of atovaquone and proguanil is also effective in preventing malaria caused by mefloquine-resistant *P. falciparum* (in the forested areas of Thailand bordering on Cambodia, Myanmar and Laos).
The combination of atovaquone and proguanil has a good safety and tolerance profile when used in the chemoprophylaxis of malaria[4]. The most common adverse events that occur during treatment are gastrointestinal (vomiting, nausea, diarrhoea and abdominal pain).

2.1.3. Therapeutic use

The Committee relies on the guidelines issued by the High Council for Public Health[5], which drafts annual directives intended for travellers, including antimalarial chemoprophylaxis procedures, depending on the areas visited. The choice of antimalarial drug depends on:

- the place visited
- the pharmacokinetics, safety and efficacy of antimalarial drugs on resistant strains
- the traveller's age
- the length of stay in a malarial area
- individual contraindications, especially in persons taking other medicines and in pregnant women.

Appendix 1 indicates the risk of malaria and recommended chemoprophylaxis according to the areas visited (classified by WHO as group 1, 2 and 3, according to the frequency of resistance to chloroquine and proguanil).

The atovaquone-proguanil combination is one of the medicines of choice, along with mefloquine and doxycycline, to prevent malaria in people travelling to areas where the prevalence of chloroquine resistance and multiresistance is high (groups 3). It is an alternative to the proguanil/chloroquine combination for preventing malaria in travellers going to areas where chloroquine resistance is rare or moderate (group 2). It can be prescribed for adults, children weighing at least 11 kg and pregnant women[6], provided that the contraindications and precautions that have been laid down are respected.

The actual benefit of these medicinal products is substantial.

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1 World Health Organization. Guidelines for the treatment of malaria.
2 Overbosch D. et al. Atovaquone-proguanil versus mefloquine for malaria prophylaxis in non-immune travelers: results from a randomized, double-blind study. Clin Infect Dis. 2001 Oct 1;33(7):1015-21.
3 Croft AMJ. Et al. Mefloquine for preventing malaria in non-immune adult travellers (review). The Cochrane library 2007, issue 3, Art. N°CD000138. DOI: 10. 1002/14651 858. CD000138 .
4 Antimalarial Drug Toxicity. Drug safety 2004: 27 (1): 25-61
5 Recommendations issued every year in the *Bulletin Epidémiologique Hebdomadaire* (BEH-Weekly Epidemiological Bulletin) published by the *Institut de Veille Sanitaire* (Health Monitoring Institute) (www.invs.sante.fr), under the sponsorship of the French Superior Council for Public Hygiene (HCSP) – Health recommendations for travellers – meeting of 12 June 2007.
6 Monitoring pregnancies that are exposed to the combination of atovaquone-proguanil cannot rule out all risk. Therefore, MALARONE may be considered for pregnant women if necessary (see SPC).

2.2. Transparency Committee recommendations

Given that French Guiana and Mayotte are classified among group 3 countries (area of high prevalence of chloroquine-resistant and multiresistant *P. falciparum* [resistance to proguanil-cycloguanil and pyrimethamine]), the only antimalarial drugs that can be used for prophylaxis are mefloquine, atovaquone-proguanil or doxycycline. However, these treatments are not suitable for small children. Atovaquone-proguanil is indicated for chemoprophylaxis in children weighing 11 kg and over and mefloquine is indicated in children weighing 15 kg and over, while doxycycline is contraindicated in children under 8 years of age and in pregnant and breast-feeding women.

In very rare cases, chloroquine + proguanil may represent an alternative to the recommended first-line antimalarial drugs (mefloquine, doxycycline, and atovaquone-proguanil) in the event of contraindications, poor tolerance or unsuitable dosage (especially in children under 2-3 years of age).

Offering chemoprophylaxis in an malaria-endemic area is only feasible for people who do not live there generally (and are therefore not immune) and who will only be staying temporarily. This chemoprophylaxis recommendation is therefore justified in French Guiana for inhabitants of the coastal strip who need to visit the interior of the region, especially along the rivers on the border.

For the inhabitants of Mayotte (malaria-endemic throughout the area), chemoprophylaxis is only justified in pregnant women by using intermittent preventive and curative treatment[7,8,9], preferably with sulphadoxine-pyrimethamine (FANSIDAR), the treatment currently recommended by the WHO (at least two doses given at least one month a part starting when the first foetal movements are felt. See Appendix 2), or by using mefloquine[10,11] chemoprophylaxis, or by using combined atovaquone-proguanil if mefloquine cannot be prescribed[12]. However, it is essential to improve the availability of insecticide-impregnated mosquito nets for the whole population, and take more effective measures against mosquito breeding areas.

The Transparency Committee recommends inclusion on the list of medicines reimbursed by National Insurance to insured residents of French Guiana who do not live in malarial areas, but pay single visit or occasional visits of under 3 months to malaria-endemic areas.

The Transparency Committee recommends inclusion on the list of medicines reimbursed by National Insurance to insured pregnant residents of Mayotte only. In the other populations, chemoprophylaxis is not justified.

2.2.1. Packaging: appropriate for the prescription conditions
2.2.2. Reimbursement rate: 65%

[7] World Health Organization: Technical Epert Group meeting on intermittent preventive treatment in pregnancy (IPTp). WHO HEADQUARTERS GENEVA 11-13 JULY 2007
[8] World Health Organisation. A Strategic Framework for Malaria Prevention and Control During Pregnancy in the African Region. Brazzaville: WHO Regional Office for Africa, 2004, AFR/MAL/04/01
[9] Organisation mondiale de la santé: Des vies en danger: le paludisme pendant la grossesse. *In: http://www.who.int/reatures/2003/04b/fr/*
[10] Steketee RW, Wirima JJ, Slutsker L et al. Malaria parasite infection during pregnancy and at delivery in mother, placenta and newborn : efficacy of chloroquine and mefloquine in rural Malawi. Am J Trop Med Hyg 1996 ; 55 : 24-32.
[11] Menendes C et al. Reducing the burden of malaria in pregnancy by preventive strategies. The Lancet Infet Dis 2007: 126-135

Appendix 1

Malaria risk and chemoprophylaxis recommended for each country (extract from BEH 24/12 June 2007).

Table 1: List of countries requiring antimalarial chemoprophylaxis, 2007		
Country [1]	**Malaria situation 2007/ chemoprophylaxis [2]**	**For a visit of under 7 days: chemoprophylaxis optional [3]**
Afghanistan	group 3	for the whole country
South Africa	Northeast: group 3; elsewhere: no prophylaxis	
Angola	Group 3	
Saudi Arabia	Southwest: group 3; elsewhere: no prophylaxis	for the whole country
Argentina (*)	North: group 1; elsewhere: no prophylaxis	for the whole country
Bangladesh	Dacca: no prophylaxis rest of country: group 3	
Belize (*)	group 1	for the whole country
Benin	group 3	
Bhutan	group 3	for the whole country
Bolivia	Amazonia: group 3; elsewhere (*): group 1	for the whole country except Amazonia
Botswana	group 3	
Brazil	Amazonia: group 3; elsewhere: no prophylaxis	
Burkina Faso	group 2	
Burundi	group 3	
Cambodia	group 3	
Cameroon	group 3	
China	Yunnan and Hainan: group 3; Northeast (*): group 1	whole country except Yunnan and Hainan
Colombia	Amazonia: group 3; elsewhere: group 2	
Comores	group 3	
Congo	group 3	
Costa Rica (*)	group 1	for the whole country
Ivory Coast	group 3	
Djibouti	group 3	
Ecuador	Amazonia: group 3; elsewhere: group 1	
Eritrea	group 3	
Ethiopia	group 3	
Gabon	group 3	
Gambia	group 3	
Ghana	group 3	
Guatemala (*)	group 1	for the whole country
Guinea	group 3	
Guinea-Bissau	group 3	
Equatorial Guinea	group 3	
Guyana	group 3	
French Guiana	Rivers: group 3; coastal areas: no prophylaxis	
Haiti	group 1	
Honduras (*)	group 1	for the whole country
India	State of Assam: group 3; elsewhere; group 2	
Indonesia	Bali: no prophylaxis; elsewhere: group 3	
Iran	Southeast: group 3; elsewhere (*): group 1	for the whole country
Iraq (*)	group 1	for the whole country
Jamaica	group 1: Kingston only	
Kenya	group 3	
Laos	group 3	
Liberia	group 3	
Madagascar	group 2	

Malaysia	urban or coastal areas: no prophylaxis; elsewhere: group 3	
Malawi	group 3	
Mali	group 2	
Mauritania	group 2	
Mayotte (departmental community)	group 3	for the whole country
Mexico (*)	group 1	for the whole country
Mozambique	group 3	
Myanmar (formerly Burma)	group 3	
Namibia	group 3	
Nepal	Terai: group 2; elsewhere: no prophylaxis	
Nicaragua (*)	group 1	for the whole country
Niger	group 2	
Nigeria	group 3	
Uganda	group 3	
Pakistan	group 3	
Panama (*)	West: group 1; East: group 3	West Panama
Papua New Guinea	group 3	
Paraguay	East (*): group 1; elsewhere: no prophylaxis	for the whole country
Peru	Amazonia: group 3; elsewhere (*): group 1	for the whole country except Amazonia
Philippines	group 3	
Dominican Republic	group 1	
Central African Republic	group 3	
Democratic Republic of Congo (formerly Zaire)	group 3	
Rwanda	group 3	
El Salvador (*)	group 1	for the whole country
São Tomé and Principe	group 3	
Solomon Islands	group 3	
Senegal	group 3	
Sierra Leone	group 3	
Somalia	group 3	
Sudan	group 3	
Sri Lanka (*)	group 2	for the whole country
Surinam	group 3	
Swaziland	group 3	
Tajikistan (*)	group 2	for the whole country
Tanzania	group 3	
Chad	group 2	
Thailand	Border areas with Cambodia, Laos, Myanmar and Malaysia: group 3; elsewhere: no prophylaxis	for the whole country except the borders with Cambodia, Laos, Myanmar and Malaysia
East Timor	group 3	
Togo	group 3	
Vanuatu	group 2	
Venezuela (Amazonia)	Amazonia: group 3; elsewhere (*): group 1	
Vietnam	Coastal strip and deltas: no prophylaxis; elsewhere: group 3	for the coastal strip and deltas
Yemen	group 3	
Zambia	group 3	
Zimbabwe	group 3	

(*) Mainly *Plasmodium vivax.*
(1) In the case of Africa, good knowledge of the areas of resistance visited by French travellers has enabled a zone 2 and a zone 3 to be identified. This distinction does not appear in the WHO or CDC recommendations. A modification should be noted of the WHO classifications since 2005, which define methods for preventing the risk of Malaria (I, II, III, IV) by combining the risk of malaria with the level of chemoresistance.
(2) Group 1: *chloroquine*; group 2: *chloroquine+proguanil* or *atovaquone+proguanil*; group 3: *mefloquine* or *atovaquone+proguanil* or *doxycycline*. See chapter 2.2.3.
(3) In these regions, chemoprophylaxis is not essential for a stay of less than 7 days provided that the traveller is in a position to consult a doctor urgently in the event of fever during the months after returning home.

2.2.3. Chemoprophylaxis according to area

COUNTRIES IN GROUP 0: non-malarial areas - no chemoprophylaxis

Africa: Egypt, Lesotho, Libya, Réunion, Saint Helena, Seychelles, Tunisia.

America: all cities (except in Amazonia) and Antigua and Barbuda, Dutch Antilles, Bahamas, Barbados, Bermuda, Canada, Chile, Cuba, Dominica, United States, Guadeloupe, Grenada, Cayman Islands, Falkland Islands, Virgin Islands, Martinique, Puerto Rico, Santa Lucia, Trinidad and Tobago, Uruguay.

Asia: all cities (except in India) and Brunei, Guam, Hong Kong, Japan, Kazakhstan, Macao, Maldives, Mongolia, Singapore, Taiwan.

Europe: all countries (including the Azores, Canaries, Cyprus, Russian Federation, Baltic States, Ukraine, Belarus and European Turkey).

Near and Middle East: all cities and Bahrain, United Arab Emirates, Israel, Jordan, Kuwait, Lebanon, Qatar.

Australasia: all cities and Australia, Fiji, Hawaii, Mariana Islands, Marshall Islands, Micronesia, New Caledonia, New Zealand, Easter Island, French Polynesia, Samoa, Tonga, Tuvalu, Wallis and Futuna, Kiribati, Cook, Western Samoa, Niue, Nauru, Palau.

COUNTRIES IN GROUPS 1, 2 and 3 (see Tables 1 and 2)
GROUP 1: *areas without chloroquine resistance*
- Chloroquine (Nivaquine® 100)

GROUP 2: areas of chloroquine resistance
- Chloroquine (Nivaquine® 100) and proguanil (Paludrine® 100)
- Combination of chloroquine-proguanil (Savarine®)
- Combination of atovaquone-proguanil (Malarone®)

GROUP 3: areas of high prevalence of chloroquine resistance and multiresistance:
- Mefloquine (Lariam® 250)
- Combination of atovaquone-proguanil (Malarone®)
- Doxycycline monohydrate.

It is not advisable for pregnant women to visit the countries in this group. Note that there are some areas of mefloquine resistance: East Timor, the forest areas of Thailand that border Cambodia, Myanmar (formerly Burma) and Laos.

SPECIAL CASES

Short stays in low-risk areas: for a short stay (under 7 days: the minimum incubation period for malaria caused by *P. falciparum*) in areas with a low risk of transmission, chemoprophylaxis is not essential, provided that the rules of protection against mosquitoes are strictly followed, that the traveller is in a position to consult a doctor urgently in the event of fever during the months after returning home and that the traveller informs the doctor that they have visited a malaria-endemic area. These regions are indicated in the third column of Table 1.

Sporadic transmission areas: chemoprophylaxis is not essential in the countries listed below, regardless of the duration of the stay. However, the traveller must be in a position to consult a doctor urgently in case of fever during the stay and during the few months that follow their return home.

Africa: Algeria, Cape Verde, Morocco, Mauritius.

Asia: Armenia, Azerbaijan, South Korea, North Korea, Southeast Georgia, Kyrgyzstan, Uzbekistan, Turkmenistan.

Near and Middle East: Oman, Syria, Southeast Turkey.

Variability of transmission levels according to regions of countries
The breakdown of areas of resistance by *Plasmodium falciparum* as indicated in Table 1 should be adjusted on the basis of transmission levels. Identifying the country of destination is insufficient; also to be taken into account are the region visited, the conditions of the stay, and the season. For example, a visit to Thailand or Vietnam not involving an overnight stay in forest areas does not normally require antimalarial prevention. Conversely, malaria is once again endemic in some cities in India and Amazonia.
Malaria is not usually transmitted above an altitude of 1500 metres in Africa and above an altitude of 2500 metres in America and Asia.

2.2.4. Long stays (over three months)

Detailed information should be given about malarial prevention. It is useful to deliver a document drawn up according to destination. It is also essential to ensure that the information given is thoroughly understood. The need for protection against mosquito bites (e.g. mosquito netting) should also be emphasised. During the first visit, it is essential for chemoprophylaxis adapted to the level of resistance to be continued for at least the first six months, except in the case of the atovaquone-proguanil combination, for which there is currently insufficient information about long-term use. Beyond that date, since it seems unrealistic for prophylaxis to continue for several years, it can be adjusted based on the advice of local doctors. Intermittent prophylaxis during the rainy season or certain journeys may be the best solution. In all cases, a doctor should be consulted rapidly in the event of fever.
Travellers should be warned that the risk of serious acute malaria persists for two months after their return from the endemic area.

2.3. Symptomatic treatment

Antimalarial treatment without medical advice during the stay should be the exception rather than the rule, and is only appropriate **if medical advice cannot be obtained within 12 hours**. It should always be based on a prescription issued by a doctor before exposure.

Table 2: Antimalarial chemoprophylaxis by resistance patterns, 2007			
Chemo-resistance group	**Adult**	**Pregnant woman**	**child**
Group 1	CHLOROQUINE (Nivaquine®) 100 mg/day Stay + 4 weeks after		CHLOROQUINE (Nivaquine®) 1.5 mg/kg/day Stay + 4 weeks after
Group 2	CHLOROQUINE + PROGUANIL 100 mg/day 200 mg/day (Nivaquine® + Paludrine®) or (Savarine®) Stay + 4 weeks after		CHLOROQUINE + PROGUANIL 1.5 mg/kg/day 3 mg/kg/day (Nivaquine®) (Paludrine®) Stay + 4 weeks after
Group 3	ATOVAQUONE 250 mg + PROGUANIL 100 mg (Malarone®) 1 tab/day Stay + 1 week after	ATOVAQUONE 250 mg + PROGUANIL 100 mg May be considered if necessary	- If < 11 kg. as above - If ≥ 11 kg and < 40 kg: ATOVAQUONE 62.5 mg + PROGUANIL 25 mg (Malarone paediatric®) 1 tab/10 kg/day Stay + 1 week after
	MEFLOQUINE 250 mg /(Lariam®) 1 tab/week 10 days before + stay + 3 weeks after		If > 15 kg: MEFLOQUINE (Lariam®) 5 mg/kg/week 10 days before + stay + 3 weeks after
	DOXYCYCLINE (doxycycline monohydrate) 100 mg/day stay + 4 weeks after	-	If > 8 years of age: DOXYCYCLINE (doxycycline monohydrate) 50 mg/day if < 40 kg stay + 4 weeks after

Box 2

Recommended interventions for malaria prevention and control during pregnancy (in areas of stable transmission)

The policy for malaria prevention and control during pregnancy in areas of stable transmission should emphasize a package of intermittent preventive treatment (IPT) and insecticide-treated nets (ITNs) and ensure effective case management of malaria illness and anaemia.

Intermittent Preventive Treatment

All pregnant women in areas of stable malaria transmission should receive at least two doses of IPT after quickening. The World Health Organization recommends a schedule of four antenatal clinic visits, with three visits after quickening. The delivery of IPT with each scheduled visit after quickening will assure that a high proportion of women receive at least two doses. IPT-SP doses should not be given more frequently than monthly.

Currently, the most effective drug for IPT is sulfadoxine-pyrimethamine (SP) because of its safety for use during pregnancy, efficacy in reproductive-age women and feasibility for use in programmes as it can be delivered as a single-dose treatment under observation by the health worker.*

Insecticide-Treated Nets

ITNs should be provided to pregnant women as early in pregnancy as possible. Their use should be encouraged for women throughout pregnancy and during the postpartum period. ITNs can be provided either through the antenatal clinic or other sources in the private and public sectors.

Effective Case Management of Malaria Illness and Anaemia

Effective case management of malaria illness for all pregnant women in malarious areas must be assured. Iron supplementation for anaemia should be given to pregnant women as part of routine antenatal care. Pregnant women should also be screened for anaemia, and those with moderate to severe anaemia should be managed according to national reproductive health guidelines.

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*Current scientific evidence suggests the following:
1) At least two IPT doses are required to achieve optimal benefit in most women;
2) One study of IPT in HIV-infected pregnant women has demonstrated that monthly dosing of IPT (with most women getting three to four doses) was necessary to achieve optimal benefit;
3) In settings with HIV prevalence in pregnant women greater than 10%, it is more cost effective to treat all women with a three-dose regimen than to screen for HIV and provide this regimen only to HIV-infected women;
4) There is no evidence that a third dose of IPT causes any additional risk, that more than three IPT doses during pregnancy offers additional benefit or that receiving three or more doses of IPT with sulfadoxine-pyrimethamine will result in an increased risk of adverse drug reactions. Research to assess the safety, efficacy and programme feasibility of other antimalarial drugs for use in IPT is ongoing.

Excerpt from: World Health Organisation. A strategic Framework for Malaria Prevention and Control During Pregnancy in the African Region. Brazzaville: WHO Regional Office for Africa, 2004. AFR/MAL/04/01