MOSQUIRIX

***Plasmodium falciparum* and hepatitis B vaccine (recombinant, AS01E adjuvanted)**

QUALITATIVE AND QUANTITATIVE COMPOSITION

Powder and suspension for suspension for injection.

After reconstitution, 1 dose (0.5 ml) contains 25 micrograms of RTS,S[1,2] adjuvanted with $AS01_E$[3].

[1] Portion of *P. falciparum* circumsporozoite protein fused with hepatitis B surface antigen (RTS), and combined with hepatitis B surface antigen (S)

[2] in the form of non-infectious virus-like particles (VLPs) produced in yeast cells (*Saccharomyces cerevisiae*) by recombinant DNA technology

[3] The GlaxoSmithKline proprietary $AS01_E$ Adjuvant System is composed of *Quillaja saponaria* Molina, fraction 21 (QS-21) (25 micrograms) and 3-O-desacyl-4'-monophosphoryl lipid A (MPL) (25 micrograms)

The powder is white.
The suspension is an opalescent, colourless to pale brownish liquid.

CLINICAL INFORMATION

Indications

Mosquirix is indicated for active immunisation of children aged 6 weeks up to 17 months against malaria caused by *Plasmodium falciparum* and against hepatitis B (see *Dosage and Administration*).

The use of Mosquirix should be based on official recommendations.

Dosage and Administration

The immunisation schedules for Mosquirix should be based on official recommendations.

Mosquirix provides protection against hepatitis B. Therefore it can replace hepatitis B vaccination in children for which prevention against malaria caused by *P. falciparum* is sought.

Posology

Vaccination in children from 6 weeks up to 17 months of age (at first dose):

- Three doses, each of 0.5 ml, should be given at monthly intervals.

- A fourth dose is recommended 18 months after the third dose, especially in areas with moderate to high malaria transmission.

Method of administration

Mosquirix is for intramuscular injection only.

The anterolateral thigh is the preferred site for injection in children younger than 5 months of age. The deltoid muscle is the preferred site for injection in children aged 5 months and older (see *Warnings and Precautions* and *Interaction*s).

For instructions on reconstitution of the medicinal product before administration, see *Use and Handling*.

Contraindications

Hypersensitivity to the active substances or to any component of the vaccine (see *Formulation and Strength* and *Excipients*) or to a previous dose of Mosquirix or hepatitis B vaccines.

Warnings and Precautions

Protection against P. falciparum malaria

Mosquirix does not provide complete protection against malaria caused by *P. falciparum* (see *Pharmacodynamic Effects*).

Protection against *P. falciparum* malaria wanes over time and vaccination may delay the acquisition of natural immunity (see Pharmacodynamic Effects) which could lead to an increased susceptibility to malaria at an older age compared with unvaccinated children. If symptoms compatible with malaria develop, appropriate diagnosis and treatment should be sought.

Data regarding the efficacy of Mosquirix are limited to children from sub-Saharan Africa.

Mosquirix will not protect against malaria caused by pathogens other than *Plasmodium falciparum*.

The use of other malaria control measures recommended locally should not be interrupted.

Protection against hepatitis B

Mosquirix should not be used for the prevention of hepatitis B in settings where prevention against malaria caused by *P. falciparum* is not sought.

An immune response against hepatitis B may not be elicited in all vaccinees.

Mosquirix will not protect against diseases caused by pathogens other than hepatitis B virus. However, it can be expected that hepatitis D will be prevented by immunisation as hepatitis D (caused by the delta agent) does not occur in the absence of hepatitis B virus infection.

Meningitis

In clinical studies, meningitis (any aetiology) has been reported more frequently in the group vaccinated with three doses of Mosquirix up to 20 months post dose 1 (27 cases out of 11,439 vaccinees) compared with the control group (4 cases out of 6,096 vaccinees).

A causal relationship to the vaccine has not been established.

Fever

A history of febrile convulsions or a family history of convulsions does not constitute a contraindication for the use of Mosquirix. Vaccinees, especially those with a history of febrile convulsions, should be closely followed up as vaccine related fever may occur after vaccination (see *Adverse Reactions*). In case of fever, antipyretic measures should be initiated according to local guidelines.

As with other vaccines, vaccination with Mosquirix should be postponed in subjects suffering from an acute severe febrile illness. The presence of a minor infection, such as a cold, should not result in the deferral of vaccination

Fever may follow each dose of Mosquirix (see *Adverse Reactions*). Clinical data generated with other paediatric vaccines suggest that the prophylactic use of paracetamol might reduce the immune response to vaccine antigens. The clinical relevance of this observation remains unknown. In absence of clinical data with Mosquirix, the routine use of prophylactic antipyretic medicinal products before vaccination is therefore not recommended.

Prior to immunisation

It is good clinical practice to precede vaccination by a review of the medical history (especially with regard to previous vaccination and possible occurrence of undesirable effects) and a clinical examination.

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of an anaphylactic event following the administration of the vaccine.

Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. It is important that procedures are in place to avoid injury from faints.

Precautions for use

Do not administer the vaccine intravascularly, intradermally or subcutaneously.

As with other vaccines administered intramuscularly, Mosquirix should be given with caution to individuals with thrombocytopenia or any coagulation disorder since bleeding may occur following an intramuscular administration to these subjects.

The potential risk of apnoea and the need for respiratory monitoring for 48 to 72 h should be considered when administering the first three doses to very preterm infants (born ≤ 28 weeks

of gestation) who remain hospitalised at the time of vaccination and particularly for those with a previous history of respiratory immaturity.

Systemic immunosuppressive medications and immunodeficiency

Limited data are available with HIV-infected children (see *Adverse reactions* and *Pharmacodynamic Effects*). There are no data in children receiving immunosuppressive treatment or children with immunodeficiencies other than HIV infection. In immunosuppressed children, it cannot be ruled out that efficacy is impaired.

Interactions

Use with other vaccines

Mosquirix can be given concomitantly with any of the following monovalent or combination vaccines: diphtheria (D), tetanus (T), whole cell pertussis (Pw), acellular pertussis (Pa), hepatitis B (HepB), *Haemophilus influenzae* type b (Hib), oral polio (OPV), measles, rubella, yellow fever, rotavirus and pneumococcal conjugate (PCV) vaccines. The co-administration of Mosquirix with PCV increases the risk of fever within 7 days post-vaccination (see *Adverse reactions*).

Concomitant administration of rotavirus and pneumococcal conjugate vaccines with Mosquirix may reduce the antibody response to the circumsporozoite (CS) antigen of Mosquirix. The impact of this observation on the level of protection induced by Mosquirix is currently unknown.

The non-inferiority of the immune response was demonstrated for D, T, Pw, Pa, Hib, polio and pneumococcal antigens (except for pneumococcal serotype 18C); although there was a trend for lower antibody geometric mean concentrations (GMCs) for these antigens when compared to the control group. These observations were considered as not clinically significant.

If Mosquirix is to be given at the same time as another injectable vaccine, the vaccines should always be administered at different injection sites.

Use with systemic immunosuppressive medications

See *Warnings and Precautions*.

Prophylactic administration of antipyretics

See *Warnings and Precautions*.

Pregnancy and Lactation

Mosquirix is not intended for use in women of childbearing potential.

Adverse Reactions

Adverse reactions after 3 doses

The safety profile presented below is based on a pooled analysis of more than 11,000 children who have been vaccinated in clinical studies with 3 doses of Mosquirix.

Adverse reactions reported are listed according to the following frequency:

Very common ≥ 1/10
Common ≥ 1/100 to < 1/10
Uncommon ≥ 1/1000 to < 1/100

Table 1: Adverse reactions reported after 3 doses of Mosquirix

System Organ Class	Frequency	Adverse reactions
Metabolism and nutrition disorders	Common	decreased appetite
Psychiatric disorders	Very common	irritability
Nervous system disorders	Common	somnolence
	Uncommon	febrile convulsions (within 7 days post-vaccination)
Gastrointestinal disorders	Common	diarrhoea
	Uncommon	vomiting
General disorders and administration site conditions	Very common	fever, injection site reactions (including swelling, erythema and pain)
	Uncommon	injection site induration

HIV-infected children

Data from clinical studies suggest that HIV-infected children are more likely to experience local and systemic reactogenicity (injection site pain and injection site erythema, fever, somnolence, irritability, decreased appetite) (Malaria-058) compared to children of unknown HIV infection status (Malaria-055).

Fever

In a clinical study (Malaria-063) in infants aged 8-12 weeks, fever was reported more frequently in infants receiving PCV in co-administration with Mosquirix, DTPa/Hib and OPV simultaneously (26%), as compared to infants receiving only Mosquirix, DTPa/Hib and OPV (14%). The frequency of grade 3 fever on co-administration (defined as axillary temperature > 39.0°C) was ≤ 1%.

Adverse reactions after the 4th dose

Clinical data in more than 4200 children who received a fourth dose of Mosquirix shows that, following this dose, decreased appetite was reported more frequently (very common) compared to the rates observed after the first three doses. All other adverse reactions occurred at the same or lower frequency as reported in Table 1.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamics

ATC Code

Pharmacotherapeutic group: *not yet assigned*, ATC code: *not yet assigned*

Mechanism of Action

Mosquirix is a pre-erythrocytic vaccine designed to help the immune system to limit the ability of *Plasmodium falciparum* to infect, mature and multiply in the liver.

The circumsporozoite (CS) protein is abundantly present at the surface of the sporozoite. Mosquirix induces the production of anti-CS antibodies and CS-specific activated T cells. Although no correlate of protection has currently been established, both humoral and cellular immune responses are considered to contribute to protection against *P. falciparum*.

Mosquirix induces antibodies against hepatitis B surface antigen (anti-HBs antibodies). An anti-HBs antibody titre ≥10 mIU/ml correlates with protection against hepatitis B virus infection.

Pharmacodynamic Effects

1. Protective efficacy against malaria

In a Phase III randomized controlled double-blind clinical efficacy study (Malaria-055) conducted at 11 centres in 7 sub-Saharan African countries with a wide range of transmission intensities, more than 15,000 children from two age groups (6-12 weeks and 5-17 months) were enrolled to evaluate efficacy and safety of Mosquirix when given according to a 0, 1, 2-month schedule. In addition, more than 4200 children (including children from both age groups) received a fourth dose, given 18 months after the third dose.

Children from the 6-12 weeks age group received Mosquirix concomitantly with DTPw-HepB+Hib and OPV vaccines, which are recommended by WHO as part of the routine Expanded Programme on Immunisation (EPI).

The primary objective of the study was efficacy against first or only episode of clinical malaria over a follow-up period of 12 months after three doses in each age group.

The secondary objectives included efficacy against all episodes of clinical malaria, efficacy against severe malaria and efficacy against hospitalisation caused by malaria over different follow-up periods after three doses in each age group.

The efficacy of Mosquirix was evaluated on top of other malaria control measures, according to local recommendations. The use of insecticide treated bed nets (ITNs) was encouraged and compliance was high in both age groups: 86% in 6-12 weeks and 78% in 5-17 months.

1.1 Infants aged 6-12 weeks (at first dose)

In infants aged 6-12 weeks, the vaccine efficacy (VE) against first or only episode of clinical malaria over 12 months of follow-up (co-primary objective) was 31% (97.5% CI: 24; 38).

In children who received three doses, a fourth dose provides additional protection of 24% (95% CI: 16; 32) against clinical malaria over 12 months of follow-up (compared to children who received three doses only).

A summary of the secondary objectives pertaining to VE over different follow-up periods, in infants who received three doses only or three doses plus a fourth dose, is given in Table 2.

Table 2: Vaccine efficacy in infants aged 6-12 weeks (at first dose)

	Vaccine efficacy against all episodes of clinical malaria (95% CI)	**Vaccine efficacy against severe malaria** (95% CI)	**Vaccine efficacy against hospitalisation caused by malaria** (95% CI)
Over 12 months follow-up from dose 3 (ATP* cohort, N = 6003)	33% (26; 39)	37% (5; 58)	32% (7; 50)
Over 18 months follow-up from dose 3 (ATP* cohort, N=6003)	27% (20; 32)	15% (-20; 39)	17% (-7; 36)
3 doses only (ATP* cohort, N=5997)			
Over 30 months follow-up from dose 3	20% (13; 27)	11% (-22; 35)	10% (-15; 30)
Over 36 months follow-up from dose 3**	18% (11; 25)	13% (-17; 35)	13% (-9; 31)
3 doses + 4th dose (ATP* cohort, N=5997)			
Over 30 months follow-up from dose 3	28% (22; 34)	17% (-14; 40)	25% (3; 42)
Over 36 months follow-up from dose 3**	27% (21; 32)	21% (-7; 42)	27% (7; 43)

* According-to-protocol (ATP) cohort: all infants immunised according to schedule, N= total number in all 3 study groups
** The follow-up period from dose 3 to study end was not the same for all subjects because the study ended on a fixed date. The median length for this follow-up period is 36 months.

1.2 Children aged 5-17 months (at first dose)

In children aged 5-17 months, the VE against first or only episode of clinical malaria over 12 months of follow-up (co-primary objective) was 56% (97.5% CI: 51; 60).

In children who received three doses, a fourth dose provides additional protection of 29% (95% CI: 22; 36) against clinical malaria over 12 months of follow-up (compared to children who received three doses only).

A summary of the secondary objectives pertaining to VE over different follow-up periods, in children who received three doses only or three doses plus a fourth dose, is given in Table 3.

Table 3: Vaccine efficacy in children aged 5-17 months (at first dose)

	Vaccine efficacy against clinical malaria (95% CI)	**Vaccine efficacy against severe malaria** (95% CI)	**Vaccine efficacy against hospitalisation caused by malaria** (95% CI)
Over 12 months follow-up from dose 3 (ATP* cohort, N=6880)	51% (47; 55)	45% (22; 60)	48% (35; 59)
Over 18 months follow-up from dose 3 (ATP* cohort, N=6885)	46% (42; 49)	36% (15; 51)	42% (29; 52)
3 doses only (ATP* cohort, N=6918)			
Over 30 months follow-up from dose 3	34% (29; 39)	2% (-28; 25)	18% (1; 32)
Over 46 months follow-up from dose 3**	26% (21; 31)	-6% (-35; 17)	12% (-5; 26)
3 doses + 4th dose (ATP* cohort, N=6918)			
Over 30 months follow-up from dose 3	46% (42; 50)	32% (10; 50)	40% (26; 52)
Over 46 months follow-up from dose 3**	39% (34; 43)	29% (6; 46)	37% (24; 49)

* According-to-protocol (ATP) cohort: all children immunised according to schedule, N= total number in all 3 study groups
** The follow-up period from dose 3 to study end was not the same for all subjects because the study ended on a fixed date. The median length for this follow-up period is 46 months.

1.3 Vaccine efficacy by P. falciparum transmission intensity

In children aged 5-17 months (at first dose) who received three doses only, the VE against clinical malaria over 30 months of follow-up was statistically significantly lower in sites with moderate or high transmission intensity compared to low transmission intensity sites. A

similar trend was observed in children who received three doses plus a fourth dose albeit not statistically significant (Table 4).

Table 4: Vaccine efficacy against clinical malaria (all episodes) over 30 months of follow-up, stratified by transmission intensity, in children aged 5-17 months (at first dose) (Malaria-055).

	Vaccine efficacy against clinical malaria (95% CI)	
	3 doses only (ATP* cohort, N=6918)	**3 doses + 4th dose** (ATP* cohort, N=6918)
Low transmission intensity (Pp** < 5%)	58% (35; 73)	58% (35; 74)
Moderate transmission intensity (Pp** 5 - 40%)	39% (30; 47)	48% (40; 56)
High transmission intensity (Pp** > 40%)	28% (21; 35)	43% (36; 49)

* According-to-protocol (ATP) cohort: all children immunised according to schedule, N= total number in all 3 study groups
** *P. falciparum* parasite prevalence (Pp)

In infants aged 6-12 weeks (at first dose) there is no statistical evidence that, over a period of 30 months of follow-up, VE against clinical malaria varied according to *P. falciparum* transmission intensity (Malaria-055).

2. Vaccine-induced immunogenicity

2.1 Immunogenicity against the circumsporozoite (CS) protein

In the Phase III efficacy study (Malaria-055), the geometric mean concentration (GMC) of antibodies against the circumsporozoite (CS) protein was measured after the third dose of Mosquirix (month 3) as well as before and after the fourth dose (months 20 and 21) in a subset within each age group.

Antibody responses for each age group are given in Table 5.

Table 5: Antibody responses to Mosquirix (anti-CS antibody)

	anti-CS antibody GMC		
	one month after the third dose (month 3) (95% CI)	**before the fourth dose (month 20)** (95% CI)	**one month after the fourth dose (month 21)** (95% CI)
Infants (aged 6-12 weeks at first dose)	N=1221	N=530	N=503
	211 EU/ml (198; 224)	6 EU/ml (5; 7)	170 EU/ml (154; 188)
Children (aged 5-17 months at first dose)	N=1034	N=442	N=426
	621 EU/ml (592; 652)	34 EU/ml (31; 39)	318 EU/ml (295; 343)

N= total number of infants/children immunised according to schedule (ATP cohort) with available results

2.2 Immunogenicity against hepatitis B

The immunogenicity of Mosquirix following a 3-dose schedule has been evaluated in infants aged 8-12 weeks (at first dose) (Malaria-063). One month post-vaccination in the ATP cohort, 100% of the infants were seroprotected for hepatitis B (N=141). These infants did not receive any other hepatitis B antigen-containing vaccine.

2.3 Immunogenicity in special sub-populations

Low weight-for-age (malnourished) children

Based on results presented in Table 6, the efficacy of Mosquirix is not expected to be substantially different in low or very low weight-for-age children as compared to the normal weight-for-age children.

Table 6: Immunogenicity in children with low and very low weight-for-age (Malaria-055)

	Infants (aged 6 – 12 weeks)			**Children (aged 5 – 17 months)**		
	normal weight-for-age[1] (N= 1121)	low weight-for-age[2] (N= 57)	very low weight-for-age[3] (N= 40)	normal weight-for-age[1] (N=838)	low weight-for-age[2] (N=156)	very low weight-for-age[3] (N=40)
anti-CS antibody GMC	210 EU/ml	217 EU/ml	213 EU/ml	607 EU/ml	728 EU/ml	534 EU/ml

Weight-for-Age z-score (WAZ): [1]WAZ > -2; [2]WAZ > -3 and ≤ -2; [3]WAZ ≤ -3

HIV-infected children

In the Phase III efficacy study Malaria-055, children were not screened for HIV infection at enrolment.

At a defined lock point, 125 children had a confirmed HIV infection. Although Mosquirix was immunogenic in HIV-infected children, the vaccine has shown to induce a lower anti-CS antibody response in HIV-infected children (GMC=193 EU/ml) as compared with children of unknown HIV infection status (GMC=492 EU/ml), one month after the third dose of Mosquirix. The clinical relevance of this observation is unknown.

In another clinical study (Malaria-058), children with HIV infection stages 1 or 2, in the context of high treatment (anti-retrovirals and co-trimoxazole) coverage, were vaccinated with 3 doses of Mosquirix (N=99) or rabies vaccine (N=101).

Mosquirix was immunogenic, inducing an anti-CS antibody response (GMC=329 EU/mL) one month after the third dose.

Over 12 months of follow-up after the third dose of Mosquirix, VE against all episodes of clinical malaria was 37% (95% CI: -27; 69).

Preterm infants

The immunogenicity of Mosquirix in 362 preterm infants born after a gestation period of less than 37 weeks (median 36 weeks, with a range of 27 to 36 weeks), was evaluated one month after the third dose. The vaccine induced a similar anti-CS response in preterm infants (GMC=262 EU/ml) as compared to infants born after at least 37 weeks of gestation (GMC=247 EU/ml).

Pharmacokinetics

Not relevant for vaccines.

Clinical Studies

See section *Pharmacodynamics*.

PHARMACEUTICAL INFORMATION

List of Excipients

Powder (RTS,S component): Sucrose, Polysorbate 80; Disodium phosphate dihydrate; Sodium dihydrogen phosphate dihydrate

Suspension ($AS01_E$ Adjuvant System): Dioleoyl phosphatidylcholine; Cholesterol; Sodium chloride; Disodium phosphate anhydrous; Potassium dihydrogen phosphate; Water for injections

Shelf Life

The expiry date is indicated on the packaging.

For shelf-life after reconstitution of the medicinal product, see *Use and Handling*.

After reconstitution:

Chemical and physical in-use stability has been demonstrated for 6 hours at 25°C.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 6 hours at 2°C to 8°C.

Storage

Store in a refrigerator (2°C – 8°C).

Do not freeze.

Store in the original package in order to protect from light.

For storage conditions after reconstitution of the medicinal product, see *Use and Handling*.

Nature and Contents of Container

- Powder for 2 doses in a vial (type I glass) with a stopper (butyl rubber)
- 1 ml suspension for 2 doses in a vial (type I glass) with a stopper (butyl rubber).

Mosquirix is available in a pack size of 50 vials of powder plus 50 vials of suspension.

Incompatibilities

This medicinal product must not be mixed with other medicinal products.

Use and Handling

The powder and suspension should be inspected visually for any foreign particulate matter and/or variation of appearance. If either is observed, do not administer the vaccine.

Mosquirix must be reconstituted prior to administration.

1. Withdraw the entire contents of the vial containing the suspension into a syringe.
2. Add the entire contents of the syringe into the vial containing the powder.
3. Shake gently until the powder is completely dissolved.

The reconstituted vaccine is an opalescent, colourless to pale brownish liquid.

The reconstituted vaccine should be inspected visually for any foreign particulate matter and/or variation of appearance. If either is observed, do not administer the vaccine.

After reconstitution, the vaccine should be used promptly; if this is not possible, the vaccine should be stored in a refrigerator (2°C – 8°C). If not used within 6 hours it should not be administered.

Each dose of 0.5 ml should be withdrawn using a sterile needle and syringe; precautions should be taken to avoid contamination of the contents.

A new needle should be used to administer each individual dose of the vaccine.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Version number: GDS10/IPI01

Date of issue: [date/month/year]

LABELLING TEXT

PARTICULARS TO APPEAR ON THE CARTON

TRADENAME OF THE VACCINE

Mosquirix

COMMON NAME

Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted)

PHARMACEUTICAL FORM

Powder and suspension for suspension for injection

ROUTE OF ADMINISTRATION

Inj.: I.M.

DESCRIPTION OF PRESENTATION

50 vials: powder (1 vial = 2 antigen doses)
50 vials: suspension (1 vial = 2 adjuvant doses)
1 dose = 0.5 ml

VACCINE COMPOSITION

After reconstitution, 1 dose (0.5 ml) contains 25 micrograms of RTS,S[1,2] adjuvanted with $AS01_E$[3].

[1] Portion of *P. falciparum* circumsporozoite protein fused with hepatitis B surface antigen (RTS), and combined with hepatitis B surface antigen (S)

[2] in the form of non-infectious virus-like particles (VLPs) produced in yeast cells (*Saccharomyces cerevisiae*) by recombinant DNA technology

[3] $AS01_E$ adjuvant is composed of *Quillaja saponaria* Molina, fraction 21 (QS-21) (25 micrograms) and 3-O-desacyl-4'- monophosphoryl lipid A (MPL) (25 micrograms)

Powder: sucrose, polysorbate 80, disodium phosphate dihydrate, sodium dihydrogen phosphate dihydrate.

Suspension: dioleoyl phosphatidylcholine (DOPC), cholesterol, sodium chloride, disodium phosphate anhydrous, potassium dihydrogen phosphate, water for injections

STORAGE CONDITIONS

Storage: 2°C – 8°C
Do not freeze
Protect from light

Vaccine without preservative
Both doses must be used within 6 hours after the reconstitution of the vaccine
Reconstituted vaccine to be discarded if not used within 6 hours

USE AND HANDLING INSTRUCTIONS

The powder must **only** be reconstituted with the suspension provided
After reconstitution **shake gently** until the powder is completely dissolved

LEGAL MENTIONS

Read the package leaflet before use
Keep out of the sight and reach of children
Medicinal product subject to medical prescription

COMPLETE NAME AND ADDRESS OF THE MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

GlaxoSmithKline Biologicals s.a.
Rue de l'Institut 89
B-1330 Rixensart - Belgium

COPYRIGHT STATEMENT

REFERENCE TO THE BATCH NUMBER, MANUFACTURING DATE AND EXPIRY DATE

LOT/MFD/EXP:

TRADE MARK PROTECTION

Trade marks owned or licensed by GSK

PARTICULARS TO APPEAR ON THE GROUP LABEL

TRADENAME OF THE VACCINE

Mosquirix

DESCRIPTION OF PRESENTATION

50 vials: powder (1 vial = 2 antigen doses)
50 vials: suspension (1 vial = 2 adjuvant doses)
1 dose = 0.5 ml

PHARMACEUTICAL FORM

Powder and suspension for suspension for injection

COMMON NAME

Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted)

VOLUME AND VACCINE COMPOSITION

After reconstitution, 1 dose (0.5 ml) contains 25 micrograms of RTS,S[1,2] adjuvanted with $AS01_E$[3].

[1] Portion of *P. falciparum* circumsporozoite protein fused with hepatitis B surface antigen (RTS), and combined with hepatitis B surface antigen (S)

[2] in the form of non-infectious virus-like particles (VLPs) produced in yeast cells (*Saccharomyces cerevisiae*) by recombinant DNA technology

[3] $AS01_E$ adjuvant is composed of *Quillaja saponaria* Molina, fraction 21 (QS-21) (25 micrograms) and 3-O-desacyl-4'- monophosphoryl lipid A (MPL) (25 micrograms)

Powder: sucrose, polysorbate 80, disodium phosphate dihydrate, sodium dihydrogen phosphate dihydrate.

Suspension: dioleoyl phosphatidylcholine (DOPC), cholesterol, sodium chloride, disodium phosphate anhydrous, potassium dihydrogen phosphate, water for injections

ROUTE OF ADMINISTRATION

Inj.: I.M.

STORAGE CONDITIONS

Storage: 2°C – 8°C
Do not freeze
Protect from light

Vaccine without preservative
Both doses must be used within 6 hours after the reconstitution of the vaccine
Reconstituted vaccine to be discarded if not used within 6 hours

USE AND HANDLING INSTRUCTIONS

The powder must **only** be reconstituted with the suspension provided
After reconstitution **shake gently** until the powder is completely dissolved

LEGAL MENTIONS

Read the package leaflet before use
Keep out of the sight and reach of children
Medicinal product subject to medical prescription

REFERENCE TO THE BATCH NUMBER, MANUFACTURING DATE AND EXPIRY DATE

LOT/MFD/EXP:

COPYRIGHT STATEMENT

TRADE MARK PROTECTION

NAME (+ CITY AND COUNTRY) OF MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

GlaxoSmithKline Biologicals s.a.
Rue de l'Institut 89
B-1330 Rixensart - Belgium

PARTICULARS TO APPEAR ON IMMEDIATE PACKAGING COMPONENTS TWO-DOSE VIAL (POWDER)

TRADENAME OF THE VACCINE

Mosquirix

NUMBER OF DOSES

2 doses (1 dose = 0.5 ml)

PHARMACEUTICAL FORM

Powder for suspension for injection

COMMON NAME

RTS,S (*Plasmodium falciparum* and hepatitis B antigen)

ROUTE OF ADMINISTRATION

Inj.: I.M.

STORAGE CONDITIONS

Storage: 2°C – 8°C
Do not freeze

REFERENCE TO THE BATCH NUMBER AND EXPIRY DATE

LOT/EXP:

NAME (+ CITY AND COUNTRY) OF MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

GSK Biologicals s.a.
Rixensart - Belgium

PARTICULARS TO APPEAR ON IMMEDIATE PACKAGING COMPONENTS TWO-DOSE VIAL (SUSPENSION)

TRADENAME OF THE VACCINE

Mosquirix

NUMBER OF DOSES

2 doses

PHARMACEUTICAL FORM

Suspension for suspension for injection

COMMON NAME

$AS01_E$ adjuvant

ROUTE OF ADMINISTRATION

Inj.: I.M.

STORAGE CONDITIONS

Storage: 2°C – 8°C
Do not freeze

REFERENCE TO THE BATCH NUMBER AND EXPIRY DATE

LOT/EXP:

NAME (+ CITY AND COUNTRY) OF MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

GSK Biologicals s.a.
Rixensart - Belgium

DETAILS FOR LEAFLET

MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Manufacturer responsible for batch release

GlaxoSmithKline Biologicals s.a.
Rue de l'Institut 89
B-1330 Rixensart - Belgium
Tel: (32) 2 656 81 11

TRADEMARK STATEMENTS

Trade marks are owned by or licensed to the GSK group of companies

COPYRIGHT STATEMENTS

LOGO(S)