

COMBIART

Artemether & Lumefantrine 80 / 480 mg Effervescent Granules

Sachets For oral use

Each sachet contains:

Artemether 80mg and Lumefantrine 480mg.

Excipients

Polysorbate 80 (SEPIPRAP 80), isomalt, saccharin sodium, flavour cherry, sodium bi carbonate, anhydrous citric acid, colloidal silicon dioxide.

DESCRIPTION

Artemether is a derivative from artemisinin, a sesquiterpene lactone isolated from the plant Artemether annua. Lumefantrine is a synthetic racemic fluorine mixture.

CLINICAL PHARMACOLOGY

Pharmacodynamic effects

This fixed dose combination contains fixed ratio of 1:6 parts of artemether and lumefantrine, respectively. The site of antiparasitic action of both components is the food vacuole of the malarial parasite, where they are thought to interfere with the conversion of haem, a toxic intermediate produced during haemozoin breakdown, to the non-toxic hemozoin malarial pigment. Lumefantrine is thought to interfere with the polymerisation process, while artemether generates reactive metabolites as a result of the interaction between its peroxide bridge and haem iron. Both artemether and lumefantrine have a secondary action involving inhibition of nucleic acid and protein synthesis within the malarial parasite.

The anti-malarial activity of the combination of artemether and lumefantrine is greater than that of either substance alone. In a double-blind comparative study in China (n=157), the 28-day cure rate of Artemether and lumefantrine when given at 4 doses was 94% compared with 90% for lumefantrine and 46% for artemether based on intent-to-treat (ITT) population, when given as monotherapy. For the evaluable population, 28-day cure rates were 100% for Artemether and lumefantrine, compared with 92% for lumefantrine and 55% for artemether when given as monotherapy.

In areas where multi-drug-resistant strains of P. falciparum malaria are common and in the resident population, 28-day cure rates with the 6-dose regimen (given over 60-96 h) were 81% and 90% for Artemether and lumefantrine versus 94% and 96% for mefloquine/artesunate, based on the ITT population. For the evaluable population, 28-day cure rates were 97% and 95% for Artemether and lumefantrine and 100% for mefloquine/artesunate.

In an open study (n=165) in adults the 28-day cure rate for Artemether and lumefantrine given as the 6-dose regimen was 96% (119/124) for the evaluable and 74.1% (120/162) for the ITT population. The main difference between the evaluable and ITT cure rates was owing to 38 patients who were excluded from the evaluable population for the following reasons: 33 patients were lost to follow up (19 of whom were not evaluated at Day 7 and 14 of whom had parasitic clearance at Day 7 but their efficacy status at Day 28 was unknown) and 5 patients took concomitant medications that were not permitted by the protocol. All these patients were considered as treatment failures in the ITT analysis.

Patients of European origin were not included in the trial with 6-dose regime. However the safety and efficacy of the 4 dose regimen were similar in European and Thai patients, similar safety and efficacy would be expected for the 6-dose regime in both populations.

In 319 patients in whom gametocytes were present, the median time to gametocyte clearance was 96h. The Artemether and lumefantrine was associated with more rapid gametocyte clearance than any comparator other than mefloquine/artesunate. Artemether and lumefantrine is active against blood stages of Plasmodium vivax, but is not active against hypnozoites. Therefore, sequential treatment with primaquine may be used to achieve hypnozoite eradication.

PHARMACOKINETICS:

Pharmacokinetic characterization of Artemether and lumefantrine is limited by the lack of an intravenous formulation, and the very high inter- and intra subject variability of artemether and lumefantrine plasma concentrations and derived pharmacokinetic parameters (AUC, C_{max}).

Absorption:

Artemether is absorbed fairly rapidly with peak plasma concentrations reached about 2 hours after dosing. Absorption of lumefantrine, a highly lipophilic compound, starts after a lag-time of up to 2 hours, with peak plasma concentration about 6-8 hours after dosing. Food enhances the absorption of both artemether and lumefantrine; in healthy volunteers the relative bioavailability of artemether was increased more than two-fold and that of lumefantrine sixteen-fold compared with fasted conditions when artemether and lumefantrine was taken after a high-fat meal.

Food effect:

Food increase the absorption of lumefantrine in patients with malaria, although to a lesser extent (approximately two-fold), most probably due to the lower fat content of the food ingested by acutely ill patients. The results of the study that absorption of lumefantrine under fasted conditions is very poor (assuming 100% absorption after a high-fat meal, the amount absorbed under fasted conditions would be <10% of the dose). Patients should therefore be encouraged to take the medication with a normal diet as soon as food can be tolerated.

Distribution

Artemether and lumefantrine are both highly bound to human serum proteins in vitro (95.4% and 99.7%, respectively). Dihydroartemisinin is also bound to human serum proteins (47-76%). Protein binding to human plasma protein is linear.

Metabolism:

Artemether is rapidly and extensively metabolised (substantial first-pass metabolism) both in vitro and in humans. Human liver microsomes metabolise artemether to the biologically active main metabolite dihydroartemisinin (demethylation), predominantly through the iso-enzyme CYP3A4/5. This metabolite has also been identified in humans in vivo. The artemether: dihydroartemisinin AUC ratio is 1.2 after a single dose and 0.3 after 6 doses given over 3 days. In vivo data indicate that artemisinins have some capacity to induce cytochrome iso-enzymes CYP2C19 and CYP3A4. Dihydroartemisinin is further converted to inactive metabolites.

Lumefantrine is N-debutylated, mainly by CYP3A4, in human liver microsomes. In vivo in animals (dogs and rats), glucuronidation of lumefantrine takes place directly and after oxidative biotransformation. In humans, the systemic exposure to the metabolite desbutyl-lumefantrine, for which the in vitro antiparasitic effect is 5 to 8 fold higher than lumefantrine, was less than 1% of the exposure to the parent drug. Desbutyl-lumefantrine data is not available specifically for an African population. In vitro, lumefantrine significantly inhibits the activity of CYP2D6 at therapeutic plasma concentrations.

Elimination: Artemether and dihydroartemisinin are rapidly cleared from plasma with an elimination half-life of about 2 hours. Lumefantrine is eliminated very slowly with a terminal half-life of 2-3 days in healthy volunteers and 4-6 days in patients with falciparum malaria. Demographic characteristics such as sex and weight appear to have no clinically relevant effects on the pharmacokinetics of Artemether and lumefantrine. No urinary excretion data are available for humans. In rats and dogs unchanged artemether has not been detected in faeces and urine due to its rapid and high-first-pass metabolism, but several metabolites (un identified) have been detected in both faeces and urine. Lumefantrine is eliminated via the bile in rats and dogs, with excretion primarily in the faeces. After oral dosing in rats and dogs qualitative and quantitative recovery of metabolites in bile and faeces was relatively low, most of the dose being recovered as parent drug.

Pharmacokinetics in special patient populations: No specific pharmacokinetic studies have been performed either in patients with hepatic or renal insufficiency, or in children or elderly patients.

INDICATIONS AND USAGE

Artemether and lumefantrine is indicated for the treatment, including standby emergency treatment, of adults, children and infants with acute, uncomplicated malaria due to P. falciparum or mixed infections including P. falciparum. Because Artemether and lumefantrine is effective against both drug-sensitive and drug-resistant P. falciparum it is also recommended for malaria infections acquired in areas where the parasites may be resistant to other anti-malarials.

Standby emergency treatment:

Prescribers are advised to issue Artemether and lumefantrine for self administration to the tourist and business travelers considered to be non immune traveling remote or isolate location far from the medical services.

Consideration should be given to official guidance regarding the appropriate use of anti-malarial agents.

CONTRAINDICATIONS

- Patients with known hypersensitivity to the active substances or to any of the excipients.
- Patients with severe malaria according to WHO definition.
- In the first trimester of pregnancy (see warning and precaution)
- Patients who are taking any drug which is metabolized by the cytochrome enzyme CYP2D6 (e.g. flecainide, metoprolol, imipramine, amitriptyline, clomipramine).
- Patients with a family history of sudden death or of congenital prolongation of the QTc interval on electrocardiograms, or with any other clinical condition known to prolong the QTc interval.
- Patients with a history of symptomatic cardiac arrhythmia or with clinically relevant bradycardia or with congestive cardiac failure accompanied by reduced left ventricle ejection fraction.
- Patients with disturbances of electrolyte balance e.g. hypokalaemia or hypomagnesaemia
- Patients taking drugs that are known to prolong the QTc interval. These drugs include:
 - Antiarrhythmics of classes Ia and III
 - Neuroleptics, antidepressive agents
 - Certain antibiotics including some agents of the following classes: fluoroquinolones, macrolides, midazole and triazole antifungal agents
 - Certain non-sedating antihistamines (terfenadine, astemizole)
 - Cisapride

WARNINGS AND PRECAUTIONS

Artemether and lumefantrine must not be used in the first trimester of pregnancy in situations where other suitable and effective anti-malarials are available.

Artemether and lumefantrine has not been evaluated for the treatment of severe malaria, including cases of cerebral malaria or other severe manifestations such as pulmonary oedema or renal failure.

Artemether and lumefantrine has not been studied in patients with severe renal or hepatic insufficiency and there for no recommendations can be made for these groups of patients.

Artemether and lumefantrine is not indicated for, and has not been evaluated in, the treatment of malaria due to P. vivax, P. malariae or P. ovale, although some patients in clinical studies had co-infection with P. falciparum and P. vivax at baseline. Artemether and lumefantrine is active against blood stages of Plasmodium vivax, but is not active against hypnozoites. Therefore, sequential treatment with primaquine may be used to achieve hypnozoite eradication.

Due to limited data on safety and efficacy, Artemether and lumefantrine should not be given concurrently with any other anti-malarial agent unless there is no other treatment option.

If a patient deteriorates whilst taking Artemether and lumefantrine, alternative treatment for malaria should be started without delay. In such cases, monitoring of the ECG is recommended and steps should be taken to correct any electrolyte disturbances.

The long elimination half-life of lumefantrine must be taken into account when administering quinine in patients previously treated with Artemether and lumefantrine.

If quinine is given after Artemether and lumefantrine, close monitoring of the ECG is advised.

If Artemether and lumefantrine is given after mefloquine, close monitoring of food intake is advised.

In patients previously treated with halofantrine, Artemether and lumefantrine should not be administered earlier than one month after the last halofantrine dose.

Artemether and lumefantrine is not indicated and has not been evaluated for prophylaxis.

Halofantrine, quinine and quinidine are known to cause QT interval prolongation.

Asymptomatic prolongation of QTc intervals by >30 ms, with an actual QTc >450 ms in males and >470 ms in females, was observed in approximately 5% of patients treated with various dose regimens of Artemether and lumefantrine in clinical trials. It is possible that these changes were disease related. In clinical trials in young children asymptomatic prolongation of QTc intervals >30 msec was observed in 35% of children weighing 5-10 kg, 34.1% of children weighing 10-15 kg and 23% of children weighing 15-25 kg.

Caution is recommended when combining Artemether and lumefantrine with drugs exhibiting variable patterns of inhibition, induction or competition for CYP3A4

Patients who remain averse to food during treatment should be closely monitored as the risk of recrudescence may be greater.

DRUG INTERACTION:

The likelihood of Artemether and lumefantrine interaction with other drug is minimal in views of its short duration of administration and wide therapeutic index; three specific pharmacokinetic and pharmacodynamic drug-drug interaction studies with ketoconazole, mefloquine and quinine have been conducted in healthy volunteers.

Interaction with anti malarial:

A drug interaction study with Artemether and lumefantrine in man involved administration of a 6-dose regimen over 60 hours in healthy volunteers which was commenced at 12 hours after completion of a 3 dose regimen of mefloquine or placebo. Plasma mefloquine concentrations from the time of addition of Artemether and lumefantrine were not affected compared with a group which received mefloquine followed by placebo.

A drug interaction study with mefloquine had no effect on plasma concentrations of artemether or the artemetherdihydroartemisinin ratio but there was a significant reduction in plasma levels of lumefantrine, possibly due to lower absorption secondary to a mefloquine-induced decrease in bile production. Patients should be encouraged to eat at dosing times to compensate for the decrease in bioavailability.

A drug interaction study in healthy male volunteers showed that the plasma concentrations of lumefantrine and quinine were not affected when i.v. quinine (10 mg/kg BW over 2 h) was given sequentially 2 h after the last (sixth) dose of Artemether and lumefantrine (so as to produce concurrent plasma peak levels of lumefantrine and quinine). Plasma concentrations of artemether and dihydroartemisinin (DHA) appeared to be lower. In this study, administration of artemether and lumefantrine to 14 subjects had no effect on QTc interval. Infusion of quinine alone in 14 other subjects caused a transient prolongation of QTc interval, which was consistent with the known cardio toxicity of quinine. This effect was slightly, but significantly, greater when quinine was infused after Artemether and lumefantrine in 14 additional subjects. It would thus appear that the inherent risk of QT-prolongation associated with i.v. quinine was enhanced by prior administration of Artemether and lumefantrine.

Interaction with CYP450 3A4 inhibitors (ketoconazole) Dose adjustment of Artemether and lumefantrine is considered unnecessary in falciparum malaria patients when administered in association with ketoconazole or other potent CYP3A4 inhibitors.

Interaction with CYP450 enzymes

Whereas in vitro studies with artemether at therapeutic concentrations revealed no significant interactions with cytochrome P450 enzymes, the artemisinins have some capacity to induce the production of the cytochrome enzyme CYP2C19, and perhaps also CYP3A4. It is possible that iso-enzyme induction could alter the therapeutic effects of drugs that are predominantly metabolised by these enzymes.

Lumefantrine was found to inhibit CYP2D6 in vivo. This may be of particular clinical relevance for compounds with a low therapeutic index. Co-administration of Artemether and lumefantrine with drugs that are metabolised by this iso-enzyme is contraindicated. In vitro studies indicated that lumefantrine metabolism is inhibited by halofantrine and quinine.

Interaction with protease inhibitor anti-retroviral drugs: Due to the low bioavailability of inhibition, induction or competition for CYP3A4 with protease inhibitor anti-retroviral drugs, use of such drugs, especially combinations of them, concomitantly with Artemether and lumefantrine, requires clinical surveillance and monitoring of clinical response/undesirable effects.

Precautions:

Administration of Artemether and lumefantrine is contra-indicated in patients taking drugs that are known to prolong the QT interval.

In patients previously treated with halofantrine, Artemether and lumefantrine should be dosed at least one month after the last halofantrine dose.

Due to the limited data on safety and efficacy, Artemether and lumefantrine should not be given concurrently with any other anti-malarial agent.

In addition, due to the propensity of some anti-malarial agents to prolong the QT interval, caution is advised when administering Artemether and lumefantrine to patients in whom there may still be detectable concentrations of these drugs in the plasma following prior treatments.

Pregnancy and lactation

There is insufficient data from the use of artemether and lumefantrine in pregnant women.

Artemether and lumefantrine treatment must not be used during the first trimester of pregnancy in situations where other suitable and effective anti-malarials are available. However, it should not be withheld in life-threatening situations, where no other effective anti-malarial is available. During the second and third trimester, treatment should only be considered if the expected benefit to the mother outweighs the risk to the foetus.

Lactation:

When taking Artemether and lumefantrine should not breast-feed their treatment. Due to the long elimination half-life of lumefantrine (4 to 6 days), it is recommended that breast feeding should not resume until at least one week after the last dose of Artemether and lumefantrine unless potential benefits to the mother and child outweigh the risks of Artemether and lumefantrine treatment.

Effects on ability to drive and use machines

Patients receiving Artemether and lumefantrine should be warned that dizziness or fatigue/asthenia may occur in which case they should not drive or use machines.

ADVERSE REACTIONS

The frequency of adverse events reported during clinical trial with Artemether and lumefantrine was similar to or lower than that of other anti-malarial drugs used as comparators.

Artemether and lumefantrine was generally well tolerated by children and adults, with most adverse events being of mild to moderate severity and duration. Many of the reported events were related to the interaction of the underlying malaria and/or to an allergic response to the treatment rather than to Artemether and lumefantrine. For other reports other alternative factors were identified as the more likely cause of the events (e.g. concomitant drugs, concomitant infection) or the information provided was too scarce to draw any conclusion.

The casual relationship with the use of Artemether and lumefantrine could not be excluded for the following adverse events.

Adverse reactions are ranked under headings of frequency, the most frequent first, using the following convention: Very common (1/100); common (1/10, <1/10); uncommon (1/1,000, <1/100); rare (1/10,000, <1/1,000); very rare (<1/10,000), including isolated reports.

Immune system disorders

Very rare: Hypersensitivity

Nervous system disorders

Very common: Headache, dizziness
Common: Sleep disorder, paraesthesia
Uncommon: Somnolence, involuntary muscle contractions, hypoaesthesia, abnormal gait, ataxia

Cardiac disorders

Common: Palpitation

Respiratory, thoracic and mediastinal disorders

Common: Cough

Gastrointestinal disorders

Very common: Abdominal pain, anorexia
Common: Diarrhoea, vomiting, nausea

Skin and subcutaneous tissue disorders

Common: Pruritus, rash

Musculoskeletal and connective tissue disorders

Common: Arthralgia, myalgia

General disorders and administration site conditions

Common: Asthenia, fatigue

Asymptomatic QTc prolongation was reported in adults, children and infants but no causal relation with Artemether and lumefantrine could be confirmed.

DOSEAGE AND ADMINISTRATION

Oral administration (For Adults)

Artemether and lumefantrine dose should be taken with food (high fat) or with milk, the food improves the absorption of the Artemether and lumefantrine.

In case of vomiting with in 1 hour of administration the dose should be repeated.

Practical scheme for administering the correct dose of artemether/lumefantrine sachets:

Recommended number of sachets						
Body weight	Day 1			Day 2		
	Morning	Evening		Morning	Evening	
> 35 kg	1	1		1	1	

Elderly:

Although no studies have been carried out in the elderly, no special precautions or dosage adjustments are considered necessary in such patients.

Dosage in patients with renal or hepatic impairment:

No specific studies have been carried out in these groups of patients and no specific dose adjustment recommendations can be made for these patients. Most patients with acute malaria present with some degree of related hepatic impairment. The adverse event profile did not differ in patients with and those without hepatic impairment. Moreover, baseline abnormalities in liver function tests improved in nearly all patients after treatment with Artemether and lumefantrine.

STORAGE

Keep out of the reach and sight of children. Store sachets below 30°C.

PRESENTATION:

Box of 6 sachets along with leaflet

List I - To be dispensed only on prescription

Manufactured by:
Strides Pharma Science Ltd
36/7, Suragajakanahalli, Indrayadi Cross,
Anekal Taluk, Bengaluru - 562 106, INDIA.



COMBIART

Artémèther & Luméfantrine 80 / 480 mg Granulés Effervescent

Sachets Par voie Orale

Chaque sachet contient:

Artémèther 80mg et Luméfantrine 480mg.

Excipients: Polysorbate 80 (SEPIPRAP 80), isomalt, saccharine de sodium, Arôme Cerise, sodium bicarbonate, acide citrique anhydre, dioxyde de silice colloïdale.

DESCRIPTION

Artémèther est un dérivé de l'artémidine, une lactone sesquiterpénique isolée de la plante Artemèther annua. Le luméfantrine est un mélange synthétique de fluor racémique.

PHARMACOLOGIE CLINIQUE

Effets pharmacodynamiques

Cette combinaison fixe contient Artémèther et Luméfantrine en proportion respective de 1 pour 6. Le site d'action antiparasite des deux composantes est la vacuole digestive du parasite où ils semblent altérer la conversion de fer, un intermédiaire toxique produit pendant la dissociation de l'hémoglobine, en hémocéine non toxique, le pigment du plasmodium. La Luméfantrine est connue pour s'interférer avec processus de polymérisation, pendant que l'artémèther produit des métabolites réactifs suite à l'interaction entre son pont de peroxyde et thème ferrique. L'artémèther et la lumefantrine bloquent ensuite la synthèse de l'acide nucléique et de protéines intraparasitaires.

L'activité antipaludique de la combinaison Artémèther et Luméfantrine est supérieure à celle de l'une ou l'autre substance administrée seule. Dans une étude comparative à double aveugle réalisée en Chine (n=157), l'analyse de la population sur la base de l'intention pour traiter (ITT), le taux de guérison à 28 jours de 94% lorsque Artémèther et Luméfantrine est administrés à 4 doses contre 90% pour la Luméfantrine et 46 % pour l'Artémèther.

Administrés isolément, Pour la population évaluable, les taux de guérison de 100% à 28 jours pour l'Artemèther et la Luméfantrine, comparés avec 92% pour l'Artemèther et 55% pour l'Artemèther administrés isolément en monothérapie.

Dans les zones où les souches multi résistantes à la malaria de P. falciparum sont communes et dans la population résidente, l'analyse en intention de traiter (ITT) a mis en évidence un taux de guérison à 28 jours 91% et 90% avec le régime à 6 doses (administrés pendant 60-96 h) contre 84% et 96% pour l'association mefloquine/artesunate. Pour la population évaluable, les taux de cure de 28 jours étaient de 97% et 95% pour l'Artemèther et la Luméfantrine et de 100 % pour l'association Mefloquine/artesunate.

Dans un essai ouvert (n=165) chez des adultes, le taux de cure de 28 jours pour l'artémèther et la lumefantrine administrés en régime à 6 doses était de 96% (119/124) pour la population évaluable et de 74.1% (120/162) pour l'ITT. La différence principale entre les taux de cure de la population évaluable et d'ITT était que à 38 patients qui ont été exclus de la population évaluable pour les raisons suivantes: 33 patients ont été perdus pour le suivi (19 d'entre eux n'ont pas été évalués au Jour 7 et 14 d'entre eux avaient eu la clairance parasitaire au Jour 7 mais leur statut d'efficacité au Jour 28 était inconnu) et 5 patients ont pris des médicaments concomitants qui n'étaient pas permises par le protocole. Tous ces patients étaient considérés avoir échoué le traitement dans l'analyse d'ITT. Les patients d'origine européenne n'ont pas été inclus dans l'essai du régime à 6 doses en raison de la sécurité et l'efficacité du dosage à 4 doses était similaires chez des patients européens et thais, une sécurité et efficacité similaires seraient attendues pour le régime à 6 doses chez les deux populations. Pour 319 patients chez lesquels les gamétocytes étaient présents, le temps moyen de clairance gamétocyte était de 96 heures. L'artémèther et la lumefantrine ont été associés à une clairance de gamétocyte que n'importe quel comparateur autre que la mefloquine/artesunate. L'artémèther et la lumefantrine sont actifs face aux étapes sanguines de Plasmodium vivax, mais ne sont pas actifs contre les hypnozoïtes. Par conséquent, le traitement séquentiel avec la primaquine peut être utilisé pour parvenir à l'éradication de l'hypnozoïte.

PHARMACOCINÉTIQUE

La caractérisation pharmacocinétique de l'artémèther et de la lumefantrine est limitée par le manque d'une formulation intraveineuse et par la variabilité très élevée inter et intra sujet de l'artémèther et des concentrations de plasma de la lumefantrine et des paramètres pharmacocinétiques dérivés (AUC, C_{max}).

Absorption:

L'artémèther est absorbé assez rapidement avec des concentrations de plasma maximales obtenues environ 2 heures après le dosage. L'absorption de lumefantrine, un composé hautement lipophile, commence après un temps de retard de près de 2 heures, avec une concentration de plasma maximale d'environ 6-8 heures après dosage. L'alimentation augmente l'absorption tant de l'artémèther que de la lumefantrine chez les volontaires sains, la biodisponibilité relative de l'artémèther a été plus que doublée et celle de la lumefantrine a augmenté plus de seize fois comparée aux conditions de jeûne lorsque l'artémèther et la lumefantrine ont été pris après un repas riche en matières grasses.

Effet des aliments:

L'alimentation augmente l'absorption de lumefantrine chez les patients avec la malaria, bien qu'à un degré modéré (approximativement 2 fois), dû à la plus probabilité que les repas contiennent des matières grasses inférieures des aliments ingérés par les patients gravement malades. Les données d'alimentation alimentaires indiquent que l'absorption de lumefantrine dans des conditions de jeûne est très faible (en supposant 100% l'absorption après un repas riche en matières grasses que la somme absorbée dans des conditions de jeûne serait < 10% de la dose). Les patients devraient donc être encouragés à prendre les médicaments avec un régime normal aussi tôt que les aliments peuvent être tolérés.

Distribution:

L'Artémèther et la lumefantrine sont tous les deux fortement liés aux protéines du sérum humain en in vitro (95.4% et 99.7%, respectivement). Le dihydroartemisinin est aussi lié aux protéines du sérum humain (47-76%). La protéine liée au plasma humain est linéaire.

Métabolisme:

L'artémèther est rapidement et largement métabolisé (métabolisme substantiel de premier passage hépatique) soit in vitro et chez l'homme. Les microsomes du foie métabolisent l'artémèther au métabolite principal biotransformation est le dihydroartemisinin (dé-méthylation), principalement à travers l'isoenzyme CYP3A4/5. Ce métabolite a aussi été détecté chez l'homme en vivo. Le ratio de l'ASC de l'artémèther/ dihydroartemisinin est 1.2 après une dose unique et 0.3 après 6 doses administrées pendant 3 jours. Les données in vivo indiquent que les artémisinines ont une certaine capacité pour induire les isoenzymes du cytochrome CYP2C19 et CYP3A4. Dihydroartemisinin est encore converti en métabolites inactifs.

Lumefantrine est N-débutylée, principalement par CYP3A4, dans les microsomes du foie humain. In vivo chez les animaux (