**atovaquone/proguanil** (a-toe-va-kwone/pro-gwa-nil)

**Malaria**

**Classification**

Therapeutic: antimalarials

**Pregnancy Category C**

**Indications**

Prevention of malaria caused by *Plasmodium falciparum*, including chloroquine-resistant strains. Treatment of acute, uncomplicated *P. falciparum* malaria, effective for many drug-resistant strains.

**Action**

Atovaquone is a selective inhibitor of parasite mitochondrial transport. Proguanil’s metabolite, cycloguanil, is a dihydrofolate reductase inhibitor. Both interfere with pyrimidine synthesis required for nucleic acids and replication, active against both erythrocytic and exoerythrocytic stages of *Plasmodium*. **Therapeutic Effects:** Prevention/treatment simultaneous illness and its sequelae.

**Pharmacokinetics**

**Absorption:** Atovaquone—variably absorbed following oral administration; food enhances absorption. Proguanil—well absorbed following oral administration.

**Distribution:** Proguanil—enters breast milk in small quantities.

**Protein Binding:** Atovaquone—99%.

**Metabolism and Excretion:** Atovaquone—undergoes enterohepatic recycling, 94% eliminated unchanged in feces; Proguanil—metabolized mostly by the CYP2C19 enzyme system and is converted to cycloguanil, the pharmacologically active metabolite.

**Half-life:** Atovaquone—adults: 2–3 days, children: 1–2 days. Cycloguanil—Adults: 8.3 hr, elderly: 14.9 hr.

**TIME/ACTION PROFILE (blood levels)**

<table>
<thead>
<tr>
<th>ROUTE</th>
<th>ONSET</th>
<th>PEAK</th>
<th>DURATION</th>
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<tbody>
<tr>
<td>PO</td>
<td>unk</td>
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<td>24 hr</td>
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</table>

† Two peaks are due to enterohepatic recycling

□ = Common drug name  ○ = Genetic Implication  □ = Discontinued

**Contraindications/Precautions**

**Contraindicated in:** Hypersensitivity to atovaquone or proguanil. Severe renal impairment (CCR < 30 mL/min).

**Use Cautiously in:**

- Nausea or vomiting; may require repeat dosing and/or prophylactic use of anti-emetics
- Severe malaria; oral agents are insufficient
- Geri: Dose carefully, considering age-related decrease in body mass, hepatic/renal/cardiac function, concurrent disease state and drug therapy.
- OB: Pregnancy; malaria is a more serious illness, consider risk/benefit of travel to endemic areas, use only if potential benefit outweighs risk to the fetus.
- Lactation: Use cautiously; proguanil enters breast milk. **Pedi:** Safe and effective use in children <5 kg has not been established.

**Adverse Reactions/Side Effects**

**Prophylaxis of Malaria**

- CNS: dizziness, dreams, headache, insomnia.
- EENT: visual difficulties.
- GI: abdominal pain, oral ulcers.

**Treatment of Malaria**

- CNS: headache, dizziness, weakness.
- GI: abdominal pain, diarrhea, nausea, vomiting, anorexia, elevated liver enzymes.
- Derm: pruritus (in children), photosensitivity.
- Hemat: neutropenias.
- Misc: allergic reactions including ANAPHYLAXIS.

**Interactions**

**Drug-Drug:** Rifampin, rifabutin, metoclopramide and tetracycline potentiate atovaquone levels. Atovaquone increases plasma levels of indinavir; use cautiously.

**Route/Dosage**

**Prevention of Malaria**

**PO (Adults and Children ≥ 40 kg):** One adult-strength tablet (atovaquone 250 mg/proguanil 100 mg) once daily 1–2 days prior to entering endemic area and continued for seven days following return.

**PO (Children 31–40 kg):** Three pediatric tablets (atovaquone 187.5 mg/proguanil 75 mg) once daily 1–2 days prior to entering endemic area and continued for seven days following return.

**PO (Children 21–30 kg):** Two pediatric tablets (atovaquone 125 mg/proguanil 50 mg) once daily 1–2 days prior to entering endemic area and continued for seven days following return.

**PO (Children 21–30 kg):** Two pediatric tablets (atovaquone 125 mg/proguanil 50 mg) once daily 1–2 days prior to entering endemic area and continued for seven days following return.

**Prevention of Malaria**

**PO (Children 11–40 kg):** Three pediatric tablets (atovaquone 107.5 mg/proguanil 50 mg) once daily 2 days prior to entering endemic area and continued for seven days following return.

**PO (Children 21–30 kg):** Two pediatric tablets (atovaquone 125 mg/proguanil 50 mg) once daily 1–2 days prior to entering endemic area and continued for seven days following return.

**PO (Children 11–40 kg):** Three pediatric tablets (atovaquone 107.5 mg/proguanil 50 mg) once daily 2 days prior to entering endemic area and continued for seven days following return.
PO (Children 11–20 kg): One pediatric tablet (atovaquone 62.5 mg/proguanil 25 mg) once daily 1–2 days prior to entering endemic area and continued for seven days following return.

Treatment of Malaria
PO (Adults and Children 40): Four adult tablets (total daily dose atovaquone 1 g/proguanil 400 mg) as a single daily dose for 3 consecutive days.

PO (Children 31–40 kg): Three adult tablets (total daily dose atovaquone 750 mg/proguanil 300 mg) once daily for 3 days.

PO (Children 21–30 kg): Two adult tablets (total daily dose atovaquone 500 mg/proguanil 300 mg) once daily for 3 days.

PO (Children 11–20 kg): One adult strength tablet (total daily dose atovaquone 250 mg/proguanil 150 mg) once daily for three days.

PO (Children 9–10 kg): Three pediatric tablets (total daily dose atovaquone 150 mg/proguanil 75 mg) once daily for three days.

PO (Children 5–8 kg): Two pediatric tablets (total daily dose atovaquone 125 mg/proguanil 75 mg) once daily for three days.

NURSING IMPLICATIONS
Assessment
- Malaria: Assess patient for improvement in signs and symptoms of condition daily throughout therapy.
- Lab Test Considerations: Monitor CBC periodically throughout therapy. May cause neutropenia. May cause AST and ALT. Monitor liver function tests periodically during therapy.

Potential Nursing Diagnoses
Risk for infection (Indications)
Deficient knowledge, related to medication regimen (Patient/Family Teaching)

Implementation
- For malaria prophylaxis, therapy should be started 1–2 days prior to potential exposures and continued for 7 days after leaving the area.
- For treatment of malaria, take once daily for 3 days.
- PO: Administer with food or a milky drink to minimize GI distress. Tablets may be crushed and mixed with condensed milk just prior to administration for children with difficulty swallowing tablets.

Patient/Family Teaching
- Instruct patient to take medication exactly as directed and continue full course of therapy, even if feeling better. If vomiting occurs within 1 hr of dose, may take a repeat dose. Take missed doses as soon as remembered, unless almost time for next dose. Do not double doses.
- Review methods of minimizing exposure to mosquitoes with patients receiving atovaquone/proguanil prophylactically. Use insect repellent, wear long sleeved shirt and long trousers, use screens or netting.
- Advise patient to wear protective clothing and sunscreen to avoid phototoxic reactions.
- Advise female patients to notify health care professional if pregnancy is planned or suspected or if breast feeding. Risk of death and serious complications in infants is higher with Falciparum malaria. Advise pregnant women anticipating travel to malaria areas discuss risks with health care professional.

Evaluation/Desired Outcomes
- Prevention of or improvement in signs and symptoms of malaria.

Why was this drug prescribed for your patient?