Tafenoquine succinate

Approved indication: malaria prevention
Kodaflex (Biocelect)
100 mg tablets
Australian Medicines Handbook section 5.7, Antiprotozoals

Tafenoquine, a primaquine analogue, is indicated for prophylaxis against malaria in adults. It is a long-acting 8-aminoquinoline that is active at all stages of the malaria life cycle, including the liver stage where the parasites can lie dormant (as hepatic hypnozoites) before entering the bloodstream. This usually occurs less than a month after the initial infection but relapse can be delayed by several years.

It is not clear how tafenoquine kills the parasite but it has been shown to be effective in preventing infection with Plasmodium falciparum and P. vivax in people living in malaria-endemic regions. Its approval in Australia is based on a comparative trial with mefloquine in healthy non-immune Australian soldiers (n=654) deployed to Timor-Leste.

Soldiers were randomised 3:1 to tafenoquine 200 mg or mefloquine 250 mg. After a loading phase of a single dose per day for three days, soldiers entered the prophylactic phase in which they received a dose once a week for 26 weeks (± 4 weeks). On returning to Australia, soldiers entered the relapse follow-up phase where those in the mefloquine group received primaquine (15 mg twice a day) for 14 days while those in the tafenoquine group received placebo. There were no malarial infections during the prophylactic phase with either treatment. However, during the relapse follow-up phase, there were four cases of P. vivax in the tafenoquine/placebo arm (4/462, 0.9%) and one case in the mefloquine/primaquine arm (1/153, 0.7%). These occurred 16–20 weeks after returning from Timor-Leste.

In a safety cohort of 825 people, there were 23 serious adverse events that were thought to be related to tafenoquine treatment. These included eye disorders (7 cases), decreased glomerular filtration rate (5 cases), infection (4 cases) and gastrointestinal disorders (4 cases). The most common adverse events that led to discontinuation were increased liver enzymes, decreased haemoglobin and decreased glomerular filtration rate.

In an ophthalmic assessment of a subgroup of soldiers in the Timor-Leste study, 93.2% (69/74) had vortex keratopathy (corneal deposits) by the end of the prophylactic phase. This did not seem to affect their vision and all cases had resolved after a year.

Like primaquine, tafenoquine can induce haemolytic anaemia in people with glucose-6-phosphate dehydrogenase (G6PD) deficiency. This is especially a concern because tafenoquine has a very long half-life of 17 days. Tafenoquine is contraindicated in G6PD deficiency and in pregnancy and lactation as the G6PD status of the infant is unlikely to be known.

Although not teratogenic in animal studies, tafenoquine caused dose-related abortions in pregnant rabbits. Women of childbearing age should use contraception while taking tafenoquine and for three months after finishing prophylaxis. This drug has not been tested in children.

Tafenoquine is also contraindicated in people with current or a history of psychosis, delusions or hallucinations. Even though people with a history of psychiatric disorders were excluded from the Timor-Leste trial, sleep disturbance, depression or depressed mood and anxiety were increased. One person attempted suicide.

Following a single oral dose of tafenoquine, maximum plasma concentrations are reached after seven hours. The drug’s half-life is 17 days. Tafenoquine should not be taken for longer than six months. The treatment course should include a 3-day loading dose before travel, weekly dosing while away and a single dose on return. The gastrointestinal effects of tafenoquine may be reduced by taking tablets with food. Dose adjustment in renal and hepatic impairment has not been studied.

Tafenoquine may inhibit drug transporters in the kidney which could lead to increased concentrations of renally excreted drugs. If tafenoquine is co-administered with drugs (e.g. dapsone) that have potential to cause haemolysis in people with normal G6DP function, they should monitor their urine for dark colour and have their haematocrit checked.

Tafenoquine seemed to be as effective as mefloquine/primaquine at preventing malaria during prolonged stays in a malaria-endemic region. However, it can cause severe haemolytic anaemia and everyone must be tested to make sure they do not have G6DP deficiency before being prescribed this drug. Tafenoquine’s once-weekly dosing may be preferred by some travellers.

REFERENCES


The Transparency Score is explained in New drugs: transparency, Vol 37 No 1, Aust Prescr 2014;37:27. At the time the comment was prepared, information about this drug was available on the Food and Drug Administration website.