PYRAMAX®: pyronaridine artesunate
A novel combination treatment for acute malaria

Background

Artemisinin combination therapy (ACT) is now the treatment of choice recommended by the World Health Organization for acute malaria. However, compliance issues, due to the administration of two or more single tablets more than once a day, and the relatively short shelf-life of current ACTs are significant drawbacks.

In 2000, in response to Medicines for Malaria Venture’s first call for proposals, the Korean pharmaceutical company Shin Poong proposed a fixed-dose combination of the artemisinin derivative, artesunate, with a known antimalarial, pyronaridine. The latter had not been used outside China for 30 years and, therefore, little chance existed of parasites in other malaria endemic countries having developed resistance to it.

A rigorous and exhaustive development programme was designed and undertaken, ensuring that pyronaridine artesunate was subjected to stringent regulatory and compliance standards (GMP/GLP/GCP).

The promise of pyronaridine artesunate will now be confirmed in large phase III trials in malaria patients to be conducted in Africa and South East Asia. The first patients have been recruited in Dakar, Senegal. Trials are also expected to be held in Gambia, Mali, Ghana, DR Congo, Kenya, Mozambique, Philippines, Indonesia, Cambodia, Thailand, Vietnam, Korea and India.

The drug to be tested will not only be in a combined tablet form for adults and children, but also in a specially-designed formulation for infants. MMV and Shin Poong aim to submit a registration package by the beginning of 2008 to the regulatory authorities in Europe (EMEA) and Korea (K-FDA), ahead of coordinated submissions at a national level in endemic countries. Shin Poong intends to work closely with MMV’s Access and Delivery Group to ensure that the drug reaches those in need in malaria-endemic countries.

The Product

Pyronaridine artesunate - PYRAMAX® is being developed as a cure for Plasmodium falciparum uncomplicated malaria and for Plasmodium vivax malaria. It is presented as a combined tablet or granule formulation, enabling adults as well as infants to be treated. Patients receive the orally-administered drug, according to their weight, once a day for three days.

Innovative pharmaceutical formulation development provides PYRAMAX® with improved pharmacokinetics and a unique stability profile which translates into a longer shelf-life, a key feature for antimalarials to be sold in developing countries.
Shin Poong has established specific contractual relationships with the Vietnamese Government for guaranteed access to artemisinin from government-managed farmers’ cooperatives, thus securing access to the key raw material. The starting material for the production of pyronaridine has also been sourced from a reliable supplier, with a second supplier identified and established. Furthermore, improved synthesis of pyronaridine has significantly reduced the cost of goods.

The strategy for addressing the potential to counterfeit pyronaridine artemunate will be to ensure that the cost of the product is such that any risk of commercial interest in counterfeiting is minimised. Tablet and granule colour is relatively unique and is thought to be difficult to mimic. Primary and secondary packaging has been addressed with prototypes which are specifically designed to be climate-appropriate, distinctive in appearance to enhance brand recognition and with compact storage requirements.