

Levamisole (as hydrochloride)

Levamisole is included in the WHO Model List of Essential Medicines. It was added as hydrochloride 50 mg and 150 mg tablets to the complementary section of section 6.1.1 Intestinal Anthelmintics for the treatment of ascariasis and mixed ascariasis/hookworm infections in 1988 and moved to the core list in 1990. The 50 mg tablet as hydrochloride was also added to section 8.2 Cytotoxic agents in 1995 and moved to the complementary list in 2002 for the treatment of colorectal carcinoma after complete resection of primary tumour together with fluorouracil.

At the 28<sup>th</sup> Annual Meeting of National centres participating in the WHO Programme for International Drug Monitoring this medicine was raised by China as one of the Problems of Current Interest. It was stated that levamisole is associated with an encephalitis-like syndrome. This levamisole-induced demyelinating encephalopathy (LIDE) was first reported in 1988. A search of the Chinese literature between 1993 and 2004 revealed 543 published reports of LIDE. The main clinical manifestations were acute or subacute diffuse cerebral lesions with early mental symptoms and motor weakness usually occurring 10-14 days after the use of levamisole. Several epidemiological studies have confirmed levamisole as the causative agent. The probable mechanism is a hypersensitivity inflammatory reaction with cerebral perivascular cuffing by mononuclear cells. Based on this benefit/risk profile, it has been withdrawn from the Chinese national formulary as an anthelmintic medicine.

It is no longer marketed as an anthelmintic agent in many countries since there are safer and more effective alternative.

The 3<sup>rd</sup> Meeting of the Advisory Committee for the Safety of Medicinal Products<sup>1</sup> suggested that the overwhelming data on toxicity should be communicated to the Expert Committee on the Use of Essential Medicines with a view to deleting it from Section 6.1.1.

<sup>1</sup>The full list of recommendations can be accessed at [http://www.who.int/medicines/areas/quality\\_safety/safety\\_efficacy/ACSoMP3.pdf](http://www.who.int/medicines/areas/quality_safety/safety_efficacy/ACSoMP3.pdf)