Direct Healthcare Professional Communication

March 2022

Ivermectin 3 mg and 6 mg Scored tablets: Risk of Disturbance of consciousness

Dear Healthcare professional,

The Egyptian Pharmaceutical Vigilance Center of the Central Administration for Pharmaceutical Care at The Egyptian Drug Authority would like to inform you of the following:

Summary

- Disturbance of consciousness from serious side effects (Incidence: unknown)
- If consciousness disorder such as coma, decreased consciousness level, or altered state of consciousness is observed, appropriate measures such as discontinuation of administration should be taken.
- Neurological toxicity including depressed level of consciousness and coma from post marketing experience
- It is important to adhere to recommended dosages. Cases of depressed level of consciousness and coma have been reported with overdosage of Ivermectin.

Background information on the security concerns

- Ivermectin 3 mg and 6 mgis indicated for the treatment of the following:
  - infections: **Strongyloidiasis of the intestinal tract** Ivermectin 3 mg and 6 mg is indicated for the treatment of intestinal (i.e., nondisseminated) strongyloidiasis due to the nematode parasite *Strongyloides stercoralis*.This indication is based on clinical studies of both comparative and open-label designs, in which 64-100% of infected patients were cured following a single 200-mcg/kg dose of ivermectin.
  - **Onchocerciasis.** Ivermectin 3 mg and 6 mg is indicated for the treatment of onchocerciasis due to the nematode parasite *Onchocerca volvulus*.This indication is based on randomized, double-blind, placebocontrolled and comparative studies conducted in 1427 patients in onchocerciasis-endemic areas of West Africa. The comparative studies used diethylcarbamazine citrate (DEC-C). Ivermectin has no activity against adult *Onchocerca volvulus* parasites. The adult parasites reside in subcutaneous nodules which are infrequently palpable. Surgical excision of these nodules (nodulectomy) may be considered in the management of patients with onchocerciasis, since this procedure will eliminate the microfilariae-producing adult parasites.
  - **Ivermectin** is a member of the avermectin class of broad-spectrum antiparasitic agents which have a unique mode of action. Compounds of the class bind selectively and with high affinity to glutamate-gated chloride ion channels which occur in invertebrate nerve and muscle cells.

21st Abdel-Aziz Al-Saud, Manial Al-Roda,Cairo
pv.head@edaegypt.gov.eg; pv.safety@edaegypt.gov.eg;
Tel.: 237484988 Ext.:1470

This leads to an increase in the permeability of the cell membrane to chloride ions with hyperpolarization of the nerve or muscle cell, resulting in paralysis and death of the parasite.

Compounds of this class may also interact with other ligand-gated chloride channels, such as those gated by the neurotransmitter gamma-aminobutyric acid (GABA).The selective activity of compounds of this class is attributable to the facts that some mammals do not have glutamate-gated chloride channels and that the avermectins have a low affinity for mammalian ligand-gated chloride channels. In addition, ivermectin does not readily cross the blood-brain barrier in humans.Ivermectin is active against various life-cycle stages of many but not all nematodes. It is active against the tissue microfilariae of *Onchocerca volvulus* but not against the adult form. Its activity against *Strongyloides stercoralis* is limited to the intestinal stages.

- Ivermectin activates and opens chloride (Cl^-) channels, especially glutamate-gated Cl^- channels found only in invertebrates. This allows increased entry of negative ions into the cell, hyperpolarizing the cell membrane and impairing function of nematode nerve and muscle cells.

Ivermectin kills parasitic worms by inducing toxic paralysis.Ivermectin can also cause human neurotoxicity by interacting with inhibitory GABA receptors in the brain. Fortunately, ivermectin taken at therapeutic doses does not effectively cross the blood-brain barrier because it is pumped out of the CNS by the P-glycoprotein (P-gp) transporter.

References

https://www.pmda.go.jp/PmdaSearch/iyakuDetail/170050_6429008F1020_2_06#CONTRAINDICATIONS

Call for reporting

The Egyptian Pharmaceutical Vigilance Center is reminding HCP and public to report any safety information regarding human medicinal products including adverse drug reactions, medications errors, lack of efficacy and other medicine related problems through the following contacts:

The Egyptian Pharmaceutical Vigilance Center
Address: 21 Abd El Aziz Al Soud Street, El-Manial, Cairo, Egypt, And PO Box: 11451
Telephone: (+2)02 25354100, Extension: 1470 Fax: +202 – 23610497
Hotline: 15301
Email: Pv.follow-up@edaegypt.gov.eg
Online reporting: https://primaryreporting.who-umc.org/EG
QR Code:

21st Abdel-Aziz Al-Saud, Manial Al-Roda,Cairo
pv.head@edaegypt.gov.eg; pv.safety@edaegypt.gov.eg;
Tel.: 237484988 Ext.:1470