ONDANSETRON HIKMA®

ACTION

Ondansetron is a potent highly selective antagonist of 5HT3 receptors, which are present peripherally on vagal nerve terminals and centrally in brain. Its precise mode of action in the control of nausea and vomiting is not known. Cytotoxic drugs and radiation appear to damage GIT mucosa causing the release of 5HT3 resulting in stimulation of 5HT3 receptors. Stimulation of 5HT3 receptors causes transmission of sensory signals to the vomiting center via vagal afferent fibers to induce vomiting. The activation of vagal afferents may cause 5HT3 release in the area postrema, located in the brain, and this may cause emesis by central mechanism. Ondansetron inhibits nausea and vomiting induced by chemotherapy and radiotherapy probably by antagonizing 5HT3 receptors both centrally and peripherally. Ondansetron has no dopamine receptor antagonist activity.

INDICATIONS

Ondansetron HIKMA is indicated for:

- Prevention of nausea and vomiting induced by cancer chemotherapy including high dose cisplatin.
- Prevention and treatment of postoperative nausea and vomiting.
- Prevention of nausea and vomiting associated with radiotherapy in patients receiving total body irradiation; single high dose fraction or daily fractions to the abdomen.

DOSAGE AND ADMINISTRATION

Chemotherapy and radiotherapy:

Adults: The dose and route of administration of Ondansetron HIKMA should be flexible within the range of 8-32 mg/day.

Emesis induced by radiotherapy and chemotherapy: Patients receiving emetogenic chemotherapy or radiotherapy, Ondansetron HIKMA 8 mg is given by slow intravenous injection before treatment or by oral administration 1-2 hours before treatment, followed by 8 mg orally every 12 hours.

Highly emetogenic chemotherapy: Patients taking highly emetogenic chemotherapy, (e.g. high dose of cisplatin), Ondansetron Hikma can be given in the following regimens over the first 24 hours of chemotherapy:

Ondansetron Hikma 8 mg single dose given by slow intravenous injection exactly before chemotherapy.

A dose of 8 mg Ondansetron Hikma by slow intravenous injection exactly before chemotherapy, followed by two doses of 8 mg intravenously two to four hours apart, or by 1 mg/hr for 24 hours as continuos infusion.

Single dose of 32 mg Ondansetron Hikma diluted in 50-100 ml of compatible infusion fluid, infused over 15 minutes before chemotherapy. Selection of the dose depends on the severity of vomiting. A single I.V. dose of 20 mg dexamethasone sodium phosphate enhances the antiemetic activity of Ondansetron Hikma. To prevent delayed emesis after the first 24 hours Ondansetron Hikma 8 mg is given twelve hourly by oral route up to 5 days after a course of treatment.

Children: Ondansetron Hikma was effective and well tolerated in children. It may be given intravenously at a dose of 5 mg/m2 exactly before chemotherapy followed by 4 mg orally after twelve hours, then continued by 4 mg/12 hour up to 5 days after chemotherapy.

Post -operative nausea and vomiting:

Adults: To prevent post-operative nausea and vomiting, Ondansetron Hikma 8 mg orally is given one hour before anesthesia followed by two doses of 8 mg every eight hours. Another recommended dose is 4 mg Ondansetron Hikma by slow intravenous injection at induction of anesthesia. To treat existing post-operative nausea and vomiting 4 mg Ondansetron Hikma given by slow intravenous injection is recommended.

Children: Dosage has not been established since there is no experience of using Ondansetron Hikma in preventing and treating post-operative nausea and vomiting in children.

Elderly: There is low experience of using Ondansetron Hikma in preventing and treating post-operative nausea and vomiting in elderly.

Patients with renal impairment: No alteration of daily dosage or frequency of dosing, or route of administration are required.

Patients with hepatic impairment: A total daily dose of 8 mg Ondansetron Hikma should not be exceeded, because the cleareance will be reduced and the serum half life of Ondansetron Hikma will be elongated in these patients.

CONTRAINDICATIONS

Ondansetron Hikma is contraindicated for patients known to have hypersensitivity to any ingredient of the preparation.

WARNINGS

Ondansetron Hikma injection should be protected from light. Ondansetron Hikma infusion is not needed to be protected from light when infusion takes place, since dilutions of Ondansetron Hikma injection in compatible I.V. infusion are stable for at least 24 hours in day light. Ondansetron Hikma injection should not be administered in the same syringe or infusion as any other medications.

Compatibility with intravenous fluids:

Ondansetron Hikma is compatible with the following intravenous infusions:

Mannitol intravenous infusion BP 10% w/v, sodium chloride intravenous infusion BP 0.9% w/v, Glucose intravenous infusion BP 5% w/v, potassium chloride 0.3% w/v and sodium chloride 0.9% w/v intravenous infusion BP, Ringers intravenous infusion, potassium chloride 0.3%w/v and glucose 5% w/v intravenous infusion BP. Dilutions of Ondansetron Hikma injection in intravenous fluids should be prepared at the infusion time.

Compatibility with other drugs:

Ondansetron Hikma Can be given by intravenous infusion at 1 mg/hour. The following drugs are compatible to be administered via the Ondansetron Hikma giving set for Ondansetron Hikma concentrations of 16 to 160 micrograms/ml (e.g 8 mg/500 ml and 8 mg /50 ml respectively).

Cisplatin: concentrations up to 0.48 mg/ml (e.g 240 mg in 500 ml) administered over one to eight hours.

5-fluorouracil: concentrations up to 0.8 mg/ml (e.g 2.4 g in 3 litres or 400 mg in 500 ml) given at a rate of 20 ml/hour (500 ml/24 hours). Higher concentrations of 5-fluorouracil may cause Ondansetron precipitation.

Carboplatin: concentrations in the range 0.18 mg/ml to 9.9 mg/ml (e.g 90 mg in 500 ml to 990 mg in 100 ml) given over ten minutes to one hour.

Etoposide: concentrations in the range 0.14 mg/ml to 0.25 mg/ ml (e.g 72 mg in 500 ml to 250 mg in 1litre) given over 30 minutes to one hour.

Cyclophosphamide: doses in the range 100 mg to 1 g, reconstituted with water for injection BP, 5 ml per 100 mg cyclophosphamide, as recommended by manufacturer and given as intravenous injection over five minutes.

Doxorubicin: doses in the range 10 mg to 100 mg reconstituted with water for injection BP, 5 ml per 10 mg doxorubicin, as recommended by manufacturer and given as intravenous injection over five minutes.

Dexamethasone: dexamethasone sodium phosphate 20 mg can be given as a slow intravenous injection via an infusion set delivering 8 or 32 mg of Ondansetron diluted in 50-100 ml of a compatible infusion fluid given over 15 minutes. Ondansetron Hikma and dexamethasone sodium phosphate were compatible through the same giving set resulting in concentrations of 32 microgram-2.5 mg/ml for dexamethasone sodium phosphate and 8 microgram to 1 mg/ml for Ondansetron Hikma.

PRECAUTIONS

Pregnancy and lactation: safety has not been established, however, Ondansetron Hikma can be given when clearly needed.

SIDE EFFECTS

Ondansetron Hikma increases large bowel transit time which may lead to constipation in some patients. Headache, a sensation of flushing or warmth in the head and epigastrium may occur. Rare reports of hypersensitivity reactions were registered.

OVERDOSAGE

Symptomatic and supportive therapy should be given if overdose was suspected.

STORAGE

Ampoules: Store between 15-25°C. Protect from light

Tablets: Store between 15-25°C.

PRESENTATIONS

Ampoules

ONDANSETRON HIKMA 4:	Ondansetron (as hydrochloride dihydrate) 4 mg/2 ml
ONDANSETRON HIKMA 8:	Ondansetron (as hydrochloride dihydrate) 8 mg/4 ml

Tablets

ONDANSETRON HIKMA 4:	Ondansetron (as hydrochloride dihydrate) 4 mg/tablet
ONDANSETRON HIKMA 8 :	Ondansetron (as hydrochloride dihydrate) 8 mg/tablet

THIS IS A MEDICAMENT.

- A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous.
- Follow the doctor's prescription strictly, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are experts in medicine, its benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.

HIKMA

Hikma Pharmaceuticals, Amman - Jordan

Keep medicament out of the reach of children

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