THE ULTIMATE WEAPON

in the battle against fungal infections

Erx code

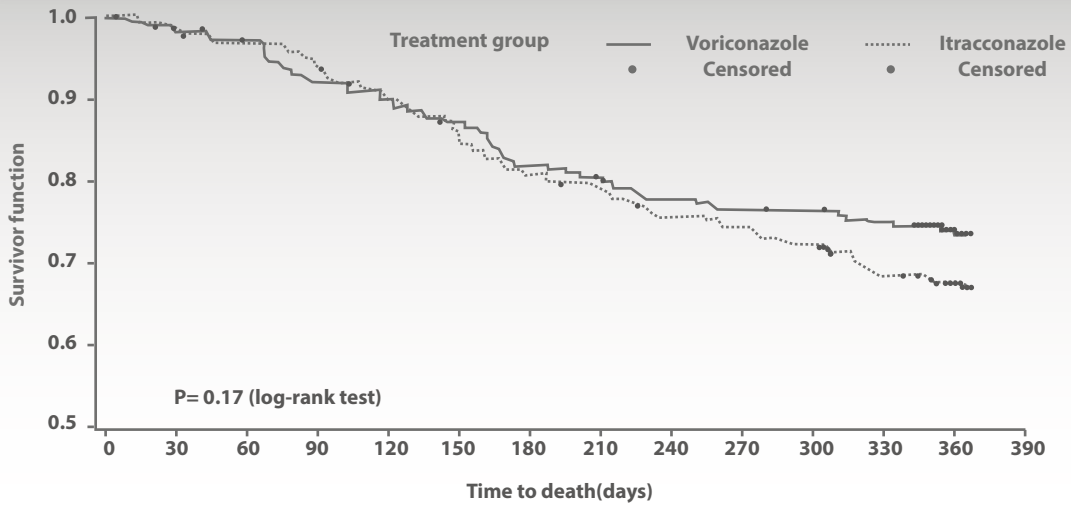
70455

Vtect

VORICONAZOLE F.C. tablets 200 mg

Voriconazole:

- Is interchangeable between intravenous and oral administration due to 96% bioavailability.
- Is superior to itraconazole in allergic bronchopulmonary aspergillosis, with better gastrointestinal tolerance and bioavailability.
- Is superior to itraconazole as antifungal prophylaxis after allogeneic haematopoietic stem-cell transplant.



Voriconazole versus itraconazole for antifungal prophylaxis following allogeneic haematopoietic stem-cell transplant

- Demonstrates superior in vitro activity against fluconazole-resistant C. glabrata and C. krusei.
- Is recommended as oral step-down therapy for patients with C. krusei, as this species is intrinsically resistant to fluconazole.

Vtect

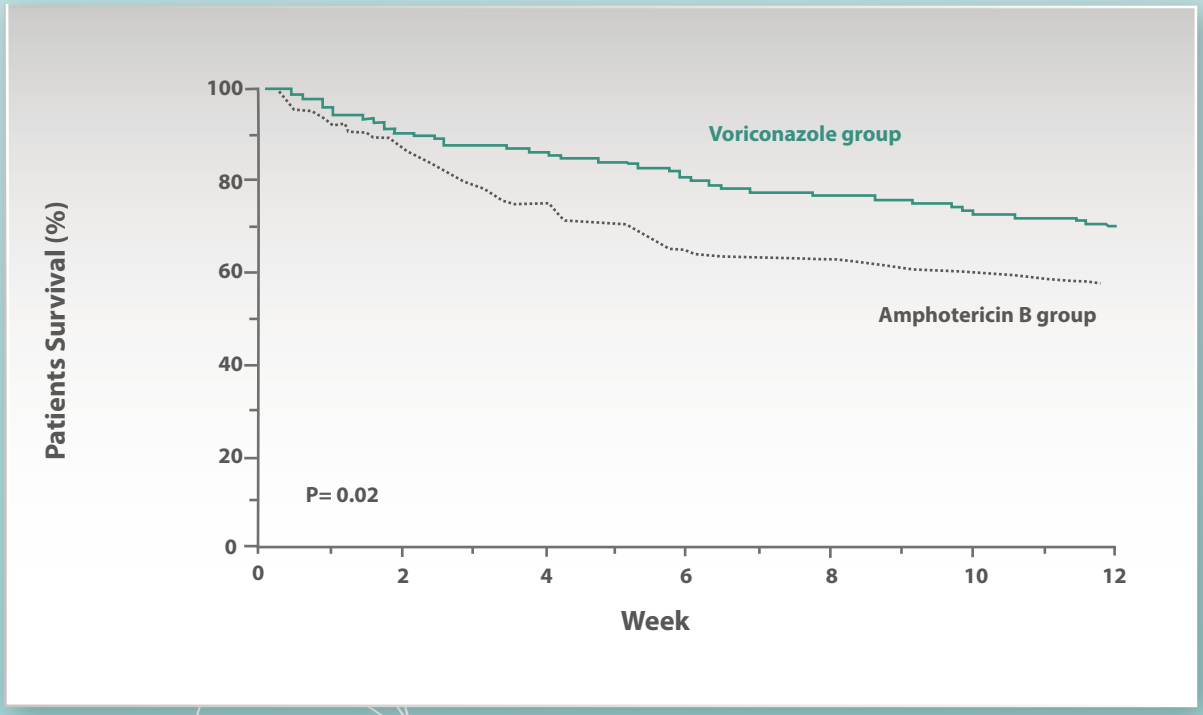
VORICONAZOLE F.C. tablets 200 mg

Has fungicidal effect against Aspergillus, despite of the fungistatic mechanism of action against Candida species.

Is the first-line agent for the treatment of chronic and invasive aspergillosis.

In comparison with amphotericin B in invasive aspergillosis has:

- **A greater likelihood of complete or partial response**
- **A lower mortality rate**
- **A lower rate of severe adverse reactions**



ACTOVERCO

Together for a healthy future

SmPC

• Name of the medicinal product:
Voriconazole film coated tablets 200 mg

• Therapeutic indications:
Voriconazole is a broad-spectrum, triazole antifungal agent and is indicated in adults and children aged 2 years and above as follows:
- Treatment of: invasive and chronic aspergillosis / candidemia in non-neutropenic patients / fluconazole-resistant serious invasive candida infections (including C. krusei)/ serious fungal infections caused by Scedosporium spp. and Fusarium spp.
- Prophylaxis of invasive fungal infections in high risk allogeneic hematopoietic stem cell transplant (HSCT) recipients.
- Voriconazole should be administered primarily to patients with progressive, possibly life-threatening infections.

• Posology and method of administration:
Electrolyte disturbances such as hypokalaemia, hypomagnesaemia and hypocalcaemia as well as liver function test should be monitored and corrected; if necessary, prior to initiation and during voriconazole therapy .
Therapy must be initiated with the specified loading dose regimen of either intravenous or oral Voriconazole to achieve plasma concentrations on day 1 that are close to steady state. On the basis of the high oral bioavailability (96%), switching between intravenous and oral administration is appropriate when clinically indicated.

12 to 14 years ≥50 kg; 15 to 17 years regardless of body weight, and adults

	Patients 40 kg and above	Patients less than 40 kg
Loading dose regimen (first 24 hours)	400 mg every 12 hours	200 mg every 12 hours
Maintenance dose (after first 24 hours)	200 mg twice daily	100 mg twice daily
Dosage adjustment for inadequate response	The maintenance dose may be increased to 300 mg twice daily	The maintenance dose may be increased to 150 mg twice daily.
Dosage adjustment for patients unable to tolerate treatment	The maintenance dose may be reduced by 50 mg steps to the 200 mg twice daily	The maintenance dose may be reduced to 100 mg twice daily

• Duration of treatment
Treatment duration should be as short as possible depending on the patient's clinical and mycological response. Long-term exposure to voriconazole greater than 180 days (6 months) requires careful assessment of the benefit-risk balance.

Children (2 to <12 years) and young adolescents with low body weight (12 to 14 years and <50 kg)

Loading dose regimen (first 24 hours)	No recommended
Maintenance Dose (after first 24 hours)	9 mg/kg twice daily (a maximum dose of 350 mg twice daily)
Dosage adjustment for inadequate response	the dose may be increased by 1 mg/kg steps (or by 50 mg steps if the maximum oral dose of 350 mg was used initially)
Dosage adjustment for patients unable to tolerate treatment	The dose may be reduced by 1 mg/kg steps (or by 50 mg steps if the maximum oral dose of 350 mg was used initially)

• Prophylaxis in Adults and Children:
Prophylaxis should be initiated on the day of transplant and may be administered for up to 100 days. Prophylaxis should be as short as possible depending on the risk for developing invasive fungal infection (IFI) as defined by neutropenia or immunosuppression. It may only be continued up to 180 days after transplantation in case of continuing immunosuppression or graft versus host disease (GvHD).
Dose: The recommended dosing regimen for prophylaxis is the same as for treatment in the respective age groups. Please refer to the treatment tables above.
Duration of prophylaxis: The safety and efficacy of voriconazole use for longer than 180 days have not been adequately studied in clinical trials.
Use of voriconazole in prophylaxis for greater than 180 days (6 months) requires careful assessment of the benefit-risk balance.

• Dose adjustment in special population:
• Elderly: No dose adjustment is necessary for elderly patients.
• Renal impairment: The pharmacokinetics of orally administered voriconazole are not affected by renal impairment. Therefore, no adjustment is necessary for oral dosing for patients with mild to severe renal impairmen
• Hepatic impairment: It is recommended that the standard loading dose regimens be used but that the maintenance dose be reduced by 50% in patients with mild to moderate hepatic cirrhosis (Child-Pugh A and B) receiving voriconazole. Voriconazole has not been studied in patients with severe chronic hepatic cirrhosis (Child-Pugh C).

• Method of administration:
Voriconazole film coated tablets are to be taken at least one hour before, or one hour following a meal.

• Contraindications:
- Hypersensitivity to the active substance or to any of the excipients.
- Coadministration with: terfenadine, astemizole, cisapride, pimozide, rifampicin, carbamazepine and phenobarbital, high-dose ritonavir, ergot alkaloids (ergotamine, dihydroergotamine).
- Coadministration with St. John's wort plant.

• Adverse effects:
- Very common: Peripheral edema, headache, visual impairment, respiratory distress, diarrhea, vomiting, abdominal pain, nausea, abnormal liver function test, rash, pyrexia
- Common: Sinusitis, agranulocytosis, pancytopenia, thrombocytopenia, leukopenia, anemia, hypoglycemia, hypokalemia, hyponatremia, depression, hallucination, anxiety, insomnia, agitation, confusional state, convulsion, syncope, tremor, hypertonia3, paresthesia, somnolence, dizziness, retinal hemorrhage, arrhythmia supraventricular, tachycardia, bradycardia, hypotension, phlebitis, acute respiratory distress syndrome, pulmonary oedema, cheilitis, dyspepsia, constipation, gingivitis, jaundice, jaundice cholestatic, hepatitis, exfoliative dermatitis, alopecia, maculo-papular rash, pruritus, erythema, acute renal failure, haematuria, back pain, chest pain, face oedema, asthenia, chills

References :
1.VFEND (voriconazole) prescribing information. http://labeling.pfizer.com/ShowLabeling.aspx?id=618 (Accessed on May 22, 2012).
2.Weiler S, Fiegl D, MacFarland R, et al. Human tissue distribution of voriconazole. Antimicrob Agents Chemother 2011; 55:925.
3.Chishimba L, Niven RM, Cooley J, Denning DW. Voriconazole and posaconazole improve asthma severity in allergic bronchopulmonary aspergillosis and severe asthma with fungal sensitization. Journal of Asthma. 2012 May 1;49(4):423-33.
4.Agarwal R, Dhooria S, Sehgal IS, Aggarwal AN, Garg M, Saikia B, Chakrabarti A. A randomised trial of voriconazole and prednisolone monotherapy in acute-stage allergic bronchopulmonary aspergillosis complicating asthma. European Respiratory Journal. 2018 Sep 1;52(3). **5.**Marks DI, Pagliuca A, Kibbler CC, Glasmacher A, Heussel CP, Kantecki M, Miller PJ, Ribaud P, Schlamm HT, Solano C, Cook G. Voriconazole versus itraconazole for antifungal prophylaxis following allogeneic haematopoietic stem-cell transplantation. British journal of haematology. 2011 Nov;155(3):318-27. **6.**Wingard JR, Carter SL, Walsh TJ, Kurtzberg J, Small TN, Baden LR, Gersten ID, Mendizabal AM, Leather HL, Confer DL, Maziarz RT. Randomized, double-blind trial of fluconazole versus voriconazole for prevention of invasive fungal infection after allogeneic hematopoietic cell transplantation. Blood, The Journal of the American Society of Hematology. 2010 Dec 9;116(24):5111-8. **7.**Pappas PG, Kauffman CA, Andes DR, Clancy CJ, Marr KA, Ostrosky-Zeichner L, Reboli AC, Schuster MG, Vazquez JA, Walsh TJ, Zaoutis TE. Clinical practice guideline for the management of candidiasis: 2016 update by the Infectious Diseases Society of America. Clinical Infectious Diseases. 2016 Feb 15;62(4):e1-50. **8.**Patterson TF, Thompson III GR, Denning DW, Fishman JA, Hadley S, Herbrecht R, Kontoyiannis DP, Marr KA, Morrison VA, Nguyen MH, Segal BH. Practice guidelines for the diagnosis and management of aspergillosis: 2016 update by the Infectious Diseases Society of America. Clinical Infectious Diseases. 2016 Aug 15;63(4):e1-60. **9.**Xu SX, Shen JL, Tang XF, Feng B, Xu HQ. Newer antifungal agents micafungin and voriconazole for fungal infection prevention during hematopoietic cell transplantation: a meta-analysis. Eur Rev Med Pharmacol Sci. 2016 Jan 1;20(2):381-90. **10.**Su HC, Hua YM, Feng IJ, Wu HC. Comparative effectiveness of antifungal agents in patients with hematopoietic stem cell transplantation: a systematic review and network meta-analysis. Infection and drug resistance. 2019;12:1311. **11.** Herbrecht R, Denning DW, Patterson TF, Bennett JE, Greene RE, Oestmann JW, Kern WV, Marr KA, Ribaud P, Lortholary O, Sylvester R. Voriconazole versus amphotericin B for primary therapy of invasive aspergillosis. New England Journal of Medicine. 2002 Aug 8;347(6):408-15.

ACTOVERCO
Together for a healthy future

No. 58, 8th St., Kooye Nasr (Gisha St.), Tehran, IR Iran,
Postal Code: 1446863914, Telefax: +98 (21) 41637000

ACT.MKT.INT.09.1403.2756

www.actoverco.com