Vardenorect

Varidenafii

Description Varidenarct Lis an oral tharapy for the treatment of excelle dysfunction. This monohytrochloride salt of varienafial is a selective inhibitor of cyclic putanosine monophosphate (COMP)-specific phosphodiosterase type 5 of PDESa) that the property of the property

metabolite (M1) is approximately 4.5 hours. After oral administration, vardenafil is excreted as metabolites predominant in the focas (approximately 91-95% of administered oral dose) and to a lesser extent in the urine (approximately 2-6% administered oral dose).

Pharmacokinetics in Special Populations:

**Prediatrics: Variential trials were not conducted in the pediatric population.

Geriatrics: In a healthy volunteer study of elderly males (>65 years) and younger males (18–45 years), mean Cmax and AUC were 34% and 52% higher, respectively, in the elderly males (see precautions, geriatric use and dosage and administration). Consequently, a lower starting dose of Vardenafil(5 mg) in patients >65 years of age should be

ministration). Consequently, a lower starting dose of Vardenafil(5 mg) in patients 56 years of age should be an understand to the patients of age should be and Insattificiency: In volunteers with mild renal impairment (CLC = 3-6-80 ml/min), the pharmacokinetics of vardenafil ser similar to those observed in a control group with normal renal function. In the moderate (CLC = 3-6-0-8 ml/min) or were (CLC = 30 ml/min) or mail impairment groups, the AUC of vardenafil was 20-30% higher compared to that served in a control group with normal renal function (CLC = 80 ml/min). Vardenafil pharmacokinetics have not been elulated in patients requiring renal dislysis (See precautions, renal insufficiency, and dosage and administration), agate insufficiency; in volunteers with mild hepatic impairment (Child-Pugh A), the Cmax and AUC following a 10 mg vardenafil dose were increased by 22% and 17%, respectively, compared to healthy control subjects. In volunteers with oddrate hepatic impairment (Child-Pugh B), the Cmax and AUC following a 10 mg vardenafil dose were increased by 20% and 160%, respectively, compared to healthy control subjects. Consequently, a starting dose of 5 mg is commended for peatients with moderate hepatic impairment, and the maximum dose should not exceed 10 mg (see ecautions and dosage and administration), Vardenafil has not been evaluated in patients with severe (Child-Pugh C) patie impairment.

recommended for patients with moderate hepatic impairment, and the maximum dose should not exceed 10 mg (see precautions and dasage and administration). Vardenafil has not been evaluated in patients with severe (Child-Pugh C) hepatic impairment.

Pharmacolypamics sure: In a clinical pharmacology study of patients with erectile dysfunction, single doses of vardenafil 20 mg caused a mean maximum decrease in supine blood pressure of 7 mmHg systolic and 8 mmHg. The dissolic (compared to placebo), accompanied by a mean 1 and 4 hours sees or coloring. Flowering the patient per manute. The dissolic (compared to placebo), accompanied by a mean 1 and 4 hours sees or coloring. Flowering the patient per manute. The dissolic (compared to placebo), accompanied by a mean 1 and 4 hours sees ording. Flowering the patient per manute. The dissolic compared to placebo pressure expenses were observed on day 3 la son day 1 Vardenafil may add to the blood pressure under the patient of the patient per sees of the patient

hypotension, the use of vardenafit by patients on nitrate therapy or on initro code donors is contraindicated (see contraindications). Electrophysiology: The effect of 10 mg and 80 mg vardenafit on OT interval was evaluated in a single-dose, doubte-bind, randomized, placebo and active-controlled (mostfloxacin 400 mg) crossover study in 69 healthy males (61% white, 12% Black, 7% Hispanio) aged 45-60 years. The OT interval was measured at one hour post dose because this interpolate point approximates the average time of peak vardenafit concentration. The 80 mg dose of Vardenafit (four times the highest recommended dose) was chosen because this dose yields plasma concentrations covering those observed upon co-administration of a low-dosen because this dose yields plasma concentrations covering those observed upon co-administration of allow-dosen of vardenafit (four times the highest recommended dose) was chosen because this dose yields plasma concentrations covering those observed upon co-administration of a low-dosen because this dose yields plasma concentrations covering those observed to recommend to the contract of the covering the contract of the covering the covering

Drug/Dose	QT Uncorrected	Fridericia QT correction	Individual QT correction
	(msec)	(msec)	(msec)
Vardenafil 10 mg	-2	8	4
	(-4,0)	(6,9)	(3,6)
Vardenafil 80 mg	-2	10	6
	(-4,0)	(8,11)	(4,7)
Moxifloxacin *400 mg	-2	8	7
	(-4,0)	(6,9)	(5,7)

'Active control (drug known to prolong QT)

Therapeutic and supratherapeutic doses of vardenafil and the active control moxifloxacin produced similar increases in QTc Interval. This study, however, was not designed to make direct statistical comparisons between the drug or the dose levels. The clinical impact of these QTc changes is unknown (see PTECAUTIONS). In a separate postmarketing study of 44 healthy volunteers, single doses of 10 mg Vardenafiliresulted in a placebo-subtracted mean change from baseline of QTCF (Friderical correction) of 5 mesc (90% CT. 28), Single doses of subtracted mean change from baseline of QTCF (Friderical correction) of 5 mesc (90% CT. 28), Single doses of gatifloxacin 400m gresulted in a placebo-subtracted mean change from baseline QTCF of 4 msec (90% CT. 1,7). When Vardenafilf long and gatifloxacin 400 mg were co-administered, the mean QTCF change from baseline was additive when compared to either drug alone and produced a mean QTCF change of 9 msec from baseline (90% CT. 1,7). The clinical impact of these QTC hanges is unknown (see PECCAUTIONS). Congenital or Acquired QT Prolongation).

Effects on Exercise Treadmill Test in Patients with Coronary Artery Disease (CAD): In two independent trials that assessed 10 mg (n=41) and 20 mg (n=43) avardenafil. respectively, vardenafil did not alter the total treadmill exercise time compared to placebo. The patient population included men aged 40-80 years with stable exercise-induced angina observable of the patients with Coronary Artery Disease (CAD): In two independent trials that assessed 10 mg (n=43) and 20 mg (n=43) avardenafil exercise time compared to placebo. The patient population included men aged 40-80 years with stable exercise-induced angina a positive stress echocardiogram or stress nuclear perfusion study, Results of these studies showed that Yardenafil did not alter the total treadmill exercise time compared to placebo (10 mg Vardenafil vs, placebo: 333±109 and 426£105 seconds; 2 mg Vardenafil vs, placebo: 354±101 and 36£105

ST-segment depression was similar to placebo in both the 10 mg and the zur mg varietient groups a transport of the property of

circically meaningful and attailetically significant improvement in the EF Domain, SEP2, and SEP3 scores compared to reprove more severe diseasely. Varidantil (5 ms. 10 ms. 10 ms. and 20 ms.) was effective in an elegistic severe severe diseasely. Varidantil (5 ms. 10 ms. 10 ms.) and 20 ms. and 20

clinical pharmacology, electrophysiology), therapeute (10 mg) and supraherapeute (80 mg) doses of Varidenstland the active control moliciacian (40 mg) produced similar increases in 10 cities of showed an additive of effect when compared and effect of combining Varidenstla with another drug of comparable of effect, showed an additive of effect when compared and effect of the compared of the compa

NTG. Potentiation of the hypotensive effects of nitrates for patients with ischemic heart disease has not been evaluated, and concomitant use of Vardenorect and nitrates is contraindicated (see clinical pharmacology, pharmacodynamics, effects on blood pressure and heart: rate when Vardenafilis combined with intrates; contraindications). Nitedipine: Vardenafilis combined with over-lease infedipine 30 gor 60 mg once daily, did not affect the relative bioavailability (AUC) or maximum concentration (Cmax) of infedipine, a drug that is metabolized via CYP3AA. Nifedipine id don't alter the plasma levels of Vardenorect when taken in combination. In these patients whose hypertension was controlled with infedipine, Vardenorect 20 mg produced mean additional supine systelic/diastolic blood pressure reductions of 615 mmHg compared to placebo.
Alpha-blockers: Blood pressure effects in patients on stable alpha-blocker treatment: Two clinical pharmacology studies were conducted in patients with benign prostatic hyperplasia (BPH) on stable-dose alpha-blocker treatment for at least four weeks.
Study 1: This study was designed to evaluate the effect of 5 mg vardenafil compared to placebo when administered to BPH patients on stohy was designed to evaluate the effect of 5 mg vardenafil compared to placebo when administered to EPH patients on chronic alpha-blocker therapy in two separate cohorts: tamsulosin 0.4 mg daily (cohort 1, n=21) and terazosin 5 or 10 mg daily (cohort 2, n=21). The design was a randomized, double binding, cross-over study with four treatments: vardenafil 5 mg or placebo administered simultaneously with the alpha-blocker of 8-bour interval after vardenafil obering 5 or 8PH results see Table 2. One patient after simultaneous treatment with 5 mg vardenafil and 10 mg terazosin 6-bourd hypotension with standing blood of mmHg occuming one hour after administration and subsequent mild duzzness and moderate lightheedeness listing for 6 hours, For varies and administration of treatments was not observed when vardena

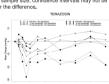
		(Study 1)	
Alpha-Blocker		Simultaneous dosing of Vardenafil 5mg and Alpha- Blocker, Placebo-subtracted	Dosing of Vardenafil 5mg and Alpha- Blocker Separated by 6 Hours, Placebo-subtracted
Terazosin 5 or 10 mg daily	Standing SBP	-3 (-6.7, 0.1)	-4 (-7.4 , - 0.5)
Terazosin 5 or 10 mg daily	Supine SBP	-4 (-6.7 ,- 0.5)	-4 (-7.1, - 0.7)
Tamsulosin 0.4mg daily	Standing SBP	-6 (-9.9, - 2.1)	-4 (- 8.3 , - 0.5)
Tamsulosin 0.4mg daily	Supine SBP	-4 (-7.0 , - 0.8)	-5 (-7.9 , -1.7)

	enatil 10 and 20 mg in BPH patients on llosin 0.4 or 0.8 mg daily (Study 2)	Stable 3 Timo (H)
	Vardenafil 10mg Placebo-s ubtracted	Vardenafil 10mg Placebo-s ubtracted
Standing SBP	-4 (-6.8 , - 0.3)	-4 (-6.8 , - 1.4)
Supine SBP	-5 (-8.2, - 0.8)	-4 (-6.3 , - 1.8)

Blood pressure effects (standing SBP) in normotensive men on stable dose tamsulosin 0.4 mg following simultaneous administration of variedness 120 mg or placebo, or following administration of variedness 120 mg or placebo, or following administration of variedness 120 mg or placebo separated by 6 hours are shown in Figure 3. The place 150 mg or placebo separated by 6 hours are shown in Figure 3. The placebo separated by 6 hours are shown in Figure 3. The placebo separated by 6 hours are shown in Figure 3. The placebo separated by 6 hours are shown in Figure 3. The placebo separated by 6 hours are shown in Figure 3. The placebo separated by 6 hours are shown in Figure 3. The placebo separated by 6 hours are shown in Figure 3. The placebo separated by 6 hours are shown in Figure 3. The placebo separated by 6 hours are shown in Figure 3. The placebo separated by 6 hours are shown in Figure 3. The placebo separated by 6 hours are shown in Figure 3. The placebo separated by 6 hours are shown in Figure 3. The placebo separated by 6 hours are shown in Figure 3. The shown in Figure 3. The placebo separated by 6 hours are shown in Figure 3. The shown in Figure 3.

healthy volunt	eers on daily alpha	blocker therapy.			
		Dosing of Vardenafil and Alpha- Blocker Separated by 6 Hours		Simultaneous dosing of Vardenafil and Alpha-Blocker	
Alpha- blocker		Vardenafil 10 mg Placebo- Subtracted	Vardenafil 20 mg Placebo- Subtracted	Vardenafil 10 mg Placebo- Subtracted	Vardenafil 20 mg Placebo- Subtracted
Terazosin 10 mg daily	Standing SBP	-7 (-10, -3)	-11 (-14, -7)	-23 (-31, 16)*	-14 (-33, 11)*
10 mg dany	Supine SBP	-5 (-8, -2)	-7 (-11, -4)	-7 (-25, 19)*	-7 (-31, 22)*
Tamsulosin 0.4 mg daily	Standing SBP	-4 (-8, -1)	-8 (-11, -4)	-8 (-14, -2)	-8 (-14, -1)
	Supine SBP	-4 (-8, 0)	-7 (-11, -3)	-5 (-9, -2)	-3 (-7, 0)

* Due to the sample size, confidence intervals may not be an accurate measure for these data. These values represent the range for the difference.



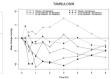


Figure 6: Mean change from baseling its standing systolic blood pressure/mmtgl) over 6 hour interval following simultaneous or 6 hr separation administration of vardenafil 10 mg, vardenafil 20 mg or placebo with terazosin (10 mg) in healthy volunteers.

Ritionaria and indinavir: Upon concomitant administration of 5 mg of Vardenored: with 800 mg BID ritionavir, the Cmax and AUC of ritionavir were reduced by approximately 20%. Upon administration of 10 mg of Vardenored: with 800 mg BID ritionavir, the Cmax and AUC of indinavir were reduced by 40% and 30%, respective the 800 mg BID ritionavir, the Cmax and AUC of indinavir were reduced by 40% and 30%, respective the 800 mg BID ritionavir, the Cmax and AUC of indinavir were reduced by 40% and 30%, respective the 800 mg TID indinavir, the Cmax and AUC of indinavir were reduced by 40% and 30%, respective the 800 mg TID indinavir, the Cmax and AUC of indinavir were reduced by 40% and 30%, respectively, and vardenafil plasma levels were observation period in healthy volunteers when administered with alcohold 6.5 g/kg body weight observed achieved to the service of the service of achieved the service of achieved the service of achieved the service of a chief the service of a chief the service of a chief the service of t



ء أقداص مغلفة

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و يقوري ؟ لا قرمى ملقف بعثوى على:

و يقوري ؟ لا قرمى ملقف بعثوى على:

الد الغير فعالة بمثل و البدائة فالدينا في المراحة و المراح

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إنتـاج: . عــناعات الدوانـــة. المحمدوعة المصدية للد

Adverse Event	Percentage of Patients Reporting Event			
	Placebo (N= 1199)	Vardenafii (N=2203)		
Headache	496	1596		
Flushing	196	1196		
Rhinitis	3%	9%		
Dyspepsia	196	496		
Accidental Injury*	2%	396		
Sinusitis	1.96	396		
Flu Syndrome	2%	396		
dizziness	1%	2%		
Increase Creatine Kinase	1%	296		
Nausea	196	2%		

Manufactured by:

