הודעה על החמרה (מידע בטיחות) בעלון לרופא ולצרכן

(מעודכן 3102.50)

תאריך _ October 15, 2013 _

שם תכשיר באנגלית ומספרי הרישום

IKACOR Tablets 40 mg: 025 25 2113 0; 80 mg: 040 02 23155 00, 120 mg: 039 47 21913 00

שם בעל הרישום__ Teva Pharmaceutical Industries Ltd., P.O.Box 3190, Petach Tikva

בעלון לרופא

טופס זה מיועד לפרוט ההחמרות בלבד !

ההחמרות המבוקשות		
פרק בעלון	**טקסט נוכחי**	**טקסט חדש**
Indication		
Contraindications	Known hypersensitivity to verapamil hydrochloride or to any other ingredient of the preparation. Acute myocardial infarction with complications. Congestive heart failure. Severe left ventricular dysfunction (see Warnings). Hypotension (less than 90 mm Hg systolic pressure) or cardiogenic shock. Sick sinus syndrome (except in patients with a functioning artificial ventricular pacemaker). Second- or third-degree AV block (except in patients with a functioning artificial ventricular pacemaker). Patients with atrial flutter or atrial fibrillation and an accessory bypass tract (e.g. Wolff-Parkinson-White, Lown-Ganong-Levine syndromes). (See Warnings).	Known hypersensitivity to verapamil hydrochloride or to any other ingredient of the preparation.<br~~Acute myocardial infarction with complications.~~<br~~Congestive heart failure~~. Heart failure with reduced ejection fraction of less than 35%, and/or pulmonary wedge pressure above 20 mm Hg (unless secondary to a supraventricular tachycardia amenable to verapamil therapy). Severe left ventricular dysfunction (see Warnings). Hypotension (less than 90 mm Hg systolic pressure) or cardiogenic shock. Sick sinus syndrome (except in patients with a functioning artificial ventricular pacemaker). Second- or third-degree AV block (except in patients with a functioning artificial ventricular pacemaker). Patients with atrial flutter or atrial fibrillation in the presence of ~~and~~ an accessory bypass tract (e.g. Wolff-Parkinson-White, Lown-Ganong-Levine syndromes). These patients are at risk to develop ventricular tachyarrhythmia including ventricular fibrillation if verapamil hydrochloride is administered (See Warnings).
Posology, dosage & administration		
Special Warnings and Special Precautions for Use	*Atrioventricular Block* The effect of verapamil on AV conduction and the SA node may lead to asymptomatic first-degree AV block and transient bradycardia, sometimes accompanied by nodal escape rhythms. PR interval prolongation is correlated with verapamil plasma concentrations, especially during the early titration phases of therapy. Higher degrees of AV block, however, were infrequently (0.8%) observed. Marked first-degree block or progressive development to second- or third-degree AV block requires a reduction in dosage or, in rare instances,	*Acute Myocardial infarction* Use with caution in acute myocardial infarction complicated by bradycardia, marked hypotension, or left ventricular dysfunction. Heart failure patients with ejection fraction higher than 35% should be compensated before starting verapamil treatment and should be adequately treated throughout. *Heart Block/ 1st Degree AV block/Bradycardia/Asystole* Verapamil hydrochloride affects the AV and SA nodes and prolongs AV conduction time. Use with caution as development of second-or third-degree AV block (contraindication) or

unifascicular, bifascicular or trifascicular bundle branch block requires discontinuation in subsequent doses of verapamil hydrochloride and institution of appropriate therapy, if needed. Verapamil hydrochloride affects the AV and SA nodes and rarely may produce second- or third degree AV block, bradycardia, and, in extreme cases, asystole. This is more likely to occur in patients with a sick sinus syndrome (SA nodal disease), which is more common in older patients. Asystole in patients other than those with sick sinus syndrome is usually of short duration (few seconds or less), with spontaneous return to AV nodal or normal sinus rhythm. If this does not occur promptly, appropriate treatment should be initiated immediately. See Adverse Reactions. ~~*Atrioventricular Block*~~ ~~The effect of verapamil on AV conduction and the SA node may lead to asymptomatic first-degree AV block and transient bradycardia, sometimes accompanied by nodal escape rhythms. PR interval prolongation is correlated with verapamil plasma concentrations, especially during the early titration phases of therapy. Higher degrees of AV block, however, were infrequently (0.8%) observed. Marked first-degree block or progressive development to second- or third-degree AV block requires a reduction in dosage or, in rare instances, discontinuation of verapamil HCl and institution of appropriate therapy depending upon the clinical situation.~~ *Antiarrhythmics, Beta-blockers* Mutual potentiation of cardiovascular effects (higher-grade AV block, higher-grade lowering of heart rate, induction of heart failure and potentiated hypotension). Asymptomatic bradycardia (36 beats/minute) with a wandering atrial pacemaker has been observed in a patient receiving concomitant timolol (a beta-adrenergic blocker) eye drops and oral verapamil hydrochloride. *Digoxin* If verapamil is administered concomitantly with digoxin, reduce digoxin dosage. See Drug Interactions *Other~~s~~ Neuromuscular transmission disorders* Verapamil should be used with caution in patients with diseases in which neuromuscular transmission is affected (myasthenia gravis, Lambert-Eaton syndrome, advanced Duchenne muscular dystrophy). Special Populations *Renal impairment* Although impaired renal function has been shown in robust comparator studies to have no effect on verapamil pharmacokinetics in patients with end-	discontinuation of verapamil HCl and institution of appropriate therapy depending upon the clinical situation. *Other* Verapamil should be used with caution in patients with diseases in which neuromuscular transmission is affected (myasthenia gravis, Lambert-Eaton syndrome, advanced Duchenne muscular dystrophy).	

stage renal failure, several case reports suggest that verapamil should be used cautiously and with close monitoring in patients with impaired renal function. Verapamil cannot be removed by hemodialysis. *Liver impairment* Use with caution in patients with severely impaired liver function (see Dosage)		
Due to its antihypertensive effect, depending on the individual response, verapamil hydrochloride may affect the ability to react to the point of impairing the ability to drive a vehicle, operate machinery or work under hazardous conditions. This applies all the more at the start of treatment, when the dose is raised, when switching from another drug and in conjunction with alcohol. Verapamil may increase the blood levels of alcohol and slow its elimination. Therefore, the effects of alcohol may be exaggerated. ~~Depending on the individual response, verapamil may affect the ability to react to the point of impairing the ability to drive a vehicle, operate machinery or work under hazardous conditions. This applies all the more at the start of treatment, when the dose is raised, when switching from another drug and in conjunction with alcohol.~~	Depending on the individual response, verapamil may affect the ability to react to the point of impairing the ability to drive a vehicle, operate machinery or work under hazardous conditions. This applies all the more at the start of treatment, when the dose is raised, when switching from another drug and in conjunction with alcohol.	**Effects on ability to drive and use machines**
Verapamil/Colchicine: Colchicine is a substrate for both CYP3A and the efflux transporter, P-glycoprotein (Pgp). Verapamil is known to inhibit CYP3A and P-gp. When verapamil and colchicine are administered together, inhibition of P-gp and/or CYP3A by verapamil may lead to increased exposure to colchicine. Colchicine levels may rise , AUC (approximately 2 fold) as well as Cmax (approximately 1.3 fold). Reduce colchicine dose. ~~Combined use is not recommended.~~ ***Verapamil/Carbamazepine/Antiepileptics:((e.g. Phenytoin)*** Verapamil therapy may increase carbamazepine concentrations during combined therapy. This may produce carbamazepine side effects such as diplopia, headache, ataxia or dizziness Carbamazepine AUC may increase by about 46% in refractory partial epilepsy patients. Verapamil plasma concentrations may be decreased upon combination with phenytoin. ***Verapamil/Doxorubicin***: In patients with small cell lung cancer doxorubicin AUC rose by 104% ~~89~~% and doxorubicin Cmax by 61% with oral verapamil administration. In patients with advanced neoplasma there was no significant change in doxorubicin PK with intravenous verapamil administration	***Verapamil/Colchicine:*** Colchicine is a substrate for both CYP3A and the efflux transporter, P-glycoprotein (Pgp). Verapamil is known to inhibit CYP3A and P-gp. When verapamil and colchicine are administered together, inhibition of P-gp and/or CYP3A by verapamil may lead to increased exposure to colchicine. . Combined use is not recommended. ***Verapamil/Carbamazepine*** Verapamil therapy may increase carbamazepine concentrations during combined therapy. This may produce carbamazepine side effects such as diplopia, headache, ataxia or dizziness Carbamazepine AUC may increase by about 46% in refractory partial epilepsy patients. ***Verapamil/Doxorubicin***: In patients with small cell lung cancer doxorubicin AUC rose by 89% and doxorubicin Cmax by 61% with oral verapamil administration. In patients with advanced neoplasma there was no significant change in doxorubicin PK with intravenous verapamil administration	**Interaction with Other Medicaments and Other Forms of Interaction**

Verapamil/Digoxin/Digitoxin: Clinical use of verapamil in digitalized patients has shown the combination to be well tolerated if digoxin doses are properly adjusted. Digoxin Cmax increases by about 44 ~~45-53~~%, digoxin C12h (about 53%) in healthy subjects, Css increases by about 44 ~~42~~% and AUC increases by about 50 ~~52~~%. In patients with hepatic cirrhosis the influence of verapamil on digoxin kinetics is magnified. Digitoxin total body clearance and extrarenal clearance are reduced by about 27% and 29%, respectively.	***Verapamil/Digoxin/Digitoxin:*** Clinical use of verapamil in digitalized patients has shown the combination to be well tolerated if digoxin doses are properly adjusted. Digoxin Cmax increases by about 45-53%, in healthy subjects, Css increases by about 42% and AUC increases by about 52%. In patients with hepatic cirrhosis the influence of verapamil on digoxin kinetics is magnified. Digitoxin total body clearance and extrarenal clearance are reduced by about 27% and 29%, respectively.	
Verapamil/Immunologics/Immunosuppressives: ***Verapamil/Cyclosporine***: Verapamil therapy may increase serum levels of cyclosporine (AUC, C_{ss}, C_{max} by ~45%). ***Verapamil/Sirolimus/Tacrolimus/Everolimus***: Possible increase in sirolimus, tacrolimus, or everolimus levels. Everolimus: AUC increase (about 3.5 fold), Cmax (about 2.3 fold); verapamil: Ctrough increases by about 2.3 fold). Concentration determinations and dose adjustments of everolimus may be necessary. Sirolimus: increased sirolimus AUC (about 2.2 fold); S-verapamil AUC increases by about 1.5 fold). Concentration determinations and dose adjustments of sirolimus may be necessary. Tacrolimus: possible increase in tacrolimus levels.	***Verapamil/Immunologics/:*** ***Verapamil/Cyclosporine***: Verapamil therapy may increase serum levels of cyclosporine (AUC, C_{ss}, C_{max} by ~45%). ***Verapamil/Sirolimus/Tacrolimus/Everolimus***: Possible increase in sirolimus, tacrolimus, or everolimus levels.	
Verapamil/Lipid Lowering Agents (HMG Co-A Reductase Inhibitors, i.e. "Statins", e.g., Atorvastatin, Lovastatin, Simvastatin): Concomitant use of these agents with verapamil hydrochloride may increase the serum levels of atorvastatin (as well as increase in AUC of verapamil by about 43 ~~42.8~~%), simvastatin or lovastatin. For simvastatin: a rise in AUC (about 2.6 fold), C_{max} (about 4.6 fold). Lovastatin levels may possibly rise; verapamil AUC may rise (63%), Cmax (32%)	***Verapamil/Lipid Lowering Agents (HMG Co-A Reductase Inhibitors, i.e. "Statins", e.g., Atorvastatin, Lovastatin, Simvastatin):*** Concomitant use of these agents with verapamil hydrochloride may increase the serum levels of atorvastatin (as well as increase in AUC of verapamil by about 42.8%), simvastatin or lovastatin. For simvastatin: a rise in AUC (about 2.6 fold), C_{max} (about 4.6 fold).	
Verapamil/Grapefruit juice: Grapefruit juice may increase the plasma levels of verapamil hydrochloride (AUC for R-verapamil increases by about 49% and for S-verapamil by about 37% verapamil AUC. Cmax for R-verapamil increases by about 75% and for the S-verapamil by about 51%. Elimination half-life and renal clearance not affected. Grapefruit juice should therefore not be ingested with verapamil	***Verapamil/Grapefruit juice:*** Grapefruit juice may increase the plasma levels of verapamil hydrochloride (AUC for R-verapamil increases by about 49% and for S-verapamil by about 37% verapamil AUC. Cmax for R-verapamil increases by about 75% and for the S-verapamil by about 51%.	
Verapami/ Lithium: Increased sensitivity to the effects of lithium (neurotoxicity) has been reported during concomitant verapamil hydrochloride-lithium therapy with either no change or an increase in serum lithium levels. The addition of verapamil hydrochloride, however, has also resulted in the lowering of the serum lithium levels in patients receiving chronic stable oral lithium. Patients receiving both drugs should	***Verapami/ Lithium:*** Oral verapamil therapy may result in a lowering of serum lithium levels in patients receiving chronic, stable oral lithium therapy. There may be increased sensitivity to lithium causing enhanced neurotoxicity. A dose adjustment of the lithium may be necessary.	

be monitored carefully. ~~Oral verapamil therapy may result in a lowering of serum lithium levels in patients receiving chronic, stable oral lithium therapy. There may be increased sensitivity to lithium causing enhanced neurotoxicity. A dose adjustment of the lithium may be necessary.~~ ***Verapamil/Inhalation Anesthetic Agents/ Neuromuscular Blocking Agents:*** Clinical data and animal studies suggest that verapamil may potentiate the activity of inhalation anesthetics and neuromuscular blocking agents (curare-like and depolarizing). It may be necessary to decrease the dose of verapamil hydrochloride and/or the dose of the neuromuscular blocking agent when the drugs are used concomitantly.	***Verapamil/Inhalation Anesthetic Agents/ Neuromuscular Blocking Agents:*** Clinical data and animal studies suggest that verapamil may potentiate the activity of inhalation anesthetics and neuromuscular blocking agents .	
Use in Pregnancy There are no adequate and well-controlled studies in pregnant women. Verapamil crosses the placenta and has been measured in umbilical cord blood. This drug should be used during pregnancy only if clearly needed. Verapamil crosses the placental barrier and can be detected in umbilical vein blood at delivery.	*Use in Pregnancy* There are no adequate and well-controlled studies in pregnant women. Verapamil crosses the placenta and has been measured in umbilical cord blood. This drug should be used during pregnancy only if clearly needed.	**Fertility, Pregnancy and Lactation**
Reproduction studies have been performed in rabbits and rats at oral verapamil doses up to 1.5 (15 mg/kg/day) and 6 (60 mg/kg/day) times the human oral daily dose, respectively, and have revealed no evidence of teratogenicity. In the rat, however, this multiple of the human dose was embryocidal and retarded fetal growth and development, probably because of adverse maternal effects reflected in reduced weight gains of the dams. This oral dose has also been shown to cause hypotension in rats. There are, however, no adequate and well-controlled studies in pregnant women.		**Preclinical Data**
The following adverse reactions have been reported with verapamil from clinical studies, postmarketing surveillance or Phase IV clinical trials and are listed below by system organ class. Frequencies are defined as: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); not known (cannot be estimated from the available data). The most commonly reported ADRs were headache, dizziness, gastrointestinal disorders: nausea, constipation and abdominal pain, as well as bradycardia, tachycardia, palpitations, hypotension, flushing, edema peripheral and fatigue. Adverse reactions reported from clinical studies with verapamil and post-marketing surveillance activities	Serious adverse reactions are uncommon when verapamil therapy is initiated with upward dose titration within the recommended single and total daily dose. The following reactions occurred at rates greater than 1% or appeared in lower rates but appeared clearly drug-related in clinical trials. *Cardiovascular* Hypotension, edema, congestive heart failure or pulmonary edema, bradycardia (HR<50/min.), AV block, flushing. *Central Nervous System* Dizziness, headache, fatigue. *Gastrointestinal* Constipation, nausea. *Pulmonary*	**Adverse events**

MedDRA System Organ Class	Common	Uncommon	Rare	Unknown
Immune system disorders				Hypersensitivity
Nervous system disorders	Dizziness, Headache		Paresthesia Tremor	Extrapyramidal disorder, paralysis (tetraparesis)[1], Seizures
Psychiatric disorders			Somnolence	
Ear and labyrinth disorders			Tinnitus	vertigo
Cardiac disorders	Bradycardia	Palpitations, Tachycardia		Atrioventricular block (1°, 2°, 3°), Cardiac failure, Sinus arrest, Sinus bradycardia; asystole
Vascular disorders	Flushing, Hypotension			
Respiratory, thoracic and mediastinal disorders				Bronchospasm
Gastrointestinal disorders	Constipation, Nausea	Abdominal pain	vomiting	Abdominal discomfort, Gingival hyperplasia, Ileus
Skin and subcutaneous tissue			Hyperhidrosis	Angioedema, Stevens-Johnson syndrome,

Dyspnea.

Skin
Rash.

Other
Elevated liver enzymes have been reported (see WARNINGS).

The following reactions, reported in 1% or less of patients, occurred under conditions where a causal relationship is uncertain
They are listed to alert the physician to a possible relationship:
Angina pectoris, atrioventricular dissociation, chest pain, claudication, myocardial infarction, palpitations, purpura (vasculitis), syncope; diarrhea, dry mouth, gastrointestinal distress, gingival hyperplasia; ecchymosis or bruising; cerebrovascular accident, confusion, equilibrium disorders, insomnia, muscle cramps, paresthesia, psychotic symptoms, shakiness (tremor), extrapyramidal disorder, somnolence; hair loss, hyperkeratosis, maculae, sweating, Stevens-Johnson syndrome, erythema multiforme; blurred vision; increased urination, spotty menstruation.
Other Adverse Reactions
Immune system disorders
Hypersensitivity.

Ear and labyrinth disorders
Vertigo, tinnitus

Cardiac disorders
Atrioventricular block (1st, 2nd, 3rd), sinus arrest, tachycardia. Heart failure may develop or existing heart failure may be exacerbated; edema peripheral.

Gastrointestinal disorders
Vomiting, ileus, abdominal pain/discomfort

Skin and subcutaneous tissue disorders
Pruritus, urticaria, angioedema, rash maculopapular.

Musculoskeletal and connective tissue disorders
Muscular weakness or muscle and joint pain.

Reproductive system and breast disorders
Impotence, gynecomastia, galactorrhea.

Nervous system disorders
There has been a single postmarketing report of paralysis (tetraparesis) associated with combined use of verapamil and colchicine. This may have been caused by

disorders				Erythema multiforme, Alopecia, Itching, Pruritus, Purpura, Rash maculopapular, Urticaria
Musculoskeletal and connective tissue disorders				Arthralgia, Muscular weakness, Myalgia
Reproductive system and breast disorders				Erectile dysfunction, Galactorrhea, Gynecomastia
General disorders and administration site conditions	Edema peripheral	Fatigue		
Investigations				Blood prolactin increased, Hepatic enzymes increased

[1] There has been a single postmarketing report of paralysis (tetraparesis) associated with the combined use of verapamil and colchicine. This may have been caused by colchicine crossing the blood-brain barrier due to CYP3A4 and P-gp inhibition by verapamil. See Drug Interactions

Reporting of suspected adverse reactions
Reporting of suspected adverse reactions is an important way to gather more information to continuously monitor the benefit/risk balance of the medicinal product.

~~Serious adverse reactions are uncommon when verapamil therapy is initiated with upward dose titration within the recommended single and total daily dose.~~

~~The following reactions occurred at rates greater than 1% or appeared in lower rates but appeared clearly drug related in clinical trials.~~

colchicine crossing the blood-brain barrier due to CYP3A4 and P-gp inhibition by verapamil. Combined use of verapamil and colchicine is not recommended.

Investigations
Elevated prolactin levels.

Cardiovascular
- Hypotension, edema, congestive heart failure or pulmonary edema, bradycardia (HR<50/min.), AV block, flushing.

Central Nervous System
- Dizziness, headache, fatigue.

Gastrointestinal
- Constipation, nausea.

Pulmonary
- Dyspnea.

Skin
- Rash.

Other
- *Elevated liver enzymes have been reported (see WARNINGS).*
-
- The following reactions, reported in 1% or less of patients, occurred under conditions where a causal relationship is uncertain
- They are listed to alert the physician to a possible relationship:

Angina pectoris, atrioventricular dissociation, chest pain, claudication, myocardial infarction, palpitations, purpura (vasculitis), syncope; diarrhea, dry mouth, gastrointestinal distress, gingival hyperplasia; ecchymosis or bruising; cerebrovascular accident, confusion, equilibrium disorders, insomnia, muscle cramps, paresthesia, psychotic symptoms, shakiness (tremor), extrapyramidal disorder, somnolence; hair loss, hyperkeratosis, maculae, sweating, Stevens-Johnson syndrome, erythema multiforme; blurred vision; increased urination, spotty menstruation.

Other Adverse Reactions

Immune system disorders

Hypersensitivity.

Ear and labyrinth disorders
- Vertigo, tinnitus

Cardiac disorders
- Atrioventricular block (1^{st}, 2^{nd}, 3^{rd}), sinus arrest, tachycardia. Heart failure may develop or existing heart failure may be exacerbated; edema peripheral.

Gastrointestinal disorders
- Vomiting, ileus, abdominal pain/discomfort

Skin and subcutaneous tissue disorders
- Pruritus, urticaria, angioedema, rash maculopapular.

Musculoskeletal and connective tissue disorders
- Muscular weakness or muscle and joint pain.

Reproductive system and breast disorders
- Impotence, gynecomastia, galactorrhea.

~~*Nervous system disorders*~~ ~~- There has been a single postmarketing report of paralysis (tetraparesis) associated with combined use of verapamil and colchicine. This may have been caused by colchicine crossing the blood-brain barrier due to CYP3A4 and P-gp inhibition by verapamil. Combined use of verapamil and colchicine is not recommended.~~ ~~*Investigations*~~ ~~- Elevated prolactin levels.~~		
Pharmacotherapeutic group: Selective calcium channel blockers with direct cardiac effects, phenylalkylamine derivatives. ATC-Code: C08DA01 **Pharmacokinetic properties** Verapamil hydrochloride is a racemic mixture consisting of equal portions of the R-enantiomer and the S-enantiomer. Verapamil is extensively metabolized. Norverapamil is one of 12 metabolites identified in urine, has 10 to 20% of the pharmacologic activity of verapamil and accounts for 6% of excreted drug. The steady-state plasma concentrations of norverapamil and verapamil are similar. Steady state after multiple once daily dosing is reached after three to four days. *Absorption* Greater than 90% of verapamil is rapidly absorbed from the small intestine after oral administration. Mean systemic availability of the unchanged compound after a single dose of verapamil is 22% owing to an extensive hepatic first-pass metabolism. Bioavailability is about two times higher with repeated administration. Peak verapamil plasma levels are reached one to two hours after administration. The peak plasma concentration of norverapamil is attained approximately one hour after administration. The presence of food has no effect on the bioavailability of verapamil. *Distribution* Verapamil is widely distributed throughout the body tissues, the volume of distribution ranging from 1.8–6.8 L/kg in healthy subjects. Plasma protein binding of verapamil is approximately 90%. *Metabolism* Verapamil is extensively metabolized. *In vitro* metabolic studies indicate that verapamil is metabolized by cytochrome P450 CYP3A4, CYP1A2, CYP2C8, CYP2C9 and CYP2C18. In healthy men, orally administered verapamil hydrochloride undergoes extensive metabolism in the liver, with 12 metabolites having been identified, most in only trace amounts. The major metabolites have been identified as various N and O-dealkylated products of verapamil. Of these metabolites, only norverapamil has any appreciable pharmacological effect		**Mechanism of Action/ Pharmacodynamics/ Pharmacokinetics**

(approximately 20% that of the parent compound), which was observed in a study with dogs. *Elimination* Following intravenous infusion, verapamil is eliminated bi-exponentially, with a rapid early distribution phase (half-life about four minutes) and a slower terminal elimination phase (half-life two to five hours). Following oral administration, the elimination half-life is three to seven hours. Approximately 50% of an administered dose is eliminated renally within 24 hours, 70% within five days. Up to 16% of a dose is excreted in the feces. About 3% to 4% of renally excreted drug is excreted as unchanged drug. The total clearance of verapamil is nearly as high as the hepatic blood flow, approximately 1 L/h/kg (range: 0.7-1.3 L/h/kg). *Special Populations* *Pediatric:* Limited information on the pharmacokinetics in the paediatric population is available. After intravenous dosing, the mean half-life of verapamil was 9.17 hours and the mean clearance was 30 L/h, whereas it is around 70 L/h for a 70-kg adult. Steady-state plasma concentrations appear to be somewhat lower in the paediatric population after oral dosing compared to those observed in adults. *Geriatrics:* Aging may affect the pharmacokinetics of verapamil given to hypertensive patients. Elimination half-life may be prolonged in the elderly. The antihypertensive effect of verapamil was found not to be age-related. *Renal insufficiency:* Impaired renal function has no effect on verapamil pharmacokinetics, as shown by comparative studies in patients with end-stage renal failure and subjects with healthy kidneys. Verapamil and norverapamil are not significantly removed by hemodialysis. *Hepatic insufficiency:* The half-life of verapamil is prolonged in patients with impaired liver function owing to lower oral clearance and a higher volume of distribution.		
Symptoms Hypotension, bradycardia up to high degree AV block and sinus arrest, hyperglycemia, stupor, metabolic acidosis Fatalities have occurred as a result of overdose. *Treatment* Treatment of overdosage should be supportive. Beta-adrenergic stimulation or parenteral administration of calcium solutions may increase calcium ion flux across the slow channel, and have been used effectively in treatment of deliberate overdosage with verapamil.	*Symptoms* Hypotension, bradycardia up to high degree AV block and sinus arrest, hyperglycemia, stupor, metabolic acidosis Fatalities have occurred as a result of overdose. *Treatment* Treatment of overdosage should be supportive. Beta-adrenergic stimulation or parenteral administration of calcium solutions may increase calcium ion flux across the slow channel, and have been used effectively in	**Overdose**

Verapamil cannot be removed by hemodialysis. Clinically significant hypotensive reactions or high degree AV block should be treated with vasopressor agents or cardiac pacing, respectively. Asystole should be handled by the usual measures including beta adrenergic stimulation (e.g., isoproterenol hydrochloride), other vasopressor agents or cardiopulmonary resuscitation.	treatment of deliberate overdosage with verapamil. Verapamil cannot be removed by hemodialysis. Clinically significant hypotensive reactions or high degree AV block should be treated with vasopressor agents or cardiac pacing, respectively. Asystole should be handled by the usual measures cardiopulmonary resuscitation	

בעלון לצרכן

טופס זה מיועד לפרוט ההחמרות בלבד !

ההחמרות המבוקשות		
פרק בעלון	**טקסט נוכחי**	**טקסט חדש**
התוויות		
מתי אין להשתמש בתכשיר?	אם רופאך מודיע שיש לך בעיות בלב כגון: לחץ דם נמוך (ערך סיסטולי מתחת ל- 90 מ"מ כספית) או לחץ דם מאוד נמוך (לדוגמא במקרה של הלם shock), אי ספיקת לב, רפרוף או פרפור פרוסדורי אליו מתלוות מסילת הולכה נוספת (לדוגמא: תופעת Wolff-Parkinson-White או Lown-Ganong-Levine).	אם רופאך מודיע שיש לך בעיות בלב כגון: לחץ דם נמוך (ערך סיסטולי מתחת ל- 90 מ"מ כספית) או לחץ דם מאוד נמוך (לדוגמא במקרה של הלם shock), ~~התקף לב עם סיבוכים~~[2], אי ספיקת לב, רפרוף או פרפור פרוסדורי אליו מתלוות מסילת הולכה נוספת (לדוגמא: תופעת Wolff-Parkinson-White או Lown-Ganong-Levine).
אזהרות מיוחדות הנוגעות לשימוש בתרופה:		
אין להשתמש בתרופה מבלי להיוועץ ברופא לפני התחלת הטיפול:		-התקף לב חד מלווה בדופק איטי וירידה גדולה בלחץ הדם.[2]
תגובות בין תרופתיות:		
הריון והנקה:		
כיצד תשתמש בתרופה:		
תופעות לוואי:	**תופעות לוואי אחרות** • עצירות , כולל החמרה של חסימת מעיים. • פריחה. • לחץ דם נמוך. • דופק איטי. • דופק מהיר. • אי ספיקת לב. • אדמימות. • התנפחות בגוף, בידיים או ברגליים. • הצטברות נוזל בריאות.	**תופעות לוואי נוספות**[2] **תופעות לוואי שכיחות (משפיעות על פחות מ 1 מתוך 10 מטופלים)** • כאב ראש • סחרחורות • עצירות, בחילות. • דופק איטי • לחץ דם נמוך • אדמומיות התנפחות בגוף, בידיים או ברגליים **תופעות לוואי שאינן שכיחות (משפיעות על**

	• סחרחורות. • כאב ראש. • עייפות. • בחילה. • בעיות בנשימה. • סחרחורת קשה (vertigo) . • זמזום באוזניים. • תופעות הקשורות למערכת העצבים (extrapyramidal). • הקאה. • צמיחה מוגברת של החניכיים (חניכיים נפוחות). • כאב בטן. • חולשת שרירים. • כאבי שרירים או מפרקים. • התפתחות מוגברת של שדיים בגבר. • יצירה מגברת של חלב בנשים הגורם לדליפה מהשדיים). • יתכן וגברים יסבלו מאימפוטנציה. • תגובות אלרגיות חרלת (פריחה מגרדת בעור) עלולות להופיע. בעיות בכבד עלולות גם להתרחש	**פחות מ 1 מתוך 100 מטופלים)** • דופק חזק • דופק מהיר • כאב בטן • עייפות **תופעות לוואי נדירות (משפיעות על פחות מ 1 מתוך 1000 מטופלים)** • תחושת נימול • רעד • נמנום • זמזום באוזניים • הקאות • זיעה מוגברת **תופעות לוואי המתחרשות במספר לא ידוע של מטופלים** • רגישות יתר • תופעות הקשורות למערכת העצבים (extrapyramidal) • סחרחורת קשה (vertigo) • אי ספיקת לב. • הפרעות בדופק הלב • עוויתות הסימפונות (בעיות בנשימה) • חוסר נוחות בבטן • צמיחה מוגברת של החניכיים (חניכיים נפוחות). • סוג של עצירות קשה (החמרה של חסימת מעיים ileus) • נפיחות בפנים, בשפתיים, בלשון ובלוע • גבשושים ושלפוחיות • מחלת Stevens Johnson(שלפוחיות בעור ובריות) • אובדן שיער • גירוד • פריחה • חרלת (פריחה מגרדת בעור) • תחושה מוגברת של דחף לשפשוף או סריטת בעור • חולשת שרירים • כאבי שרירים או מפרקים. • אין אונות • יצירה מגברת של חלב בנשים הגורם לדליפה מהשדיים). • התפתחות מוגברת של שדיים בגבר • עליה ברמת אנזימי הכבד ~~**תופעות לוואי אחרות**~~ • ~~עצירות , כולל החמרה של חסימת מעיים.~~ • ~~פריחה.~~ • ~~לחץ דם נמוך.~~ • ~~דופק איטי.~~ • ~~דופק מהיר.~~ • ~~אי ספיקת לב.~~

		~~אדמימות.~~ ~~התנפחות בגוף, בידיים או ברגליים.~~ ~~הצטברות נוזל בריאות.~~ ~~סחרחורות.~~ ~~כאב ראש.~~ ~~עייפות.~~ ~~בחילה.~~ ~~בעיות בנשימה.~~ ~~סחרחורת קשה (vertigo) .~~ ~~זמזום באוזניים.~~ ~~תופעות הקשורות למערכת העצבים (extrapyramidal).~~ ~~הקאה.~~ ~~צמיחה מוגברת של החניכיים (חניכיים נפוחות).~~ ~~כאב בטן.~~ ~~חולשת שרירים.~~ ~~כאבי שרירים או מפרקים.~~ ~~התפתחות מוגברת של שדיים בגבר.~~ ~~יצירה מוגברת של חלב בנשים הגורם לדליפה מהשדיים).~~ ~~יתכן וגברים יסבלו מאימפוטנציה.~~ ~~תגובות אלרגיות חריגות (פריחה מגרדת בעור) עלולות להופיע.~~ ~~בעיות בכבד עלולות גם להתרחש, אשר ניתנים לאבחון ע"י בדיקות רפואיות.~~