הודעה על החמרה (מידע בטיחות) בעלון לרופא
(מעודכן 3102.50)

תאריך: 6.5.2013

שם תכשיר באנגלית ומספר הרישום:

Tasigna 200 mg [138-17-31681], Tasigna 150 mg [145-84-33271]

שם בעל הרישום: Novartis Pharma Services AG.

טופס זה מיועד לפרוט ההחמרות בלבד !

ההחמרות המבוקשות		
פרק בעלון	**פרק בעלון**	**פרק בעלון**
Monitoring recommendations and dose adjustments … Increases in serum cholesterol levels have been reported with Tasigna therapy (see Section 4.4 Special warnings and precautions for use). Lipid profiles should be assessed prior to initiating Tasigna therapy and as clinically indicated during treatmen ...	**Monitoring recommendations and dose adjustments**	**Posology and method of administration**
Laboratory tests and monitoring In a Phase III study in newly diagnosed CML patients, 1.1% of the patients treated with 400 mg nilotinib twice a day had a grade 3/4 elevation in cholesterol; however, there were no grade 3/4 elevations in the 300 mg twice a day dose group. It is recommended that the lipid profile should be assessed before initiating treatment with Tasigna and monitored during treatment, as clinically indicated (see section 4.2 Posology and method of administration). If lipid lowering agents are needed, please refer to section 4.5 (Interaction with other medicinal products and other forms of interaction) before starting treatment since many cholesterol lowering drugs are also metabolized by the CYP3A4 pathway.		**Special warnings and precautions for use**

ההחמרות המבוקשות		
Women of childbearing potential Women of childbearing potential must be advised to use highly effective contraception during treatment with TASIGNA.	**Women of childbearing potential** Women of childbearing potential must be advised to use effective contraception during treatment with TASIGNA.	**Pregnancy and lactation**
In patients with newly diagnosed Ph+ CML-CP … Non-hematologic adverse drug reactions (ADRs) reported with very common frequency (≥10%) were rash, pruritus, headache, nausea, fatigue, alopecia and myalgia. Most of these ADRs were mild to moderate in severity (Grade 1 or 2). Upper abdominal pain, , constipation, diarrhea, dry skin, muscle spasms, arthralgia, abdominal pain, peripheral edema, vomiting, and asthenia were observed less commonly (< 10% and ≥ 5%) and have been of mild to moderate severity, manageable and generally did not require dose reduction. Pleural and pericardial effusions, regardless of causality, occurred in 1% and <1% of patients, respectively, receiving TASIGNA 300 mg twice daily. Gastrointestinal hemorrhage, regardless of causality, was reported in 3% of these patients. **…**	**In patients with newly diagnosed Ph+ CML-CP** … Non-hematologic adverse drug reactions (ADRs) reported with very common frequency (≥10%) were rash, pruritus, headache, nausea, fatigue and myalgia. Most of these ADRs were mild to moderate in severity (Grade 1 or 2). Upper abdominal pain, alopecia, constipation, diarrhea, dry skin, muscle spasms, arthralgia, abdominal pain, peripheral edema, vomiting, pain in extremity, dyspepsia and asthenia were observed less commonly (< 10% and ≥ 5%) and have been of mild to moderate severity, manageable and generally did not require dose reduction. Pleural and pericardial effusions, regardless of causality, occurred in 1% and <1% of patients, respectively, receiving TASIGNA 300 mg twice daily. Gastrointestinal hemorrhage, regardless of causality, was reported in 2.5% of these patients. **…**	**Undesirable effects**
In patients with newly diagnosed Ph+ CML-CP … The change from baseline in mean time-averaged QTcF interval at steady state in the nilotinib recommended dose of 300 mg twice daily was 6 msec. In the nilotinib 400 mg twice daily group and the imatinib 400 mg once daily group the mean time-averaged QTcF interval at steady state were 6 msec and 3 msec respectively. No patient had an absolute QTcF of >500 msec while on study drug in any of the treatment groups and no events of Torsade de Pointes were observed. QTcF increase from baseline that exceeds 60 msec was observed in 5 patients while on study (one in the 300 mg twice daily treatment group and four in the 400 mg twice daily treatment group). …	**In patients with newly diagnosed Ph+ CML-CP** … The change from baseline in mean time-averaged QTcF interval at steady state in the nilotinib recommended dose of 300 mg twice daily was 6 msec. In the nilotinib 400 mg twice daily group and the imatinib 400 mg once daily group the mean time-averaged QTcF interval at steady state were 6 msec and 3 msec respectively. No patient had an absolute QTcF of >500 msec while on study drug in any of the treatment groups and no events of Torsade de Pointes were observed. QTcF increase from baseline that exceeds 60 msec was observed in 4 patients while on study (one in the 300 mg twice daily treatment group and three in the 400 mg twice daily treatment group). …	**Undesirable effects**

ההחמרות המבוקשות		
Table 2 Most Frequently Reported Non-hematologic Adverse Drug Reactions (≥5% in any TASIGNA Group) אנא ראו טבלה מצורפת בנספח 2	Table 2 Most Frequently Reported Non-hematologic Adverse Drug Reactions (≥5% in any TASIGNA Group) אנא ראו טבלה מצורפת בנספח 1	**Undesirable effects**
Blood and Lymphatic System Disorders: *Common:* eosinophilia, febrile neutropenia, pancytopenia, lymphopenia. *Unknown frequency:* thrombocythemia, leukocytosis.	**Blood and Lymphatic System Disorders**: *Common:* febrile neutropenia, pancytopenia, lymphopenia. *Unknown frequency:* thrombocythemia, leukocytosis, eosinophilia.	**Undesirable effects**
Metabolism and Nutrition Disorders: *Very Common:* hypophosphatemia (including blood phosphorus decreased). *Common:* electrolyte imbalance (including hypomagnesemia, hyperkalemia, hypokalemia, hyponatremia, hypocalcemia, hypercalcemia, hyperphosphatemia), diabetes mellitus, hyperglycemia, hypercholesterolemia, hyperlipidemia, hypertriglyceridemia. Uncommon: gout, dehydration, increased appetite, dyslipidemia. *Unknown frequency:* hyperuricemia, hypoglycemia.	**Metabolism and Nutrition Disorders**: *Very Common:* hypophosphatemia (including blood phosphorus decreased). *Common:* electrolyte imbalance (including hypomagnesemia, hyperkalemia, hypokalemia, hyponatremia, hypocalcemia, hypercalcemia, hyperphosphatemia), diabetes mellitus, hyperglycemia, hypercholesterolemia, hyperlipidemia. Uncommon: gout, dehydration, increased appetite. *Unknown frequency:* hyperuricemia, hypoglycemia, dyslipidemia.	**Undesirable effects**
Vascular Disorders: *Common:* hypertension, flushing. *Uncommon:* hypertensive crisis, peripheral arterial occlusive disease, hematoma, arteriosclerosis. *Unknown frequency:* shock hemorrhagic, hypotension, thrombosis.	**Vascular Disorders**: *Common:* hypertension, flushing. *Uncommon:* hypertensive crisis, peripheral arterial occlusive disease, hematoma. *Unknown frequency:* shock hemorrhagic, hypotension, thrombosis, arteriosclerosis.	**Undesirable effects**
Gastrointestinal Disorders: *Common:* pancreatitis, abdominal discomfort, abdominal distension, dyspepsia, dysgeusia, flatulence. *Uncommon:* gastrointestinal hemorrhage, melena, mouth ulceration, gastroesophageal reflux, stomatitis, esophageal pain, dry mouth, gastritis, sensitivity of teeth,. *Unknown frequency:* gastrointestinal ulcer perforation, retroperitoneal hemorrhage, haematemesis, gastric ulcer, esophagitis ulcerative, subileus, enterocolitis, hemorrhoids, hiatus hernia, rectal hemorrhage, gingivitis.	**Gastrointestinal Disorders**: *Common:* pancreatitis, abdominal discomfort, abdominal distension, dyspepsia, dysgeusia, flatulence. *Uncommon:* gastrointestinal hemorrhage, melena, mouth ulceration, gastroesophageal reflux, stomatitis, esophageal pain, dry mouth, sensitivity of teeth,. *Unknown frequency:* gastrointestinal ulcer perforation, retroperitoneal hemorrhage, haematemesis, gastric ulcer, esophagitis ulcerative, subileus, gastritis, enterocolitis, hemorrhoids, hiatus hernia, rectal hemorrhage, gingivitis.	**Undesirable effects**
Investigations: *Very Common:* alanine aminotransferase increased, aspartate aminotransferase increased, lipase increased. *Common:* hemoglobin decreased, blood amylase increased, gamma-glutamyltransferase increased, blood creatinine phosphokinase increased, blood alkaline phosphatase increased, blood insulin increased, weight decreased, weight increased,	**Investigations**: *Very Common:* alanine aminotransferase increased, aspartate aminotransferase increased, lipase increased. *Common:* hemoglobin decreased, blood amylase increased, gamma-glutamyltransferase increased, blood creatinine phosphokinase increased, blood alkaline phosphatase increased, weight decreased, weight increased. *Uncommon:*	**Undesirable effects**

ההחמרות המבוקשות		
lipoprotein increased (including very low density and high density). *Uncommon:* blood lactate dehydrogenase increased, blood urea increased, globulins decreased. *Unknown frequency:* troponin increased, blood bilirubin unconjugated increased, blood insulin decreased, insulin C-peptide decreased, blood parathyroid hormone increased.	blood lactate dehydrogenase increased, blood urea increased, globulins decreased. *Unknown frequency:* troponin increased, blood bilirubin unconjugated increased, blood insulin increased, blood insulin decreased, insulin C-peptide decreased, lipoprotein increased (including very low density and high density), blood parathyroid hormone increased.	
Table 3 Grade 3/4 Laboratory Abnormalities אנא ראו טבלה מצורפת בנספח 4	Table 3 Grade 3/4 Laboratory Abnormalities אנא ראו טבלה מצורפת בנספח 3	**Undesirable effects**
CLINICAL STUDIES / **Progression to AP/BC on treatment** … Including clonal evolution as a criterion for progression, a total of 25 patients progressed to AP or BC on treatment by the cut-off date (3 in the nilotinib 300 mg twice daily group, 5 in the nilotinib 400 mg twice daily group and 17 in the imatinib 400 mg once daily group). The estimated rates of patients free from progression to AP or BC including clonal evolution at 48 months were 98.5%, 97.9% and 93.2%, respectively (HR=0.1619 and stratified log-rank p=0.0009 between nilotinib 300 mg BID and imatinib, HR = 0.2848 and stratified log-rank p=0.0085 between nilotinib 400 mg BID and imatinib).	**CLINICAL STUDIES /** **Progression to AP/BC on treatment** … Including clonal evolution as a criterion for progression, a total of 24 patients progressed to AP or BC on treatment by the cut-off date (2 in the nilotinib 300 mg twice daily group, 5 in the nilotinib 400 mg twice daily group and 17 in the imatinib 400 mg once daily group). The estimated rates of patients free from progression to AP or BC including clonal evolution at 36 months were 99.3%, 97.9% and 93.2%, respectively (HR=0.1106 and stratified log-rank p=0.0003 between nilotinib 300 mg BID and imatinib, HR = 0.2848 and stratified log-rank p=0.0085 between nilotinib 400 mg BID and imatinib). **…**	**Pharmacodynamic properties**
CLINICAL STUDIES / **Overall survival (OS)** A total of 43 patients died during treatment or during the follow-up after discontinuation of treatment (15 in the nilotinib 300 mg twice daily group, 9 in the nilotinib 400 mg twice daily group and 19 in the imatinib 400 mg once daily group). Twenty-two (22) of these 43 deaths were related to CML (5 in the nilotinib 300 mg twice daily group, 4 in the nilotinib 400 mg twice daily group and 13 in the imatinib 400 mg once daily group). The estimated rates of patients alive at 48 months were 94.3%, 96.7% and 93.3%, respectively (HR=0.7768 and stratified log-rank p = 0.4636 between nilotinib 300 mg twice daily and imatinib, HR=0.4611 and stratified log-rank p = 0.0498 between nilotinib 400 mg twice daily	**CLINICAL STUDIES /** **Overall survival (OS)** A total of 38 patients died during treatment or during the follow-up after discontinuation of treatment (13 in the nilotinib 300 mg twice daily group, 8 in the nilotinib 400 mg twice daily group and 17 in the imatinib 400 mg once daily group). Twenty-three (23) of these 38 deaths were related to CML (5 in the nilotinib 300 mg twice daily group, 4 in the nilotinib 400 mg twice daily group and 14 in the imatinib 400 mg once daily group). The estimated rates of patients alive at 36 months were 95.1%, 97.0% and 94.0%, respectively (HR=0.7537 and stratified log-rank p = 0.4413 between nilotinib 300 mg twice daily and imatinib, HR=0.4607 and stratified log-rank p = 0.0639 between nilotinib 400 mg twice daily	**Pharmacodynamic properties**

ההחמרות המבוקשות		
and imatinib). Considering only CML-related deaths as events, the estimated rates of OS at 48 months were 98.1%, 98.5% and 95.4%, respectively (HR=0.3782 and stratified log-rank p = 0.0547 between nilotinib 300 mg twice daily and imatinib, HR=0.2290 and stratified log-rank p = 0.0250 between nilotinib 400 mg twice daily and imatinib).	and imatinib). Considering only CML-related deaths as events, the estimated rates of OS at 36 months were 98.1%, 98.5% and 95.2%, respectively (HR=0.3511 and stratified log-rank p = 0.0356 between nilotinib 300 mg twice daily and imatinib, HR=0.2784 and stratified log-rank p = 0.0159 between nilotinib 400 mg twice daily and imatinib).	

Table 2 Most Frequently Reported Non-haematologic Adverse Drug Reactions (≥5% in any TASIGNA Group)

			Newly Diagnosed Ph+ CML-CP						Resistant or Intolerant Ph+ CML-CP and CML-AP			
			36-month analysis						24-month analysis			
			TASIGNA 300 mg twice daily	TASIGNA 400 mg twice daily	IMATINIB 400 mg once daily	TASIGNA 300 mg twice daily	TASIGNA 400 mg twice daily	IMATINIB 400 mg once daily	TASIGNA 400 mg twice daily			
			ALL GRADES (%)			GRADE 3 or 4 (%)			ALL GRADES (%)	GRADE 3/4 (%)	CML -CP GRADE 3/4 (%)	CML -AP GRADE 3/4 (%)
System Organ Class	**Frequency**	**Adverse Reaction**	**N=279 %**	**N=277 %**	**N=280 %**	**N=279 %**	**N=277 %**	**N=280 %**	**N=458 %**	**N=458 %**	**N=321 %**	**N=137 %**
Metabolism and nutrition disorders	Common	Decreased apetite	4	4	3	0	0	0	8	<1	<1	0
Nervous system disorders	Very common	Headache	15	22	9	1	1	<1	15	1	2	<1
Gastrointestinal disorders	Very common	Nausea	14	21	34	<1	1	0	20	<1	<1	<1
	Very common	Constipation	10	7	3	0	<1	0	12	<1	<1	0
	Very common	Diarrhea	9	7	30	<1	0	2	11	2	2	<1
	Very Common	Vomiting	6	9	18	0	1	0	10	<1	<1	0
	Common	Abdominal pain upper	10	8	8	1	0	<1	5	<1	<1	0
	Common	Abdominal pain	6	5	4	0	<1	0	6	<1	<1	<1
	Common	Dyspepsia	5	6	5	0	<1	0	3	0	0	0
Skin and subcutaneous tissue disorders	Very common	Rash	33	37	14	<1	3	2	28	1	2	0
	Very common	Pruritus	18	14	5	<1	<1	0	24	<1	<1	0
	Very common	Alopecia	10	14	5	0	0	0	9	0	0	0
	Very Common	Dry Skin	9	10	5	0	0	0	5	0	0	0
	Common	Erythema	2	6	3	0	0	0	5	<1	<1	0
Musculoskeletal and connective tissue disorders	Very common	Myalgia	10	11	12	<1	<1	<1	10	<1	<1	<1
	Common	Arthralgia	7	9	8	<1	0	<1	7	<1	1	0
	Common	Muscle spasms	9	8	29	0	<1	1	8	<1	<1	0
	Common	Bone pain	4	5	3	0	<1	<1	6	<1	<1	0
	Common	Pain in extremity	5	3	7	<1	<1	<1	5	<1	<1	<1
General disorders and administration site conditions	Very common	Fatigue	11	10	10	0	<1	<1	17	1	1	<1
	Common	Asthenia	9	5	8	<1	<1	0	6	0	0	0
	Common	Edema peripheral	5	6	17	<1	0	0	6	0	0	0

Table 2 Most Frequently Reported Non-hematologic Adverse Drug Reactions (≥5% in any TASIGNA Group)

			Newly Diagnosed Ph+ CML-CP						Resistant or Intolerant Ph+ CML-CP and CML-AP			
			48-month analysis						24-month analysis			
			TASIGNA 300 mg twice daily	TASIGNA 400 mg twice daily	IMATINIB 400 mg once daily	TASIGNA 300 mg twice daily	TASIGNA 400 mg twice daily	IMATINIB 400 mg once daily	TASIGNA 400 mg twice daily			
			ALL GRADES (%)			GRADE 3 or 4 (%)			ALL GRADES (%)	GRADE 3/4 (%)	CML -CP GRADE 3/4 (%)	CML -AP GRADE 3/4 (%)
System Organ Class	**Frequency**	**Adverse Reaction**	**N=279 %**	**N=277 %**	**N=280 %**	**N=279 %**	**N=277 %**	**N=280 %**	**N=458 %**	**N=458 %**	**N=321 %**	**N=137 %**
Metabolism and nutrition disorders	Common	Decreased apetite[1]	4	4	3	0	0	0	8	<1	<1	0
Nervous system disorders	Very common	Headache	16	22	10	1	1	<1	15	1	2	<1
Gastrointestinal disorders	Very common	Nausea	14	21	35	<1	1	0	20	<1	<1	<1
	Very common	Constipation	10	7	3	0	<1	0	12	<1	<1	0
	Very common	Diarrhea	8	7	30	<1	0	3	11	2	2	<1
	Very Common	Vomiting	6	9	18	0	1	0	10	<1	<1	0
	Common	Abdominal pain upper	10	8	8	1	0	<1	5	<1	<1	0
	Common	Abdominal pain	6	5	4	0	<1	0	6	<1	<1	<1
	Common	Dyspepsia	5	5	6	0	<1	0	3	0	0	0
Skin and subcutaneous tissue disorders	Very common	Rash	33	38	14	<1	3	2	28	1	2	0
	Very common	Pruritus	18	15	6	<1	<1	0	24	<1	<1	0
	Very common	Alopecia	10	14	5	0	0	0	9	0	0	0
	Very Common	Dry Skin	10	11	5	0	0	0	5	0	0	0
	Common	Erythema	3	6	3	0	0	0	5	<1	<1	0
Musculoskeletal and connective tissue disorders	Very common	Myalgia	10	11	12	<1	<1	<1	10	<1	<1	<1
	Common	Arthralgia	8	10	8	<1	0	<1	7	<1	1	0
	Common	Muscle spasms	9	8	29	0	<1	1	8	<1	<1	0
	Common	Bone pain	4	5	4	0	<1	<1	6	<1	<1	0
	Common	Pain in extremity	5	3	8	<1	<1	<1	5	<1	<1	<1
General disorders and administration site conditions	Very common	Fatigue	13	11	13	0	<1	1	17	1	1	<1
	Common	Asthenia	10	5	8	<1	<1	0	6	0	0	0
	Common	Edema peripheral	5	7	17	<1	0	0	6	0	0	0

Table 3 Grade 3/4 Laboratory Abnormalities

	Newly diagnosed Ph+ CML-CP			Resistant or intolerant Ph+	
	TASIGNA 300 mg twice daily N = 279	TASIGNA 400 mg twice daily N = 277	IMATINIB 400 mg once daily N = 280	CML-CP N=321	CML-AP N=137
Haematologic Parameters					
Myelosuppression					
-Neutropenia	12%	11%	21%	31%	42%
-Thrombocytopenia	10%	12%	9%	30%	42%
-Anaemia	4%	5%	6%	11%	27%
Biochemistry Parameters					
-Elevated creatinine	0%	0%	<1%	1%	<1%
-Elevated lipase	8%	8%	4%	18%	18%
-Elevated SGOT (AST)	1%	3%	1%	3%	2%
-Elevated SGPT (ALT)	4%	9%	3%	4%	4%
-Hypophosphataemia	6%	8%	9%	17%	15%
-Elevated Bilirubin (total)	4%	8%	<1%	7%	9%

Table 3 Grade 3/4 Laboratory Abnormalities

	Newly diagnosed Ph+ CML-CP			Resistant or intolerant Ph+	
	TASIGNA 300 mg twice daily N = 279	TASIGNA 400 mg twice daily N = 277	IMATINIB 400 mg once daily N = 280	CML-CP N=321	CML-AP N=137
Haematologic Parameters					
Myelosuppression					
-Neutropenia	12%	11%	21%	31%	42%
-Thrombocytopenia	10%	12%	9%	30%	42%
-Anaemia	4%	5%	6%	11%	27%
Biochemistry Parameters					
-Elevated creatinine	0%	0%	<1%	1%	<1%
-Elevated lipase	9%	9%	4%	18%	18%
-Elevated SGOT (AST)	1%	3%	1%	3%	2%
-Elevated SGPT (ALT)	4%	9%	3%	4%	4%
-Hypophosphataemia	7%	9%	10%	17%	15%
-Elevated Bilirubin (total)	4%	9%	<1%	7%	9%

הודעה על החמרה (מידע בטיחות) בעלון לצרכן
(מעודכן 3102.50)

תאריך: 6.5.2013

שם תכשיר באנגלית ומספר הרישום:

Tasigna 200 mg [138-17-31681], Tasigna 150 mg [145-84-33271]

שם בעל הרישום: Novartis Pharma Services AG.

טופס זה מיועד לפרוט ההחמרות בלבד !

ההחמרות המבוקשות		
פרק בעלון	**טקסט נוכחי**	**טקסט חדש**
כיצד תשתמש בתרופה	**בדיקות ומעקב:** בתקופת הטיפול בתרופה זו יש לבצע בדיקות באופן סדיר כולל בדיקות דם. בדיקות אלו ינטרו את רמת תאי הדם (תאי דם לבנים, תאי דם אדומים וטסיות), ואת תפקודי הלבלב והכבד כדי לראות את סבילותך לטסיגנה. בדיקות הדם ינטרו גם את האלקטרוליטים בגופך (אשלגן, מגנזיום) ; אלו בעלי חשיבות בתפקוד הלב. קצב הלב שלך ייבדק גם באמצעות מכשיר אשר מודד את הפעילות החשמלית של הלב (בדיקה הנקראת "א.ק.ג."). ...	**בדיקות ומעקב:** בתקופת הטיפול בתרופה זו יש לבצע בדיקות באופן סדיר כולל בדיקות דם. בדיקות אלו ינטרו את רמת תאי הדם (תאי דם לבנים, תאי דם אדומים וטסיות), ואת תפקודי הלבלב והכבד כדי לראות את סבילותך לטסיגנה. בדיקות הדם ינטרו גם את האלקטרוליטים בגופך (אשלגן, מגנזיום) ; אלו בעלי חשיבות בתפקוד הלב. קצב הלב שלך ייבדק גם באמצעות מכשיר אשר מודד את הפעילות החשמלית של הלב (בדיקה הנקראת "א.ק.ג."). בדיקות הדם ינטרו גם את רמת השומנים בדמך. ...
תופעות לוואי	**יש לדווח מיד לרופא במקרים הבאים:** ... • קשיים או כאבים בזמן נשימה, שיעול, צפצוף (סימנים להפרעות בריאות). ...	**יש לדווח מיד לרופא במקרים הבאים:** ... • קשיים או כאבים בזמן נשימה, שיעול, צפצוף עם או ללא חום (סימנים להפרעות בריאות). ...
תופעות לוואי	**<u>תופעות לוואי נוספות:</u>** ... במהלך הטיפול בטסיגנה, ייתכן כי יהיו לך תוצאות בדיקות דם שאינן תקינות כגון רמת תאי דם נמוכה (תאי דם לבנים, תאי דם אדומים, טסיות דם), רמה גבוהה של ליפאז או אמילאז בדם (תפקוד לבלב), רמה גבוהה של בילירובין בדם (תפקוד כבד), רמה גבוהה של קראטינין בדם (תפקוד כליות), רמה גבוהה של אשלגן או רמה נמוכה של מגנזיום, רמה נמוכה או גבוהה בדם של אינסולין (הורמון המווסת רמות סוכר בדם). ...	**<u>תופעות לוואי נוספות:</u>** ... במהלך הטיפול בטסיגנה, ייתכן כי יהיו לך תוצאות בדיקות דם שאינן תקינות כגון רמת תאי דם נמוכה (תאי דם לבנים, תאי דם אדומים, טסיות דם), רמה גבוהה של ליפאז או אמילאז בדם (תפקוד לבלב), רמה גבוהה של בילירובין בדם (תפקוד כבד), רמה גבוהה של קראטינין בדם (תפקוד כליות), רמה גבוהה של אשלגן או רמה נמוכה של מגנזיום, רמה נמוכה או גבוהה בדם של אינסולין (הורמון המווסת רמות סוכר בדם). רמה גבוהה של שומנים בדם. ...

תופעות לוואי	**<u>תופעות לוואי נוספות:</u>** ... אם התופעות שצוינו לעיל משפיעות עליך בצורה חמורה, עליך ליידע את הרופא. ...	**<u>תופעות לוואי נוספות:</u>** ... אם אחת מהתופעות שצוינו לעיל משפיעות עליך, עקוב אחר עצת הרופא שלך. ...

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