הודעה על החמרה (מידע בטיחות) בעלון לרופא

תאריך 15-05-2017

שם התכשיר באנגלית ומספר הרישום

Nuvigil 50 mg Reg.No. 155-83-34388

Nuvigil 150 mg Reg.No. 155-84-34389

Nuvigil 250 mg Reg.No. 155-85-34390

שם בעל הרישום Abic Marketing Ltd.

טופס זה מיועד לפרוט ההחמרות בלבד!

ההחמרות המבוקשות		
פרק בעלון	**טקסט נוכחי**	**טקסט חדש**

5.1 Serious Dermatologic Reactions, including Stevens-Johnson Syndrome and Toxic Epidermal Necrosis … In clinical trials of modafinil, the incidence of rash resulting in discontinuation was approximately 0.8% (13 per 1,585) in pediatric patients (age <17 years); these rashes included 1case of possible Stevens-Johnson syndrome (SJS) and 1 case of apparent multi-organ hypersensitivity reaction / Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) [*see Warnings and Precautions (5.2)]*. Several of the cases were associated with fever and other abnormalities (e.g., vomiting, leukopenia). The median time to rash that resulted in discontinuation was 13 days. No such cases were observed among 380 pediatric patients who received placebo. Skin and mouth sores, blistering and ulceration have been reported with modafinil and NUVIGIL in the postmarketing setting. Recurrence of signs and symptoms of serious dermatologic reactions following rechallenge has been reported in some cases. (4) Rare cases of serious or life-threatening rash, including SJS, and toxic epidermal necrolysis (TEN) have been reported in adults and children in worldwide postmarketing experience. There are no factors, including duration of therapy, that are known to predict the risk of occurrence or the severity of rash associated with modafinil In cases where the time to onset was reported, serious rash occurred 1 day to 2 months after initiation of treatment, but isolated cases of serious dermatologic reactions have been reported with symptoms beginning after prolonged treatment (e.g., 3 months). Although benign rashes also occur with NUVIGIL, it is not possible to reliably predict which rashes will prove to be serious. Accordingly, NUVIGIL should be discontinued at the first sign of rash, skin or mouth sores, or blistering or ulceration, unless the rash is clearly not drug-related. Discontinuation of treatment may not prevent a rash from becoming life-threatening or permanently disabling or disfiguring.	**5.1 Serious ~~Rash~~, including Stevens-Johnson Syndrome** … In clinical trials of modafinil, the incidence of rash resulting in discontinuation was approximately 0.8% (13 per 1,585) in pediatric patients (age <17 years); these rashes included 1 case of possible Stevens-Johnson Syndrome (SJS) and 1 case of apparent multi-organ hypersensitivity reaction. Several of the cases were associated with fever and other abnormalities (e.g., vomiting, leukopenia). The median time to rash that resulted in discontinuation was 13 days. No such cases were observed among 380 pediatric patients who received placebo. Rare cases of serious or life-threatening rash, including SJS, Toxic Epidermal Necrolysis (TEN), ~~and Drug Rash with Eosinophilia and Systemic Symptoms (DRESS)~~ have been reported in adults and children in worldwide post-marketing experience. ~~The reporting rate of TEN and SJS associated with modafinil use, which is generally accepted to be an underestimate due to underreporting, exceeds the background incidence rate. Estimates of the background incidence rate for these serious skin reactions in the general population range between 1 to 2 cases per million person years.~~ Cases of serious rash similar to those observed with modafinil including skin and mouth blistering have been reported in adults in postmarketing experience with NUVIGIL. There are no factors that are known to predict the risk of occurrence or the severity of rash associated with modafinil ~~or armodafinil. Nearly all cases of serious rash associated with these drugs occurred within 1 to 5 weeks after treatment initiation. However, isolated cases have been reported after prolonged treatment (e.g., 3 months). Accordingly, duration of therapy cannot be relied upon as a means to predict the potential risk heralded by the first appearance of a rash~~. Although benign rashes also occur with NUVIGIL, it is not possible to reliably predict which rashes will prove to be serious. Accordingly, NUVIGIL should be discontinued at the first sign of rash, unless the rash is clearly not drug-related. Discontinuation of treatment may not prevent a rash from becoming life-threatening or permanently disabling or disfiguring.	**5. Warnings and Precautions**

5.2 Drug Reaction with Eosinophilia and System Symptoms (DRESS) / Multiorgan Hypersensetivity DRESS, also known as multi-organ hypersensitivity, has been reported with NUVIGIL. DRESS typically, although not exclusively, presents with fever, rash, lymphadenopathy, and/or facial swelling, in association with other organ system involvement, such as hepatitis, nephritis, hematologic abnormalities, myocarditis, or myositis, sometimes resembling an acute viral infection. Eosinophilia is often present. This disorder is variable in its expression, and other organ systems not noted here may be involved. It is important to note that early manifestations of hypersensitivity (e.g., fever, lymphadenopathy) may be present even though rash is not evident. One fatal case of DRESS that occurred in close temporal association (3 weeks) with the initiation of NUVIGIL treatment has been reported in the postmarketing setting. In addition, multi-organ hypersensitivity reactions, including at least one fatality in postmarketing experience, have occurred in close temporal association (median time to detection 13 days; range 4-33) to the initiation of modafinil. Although there have been a limited number of reports, multi-organ hypersensitivity reactions may result in hospitalization or be life-threatening. If a multi-organ hypersensitivity reaction is suspected, NUVIGIL should be discontinued. Although there are no case reports to indicate cross-sensitivity with other drugs that produce this syndrome, the experience with drugs associated with multi-organ hypersensitivity would indicate this to be a possibility.	~~5.3~~ **Multi-organ Hypersensitivity Reactions** Multi-organ hypersensitivity reactions, including at least one fatality in post-marketing experience, have occurred in close temporal association (median time to detection 13 days: range 4-33) to the initiation of modafinil. ~~A similar risk of multi-organ hypersensitivity reactions with armodafinil cannot be ruled out.~~ Although there have been a limited number of reports, multi-organ hypersensitivity reactions may result in hospitalization or be life-threatening. ~~There are no factors that are known to predict the risk of occurrence or the severity of multi-organ hypersensitivity reactions. Signs and symptoms of this disorder were diverse; however, patients typically, although not exclusively,~~ presented with fever and rash associated with other organ system involvement. ~~Other associated manifestations included~~ myocarditis, hepatitis~~, liver function test abnormalities~~, hematological abnormalities ~~(e.g.,~~ eosinophilia~~, leukopenia, thrombocytopenia), pruritus, and asthenia.~~ Because multi-organ hypersensitivity is variable in its expression, other organ system symptoms and signs, not noted here, may occur. If a multi-organ hypersensitivity reaction is suspected, NUVIGIL should be discontinued. Although there are no case reports to indicate cross-sensitivity with other drugs that produce this syndrome, the experience with drugs associated with multi-organ hypersensitivity would indicate this to be a possibility.	
5.5 Psychiatric Symptoms **…** Post-marketing adverse reactions associated with the use of Nuvigil, some of which resulted in hospitalization, have included mania, delusions, hallucinations, suicidal ideation, and aggression. Many, but not all, patients who developed psychiatric adverse reactions had a prior psychiatric history. In these cases, reported NUVIGIL total daily doses ranged from 50 mg to 450 mg, which includes doses below and above the recommended dosages.	~~5.4~~ **Psychiatric Symptoms** … Post-marketing adverse reactions associated with the use of modafinil have included mania, delusions, hallucinations, suicidal ideation, and aggression, some resulting in hospitalization. Many, but not all, patients had a prior psychiatric history. ~~One healthy male volunteer developed ideas of reference, paranoid delusions, and auditory hallucinations in association with multiple daily 600 mg doses of modafinil and sleep deprivation. There was no evidence of psychosis 36 hours after drug discontinuation.~~	

The following serious adverse reactions are described below and elsewhere in the labeling: • Serious Dermatologic Reactions *[see Warnings and Precautions (5.1)]* • Drug Reaction with Eosinophilia and System Symptoms (DRESS)/Multiorgan Hypersensitivity *[see Warnings and Precautions (5.2)]* • Angioedema and Anaphylaxis Reactions *[see Warnings and Precautions (5.3)]* • Persistent Sleepiness *[see Warnings and Precautions (5.4)]* • Psychiatric Symptoms *[see Warnings and Precautions (5.5)]* • Effects on Ability to Drive and Use Machinery *[see Warnings and Precautions (5.6)]* • Cardiovascular Events *[see Warnings and Precautions (5.7)]* **6.2. Postmarketing Experience** The following adverse reactions have been identified during post approval use of NUVIGIL. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. Gastrointestinal Disorders: Mouth Sores (including mouth blistering and ulceration).	The following serious adverse reactions are described below and elsewhere in the labeling: • Serious ~~Rash, including Stevens-Johnson~~ Syndrome *[see Warnings and Precautions (5.1)]* • Angioedema and Anaphylaxis Reactions *[see Warnings and Precautions (5.2)]* • Multi-organ Hypersensitivity Reactions *[see Warnings and Precautions (5.3)]* • Persistent Sleepiness *[see Warnings and Precautions (5.4)]* • Psychiatric Symptoms *[see Warnings and Precautions (5.5)]* • Effects on Ability to Drive and Use Machinery *[see Warnings and Precautions (5.6)]* • Cardiovascular Events *[see Warnings and Precautions (5.7)]*	**6. Adverse Reactions**
8.1 Pregnancy Risk Summary Limited available data on armodafinil use in pregnant women are insufficient to inform a drug associated risk of adverse pregnancy outcomes. Intrauterine growth restriction and spontaneous abortion have been reported in association with armodafinil and modafinil. Although the pharmacology of armodafinil is not identical to that of the sympathomimetic amines, armodafinil shares some pharmacologic properties with this class *[see Clinical Pharmacology (12.1)]*. Some sympathomimetics have been associated with intrauterine growth restriction and spontaneous abortions. In animal reproduction studies of armodafinil (R-modafinil) and modafinil (a mixture of R- and S-modafinil) conducted in pregnant rats (armodafinil, modafinil) and rabbits (modafinil) during organogenesis, evidence of developmental toxicity (increased embryofetal and offspring mortality, decreased fetal growth) was observed at clinically relevant plasma exposures. All pregnancies have a background risk of birth defects, loss, or other adverse outcomes. The estimated background risk of major birth defects and miscarriage for the indicated populations is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized	**8.1 Pregnancy** ~~There are no adequate and well-controlled studies of armodafinil in pregnant women.~~ Intrauterine growth restriction and spontaneous abortion have been reported in association with armodafinil and modafinil. Although the pharmacology of armodafinil is not identical to that of the sympathomimetic amines, it does share some pharmacologic properties with this class. Certain of these drugs have been associated with intrauterine growth restriction and spontaneous abortions. ~~Whether the cases reported with armodafinil are drug-related is unknown.~~ In studies of armodafinil (R-modafinil) and modafinil (a mixture of R- and S-modafinil) conducted in rats (armodafinil, modafinil) and rabbits (modafinil), developmental toxicity was observed at clinically relevant plasma exposures. ~~NUVIGIL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.~~	**8. Use in Specific Populations**

pregnancies is 2-4% and 15-20%, respectively. Data *Animal Data* Oral administration of armodafinil (60, 200, or 600 mg/kg/day) to pregnant rats throughout organogenesis resulted in decreased fetal body weight and increased incidences of fetal variations indicative of growth delay at the highest dose, which was also maternally toxic. The highest no-effect dose for embryofetal developmental toxicity in rat (200 mg/kg/day) was associated with a plasma armodafinil exposure (AUC) less than that in humans at the maximum recommended human dose (MRHD) of NUVIGIL (250 mg/day). Modafinil (50, 100, or 200 mg/kg/day) administered orally to pregnant rats throughout organogenesis produced an increase in resorptions and an increased incidence of fetal variations at the highest dose tested. The higher no-effect dose for embryofetal developmental toxicity (100 mg/kg/day) was associated with a plasma armodafinil AUC less than that in humans at the MRHD of NUVIGIL. However, in a subsequent rat study of up to 480 mg/kg/day of modafinil, no adverse effects on embryofetal development were observed. In a study in which modafinil (45, 90, or 180 mg/kg/day) was orally administered to pregnant rabbits during organogenesis, embryofetal death was increased at the highest dose. The highest no-effect dose for developmental toxicity (100 mg/kg/day) was associated with a plasma armodafinil AUC less than that in humans at the MRHD of NUVIGIL. Modafinil administration to rats throughout gestation and lactation at oral doses of up to 200 mg/kg/day resulted in decreased viability in the offspring at doses greater than 20 mg/kg/day, a dose resulting in a plasma armodafinil AUC less than that in humans at the MRHD of NUVIGIL. No effects on postnatal developmental and neurobehavioral parameters were observed in surviving offspring. **8.2 Lactation** Risk Summary There are no data on the presence of armodafinil or its metabolites in human milk, the effects on the breastfed infant, or the effect of this drug on milk production. Modafinil was present in rat milk when animals were dosed during the lactation period. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for armodafinil and any potential adverse effects on the breastfed child from	Oral administration of armodafinil (60, 200, or 600 mg/kg/day) to pregnant rats throughout organogenesis resulted in increased incidences of fetal ~~visceral and skeletal~~ variations ~~and decreased fetal body weight at the highest dose.~~ The highest no-effect dose for embryofetal developmental toxicity in rat (200 mg/kg/day) was associated with a plasma armodafinil exposure (AUC) less than that in humans at the maximum recommended human dose (MRHD) of NUVIGIL (250 mg/day). Modafinil (50, 100, or 200 mg/kg/day) administered orally to pregnant rats throughout organogenesis ~~caused, in the absence of maternal toxicity,~~ an increase in resorptions and an increased incidence of ~~visceral and skeletal~~ variations in the offspring at the highest dose tested. The higher no-effect dose for embryofetal developmental toxicity ~~in rat~~ (100 mg/kg/day) was associated with a plasma armodafinil AUC less than that in humans at the MRHD of NUVIGIL. However, in a subsequent study of up to 480 mg/kg/day of modafinil, no adverse effects on embryofetal development were observed. ~~Modafinil administered orally to pregnant rabbits throughout organogenesis at doses of up to 100 mg/kg/day had no effect on embryofetal development; however, the doses used were too low to adequately assess the effects of modafinil on embryofetal development. In a subsequent developmental toxicity study evaluating doses of 45, 90, and 180 mg/kg/day in pregnant rabbits, the incidences of fetal structural alterations and embryofetal death were increased at the highest dose.~~ The highest no-effect dose for developmental toxicity (100 mg/kg/day) was associated with a plasma armodafinil AUC less than that in humans at the MRHD of NUVIGIL. Modafinil administration to rats throughout gestation and lactation at oral doses of up to 200 mg/kg/day resulted in decreased viability in the offspring at doses greater than 20 mg/kg/day, a dose resulting in a plasma armodafinil AUC less than that in humans at the MRHD of NUVIGIL. No effects on postnatal developmental and neurobehavioral parameters were observed in surviving offspring. ~~**8.3 Nursing Mothers**~~ ~~It is not known whether armodafinil or its metabolites are excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when NUVIGIL is administered to a nursing woman.~~	

armodafinil or from the underlying maternal condition. **8.3 Females and Males of Reproductive Potential** The effectiveness of hormonal contraceptives may be reduced when used with NUVIGIL and for one month after discontinuation of therapy. Advise women who are using a hormonal method of contraception to use an additional barrier method or an alternative non-hormonal method of contraception during treatment with NUVIGIL and for one month after discontinuation of NUVIGIL treatment *[see Drug Interactions (7) and Clinical Pharmacology (12.3)]*.		

9.2 Abuse Abuse of NUVIGIL has been reported in patients treated with NUVIGIL. Patterns of abuse have included euphoric mood and use of increasingly large doses or recurrent use of NUVIGIL for a desired effect. Drug diversion has also been noted. During the postmarketing period, misuse of NUVIGIL has been observed (e.g., taking NUVIGIL against a physician's advice, and obtaining NUVIGIL from multiple physicians). Abuse of armodafinil, the active ingredient of NUVIGIL, poses a risk of overdosage similar to that seen for modafinil, which may lead to tachycardia, insomnia, agitation, dizziness, anxiety, nausea, headache, dystonia, tremor, chest pain, hypertension, seizures, delirium, or hallucinations. Other signs and symptoms of CNS stimulant abuse include tachypnea, sweating, dilated pupils, hyperactivity, restlessness, decreased appetite, loss of coordination, flushed skin, vomiting, and abdominal pain. In humans, modafinil produces psychoactive and euphoric effects, alterations in mood, perception, thinking and feelings, typical of other CNS stimulants. In in vitro binding studies, modafinil binds to the dopamine reuptake site and causes an increase in extracellular dopamine, but no increase in dopamine release. Modafinil is reinforcing, as evidenced by its self-administration in monkeys previously trained to self-administer cocaine. In some studies, modafinil was also partially discriminated as stimulant-like. Physicians should follow patients closely, especially those with a history of drug and/or stimulant (e.g., methylphenidate, amphetamine, or cocaine) abuse. Patients should be observed for signs of misuse or abuse (e.g., incrementation of doses or drug-seeking behavior). The abuse potential of modafinil (200, 400, and 800 mg) was assessed relative to methylphenidate (45 and 90 mg) in an inpatient study in individuals experienced with drugs of abuse. Results from this clinical study demonstrated that modafinil produced psychoactive and euphoric effects and feelings consistent with other scheduled CNS stimulants (methylphenidate).	**9.1 Abuse** ~~Although the abuse potential of armodafinil has not been specifically studied, its abuse potential is likely to be similar to that of modafinil~~. In humans, modafinil produces psychoactive and euphoric effects, alterations in mood, perception, thinking and feelings typical of other CNS stimulants. In in vitro binding studies, modafinil binds to the dopamine reuptake site and causes an increase in extracellular dopamine, but no increase in dopamine release. Modafinil is reinforcing, as evidenced by its self-administration in monkeys previously trained to self-administer cocaine. In some studies, modafinil was also partially discriminated as stimulant-like. Physicians should follow patients closely, especially those with a history of drug and/or stimulant (e.g., methylphenidate, amphetamine, or cocaine) abuse. Patients should be observed for signs of misuse or abuse (e.g., incrementation of doses or drug-seeking behavior). The abuse potential of modafinil (200, 400, and 800 mg) was assessed relative to methylphenidate (45 and 90 mg) in an inpatient study in individuals experienced with drugs of abuse. Results from this clinical study demonstrated that modafinil produced psychoactive and euphoric effects and feelings consistent with other scheduled CNS stimulants (methylphenidate).	**9. Drug Abuse and Dependence**
9.3 Dependence Physical dependence is a state that develops as a result of physiological adaptation in response to repeated drug use, manifested by withdrawal signs and symptoms after abrupt discontinuation or a significant dose reduction of a drug. Physical dependence can occur in patients treated with NUVIGIL. Abrupt cessation or dose reduction following chronic use can result in withdrawal symptoms, including shaking, sweating, chills, nausea, vomiting, confusion, aggression, and atrial		

fibrillation. Drug withdrawal convulsions, suicidality, fatigue, insomnia, aches, depression and headache have also been observed during the postmarketing period. Also, abrupt withdrawal has caused deterioration of psychiatric symptoms such as depression. Tolerance is a physiological state characterized by a reduced response to a drug after repeated administration (i.e., a higher dose of a drug is required to produce the same effect that was once obtained at a lower dose). Multiple cases of development of tolerance to NUVIGIL have been reported during the postmarketing period.		
Fatal overdoses involving modafinil alone or involving NUVIGIL or modafinil in combination with other drugs have been reported in the postmarketing setting. Symptoms most often accompanying NUVIGIL or modafinil overdose, alone or in combination with other drugs, have included anxiety, dyspnea, insomnia; central nervous system symptoms such as restlessness, disorientation, confusion, excitation and hallucination; digestive changes such as nausea and diarrhea; and cardiovascular changes such as tachycardia, bradycardia, hypertension, and chest pain. No specific antidote exists for the toxic effects of a NUVIGIL overdose. Such overdoses should be managed with primarily supportive care, including cardiovascular monitoring.	~~There were no overdoses reported in the NUVIGIL clinical studies. Symptoms of NUVIGIL overdose are likely to be similar to those of modafinil. Symptoms of overdose in modafinil clinical trials included excitation or agitation, insomnia, and slight or moderate elevations in hemodynamic parameters. From post-marketing experience with modafinil, there have been reports of fatal overdoses involving modafinil alone or in combination with other drugs. Symptoms most often accompanying modafinil overdose, alone or in combination with other drugs have included~~ insomnia; central nervous system symptoms such as restlessness, disorientation, confusion, excitation and hallucination; digestive changes such as nausea and diarrhea; and cardiovascular changes such as tachycardia, bradycardia, hypertension and chest pain. No specific antidote exists for the toxic effects of a NUVIGIL overdose. Such overdoses should be managed with primarily supportive care, including cardiovascular monitoring.	**10. Overdosage**

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ההחמרות המבוקשות		
פרק בעלון	**טקסט נוכחי**	**טקסט חדש**
2. לפני השימוש בתרופה	**אין להשתמש בתרופה אם** אתה רגיש (אלרגי) לחומר הפעיל ארמודפיניל (armodafinil), או לכל אחד ממרכיבי התרופה האחרים (ראה סעיף 6 - "מידע נוסף" בעלון זה). אתה רגיש (אלרגי) למודפיניל (modafinil) – פרוויג'יל (Provigil)	**אין להשתמש בתרופה אם** אתה רגיש (אלרגי) לחומר הפעיל ארמודפיניל (armodafinil), או לכל אחד ממרכיבי התרופה האחרים (ראה סעיף 6 - "מידע נוסף" בעלון זה). אתה רגיש (אלרגי) למודפיניל (modafinil) – פרוויג'יל (Provigil) היתה לך פריחה או תגובה אלרגית לארמודפיניל (נוביג'יל) או למודפיניל (פרוויג'יל). אלו תרופות דומות מאוד
	אם אתה לוקח או לקחת לאחרונה **<u>חשוב</u>** אם את משתמשת באמצעי למניעת היריון על בסיס הורמונלי, כגון גלולות למניעת היריון, זריקות, שתלים, מדבקות, טבעות לנרתיק, והתקנים תוך רחמיים (IUD) ספרי על כך לרופא. יעילות אמצעי מניעת היריון על בסיס הורמונלי עלולה לקטון בזמן נטילת נוביג'יל, והסיכוי להיכנס להיריון תוך כדי נטילת נוביג'יל ולמשך חודש לאחר הפסקת הנוביג'יל גדל. יש להתיעץ עם הרופא לגבי בחירת אמצעי למניעת הריון בתקופת הטיפול בתרופה.	**אם אתה לוקח או לקחת לאחרונה** **<u>חשוב</u>** אם את משתמשת באמצעי למניעת היריון על בסיס הורמונלי, כגון גלולות למניעת היריון, זריקות, שתלים, מדבקות, טבעות לנרתיק, והתקנים תוך רחמיים (IUD) ספרי על כך לרופא. יעילות אמצעי מניעת היריון על בסיס הורמונלי עלולה לקטון בזמן נטילת נוביג'יל, והסיכוי להיכנס להיריון תוך כדי נטילת נוביג'יל ולמשך חודש לאחר הפסקת הנוביג'יל גדל. עלייך להשתמש באמצעי מניעה יעילים במהלך נטילת נוביג'יל ובמשך חודש לאחר נטילת המנה האחרונה. יש להתיעץ עם הרופא לגבי בחירת אמצעי למניעת הריון בתקופת הטיפול בתרופה, ועד חודש לאחר הפסקת הטיפול.
	שימוש בילדים תרופה זו אינה מאושרת לשימוש בילדים או במתבגרים. יעילות ובטיחות התרופה לא נבדקו בילדים מתחת לגיל ~~17~~.	**שימוש בילדים** תרופה זו אינה מאושרת לשימוש בילדים או במתבגרים. יעילות ובטיחות התרופה לא נבדקו בילדים מתחת לגיל 18.
3. כיצד תשתמש	תסמינים של מינון יתר של נוביג'יל כוללים: קשיי שינה, אי שקט, בלבול, חוסר התמצאות,	תסמינים של מינון יתר של נוביג'יל כוללים: קשיי שינה, אי שקט, בלבול, חוסר התמצאות,

בתרופה	התרגשות, הזיות (שמיעה, ראיה או הרגשה של דברים שאינם מציאותיים), הקאה ושלשול, דופק מהיר או איטי, כאב בחזה, עליה בלחץ הדם	התרגשות, הזיות (שמיעה, ראיה או הרגשה של דברים שאינם מציאותיים), הקאה ושלשול, דופק מהיר או איטי, כאב בחזה, עליה בלחץ הדם, חרדה, קוצר נשימה
4. תופעות לוואי	**יש להפסיק את נטילת התרופה ולפנות לרופא מיד אם מופיע:** • פריחה בעור, חרלת, פצעים בפה, שלפוחיות וקילוף העור. אם אתה סובל מפריחה חמורה, הפסקת השימוש בנוביג'יל לאו דווקא תמנע מהפריחה ~~להחמיר~~, להפוך למסכנת חיים או לגרום לנכות או להשחתת המראה. • נפיחות בפנים, בעיניים, בשפתיים, בלשון או בגרון. • קשיי בליעה או נשימה. • חום, קוצר נשימה, נפיחות ברגליים, הצהבת העור או לובן העיניים, או שתן כהה.	**יש להפסיק את נטילת התרופה ולפנות לרופא מיד אם מופיע:** **פריחה חמורה בעור או תגובה אלרגית חמורה** • פריחה בעור, חרלת, פצעים בפה, שלפוחיות וקילוף העור. אם אתה סובל מפריחה חמורה, הפסקת השימוש בנוביג'יל לאו דווקא תמנע מהפריחה להפוך למסכנת חיים או לגרום לנכות או להשחתת המראה לצמיתות. • נפיחות בפנים, בעיניים, בשפתיים, בלשון או בגרון. • קשיי בליעה, נשימה או צרידות. • חום, קוצר נשימה, נפיחות ברגליים, הצהבת העור או לובן העיניים, או שתן כהה.