Mornigag 10/10 mg

Delayed Release Tablet
Doxylamine succinate and pyridoxine hydrochloride

• 1- INDICATIONS AND USAGE
MORNIGAG is indicated for the treatment of nausea and vomiting of pregnancy in women who do not respond to conservative management.
Limitations of Use
MORNIGAG has not been studied in women with hyperemesis gravidarum.
• 2- DOSAGE AND ADMINISTRATION
2.1 Dosage Information
Initially, take two **MORNIGAG** delayed-release tablets orally at bedtime (Day 1). If this dose adequately controls symptoms the next day, continue taking two tablets daily at bedtime. However, if symptoms persist into the afternoon of Day 2, take the usual dose of two tablets at bedtime that night then take three tablets starting on Day 3 (one tablet in the morning and two tablets at bedtime). If these three tablets adequately control symptoms on Day 4, continue taking three tablets daily. Otherwise take four tablets starting on Day 4 (one tablet in the morning, one tablet mid-afternoon and two tablets at bedtime). The maximum recommended dose is four tablets (one in the morning, one in the mid-afternoon and two at bedtime) daily. Take on an empty stomach with a glass of water [see Clinical Pharmacology (12.3)]. Swallow tablets whole. Do not crush, chew, or split MORNIGAG tablets. Take as a daily prescription and not on an as needed basis. Reassess the woman for continued need for **MORNIGAG** as her pregnancy progresses.
• 3- CONTRAINDICATIONS
MORNIGAG is contraindicated in women with any of the following conditions:
Known hypersensitivity to doxylamine succinate, other ethanolamine derivative antihistamines, pyridoxine hydrochloride or any inactive ingredient in the formulation
Monoamine oxidase (MAO) inhibitors intensify and prolong the adverse central nervous system effects of MORNIGAG [see Drug Interactions (7.1)].
• 4- WARNINGS AND PRECAUTIONS
4.1 Activities Requiring Mental Alertness
MORNIGAG may cause somnolence due to the anticholinergic properties of doxylamine succinate, an antihistamine. Women should avoid engaging in activities requiring complete mental alertness, such as driving or operating heavy machinery, while using **MORNIGAG** until cleared to do so by their healthcare provider.
MORNIGAG use is not recommended if a woman is concurrently using central nervous system (CNS) depressants including alcohol. The combination may result in severe drowsiness leading to falls or accidents [see Drug Interactions (7.1)].
4.2 Concomitant Medical Conditions
MORNIGAG has anticholinergic properties and, therefore, should be used with caution in women with: asthma, increased intraocular pressure, narrow angle glaucoma, stenosing peptic ulcer, pyloroduodenal obstruction and urinary bladder-neck obstruction.
4.3 Interference with Urine Screen for Methadone, Opiates and Phencyclidine Phosphate (PCP)
There have been reports of false positive urine screening tests for methadone, opiates, and PCP with doxylamine succinate/pyridoxine hydrochloride use [see Drug Interactions (7.3)].
4.4 This product contains lactose, Patients with rare hereditary problems of galactose intolerance, the Lapp lactose deficiency or glucose-galactose malabsorption should not take this medicine.
• 5- ADVERSE REACTIONS
The following adverse reactions are discussed elsewhere in the labeling:
o Somnolence [see Warnings and Precautions (5.1)]
o Falls or other accidents resulting from the effect of the combined use of **MORNIGAG** with CNS depressants including alcohol [see Warnings and Precautions (5.1)]
5.1 Clinical Trial Experience
Number (Percent) of Subjects with ≥ 5 Percent Adverse Reactions in a 15 Day Placebo-Controlled Study of Doxylamine succinate and pyridoxine hydrochloride (Only Those Adverse Reactions Occurring at an Incidence ≥ 5 Percent and at a Higher Incidence with Doxylamine succinate and Pyridoxine hydrochloride than Placebo are Shown) Somnolence (14.3%)
5.2 Postmarketing Experience
The following adverse events, listed alphabetically, have been identified during post-approval use of the combination of 10 mg doxylamine succinate and 10 mg pyridoxine hydrochloride. 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.
Cardiac disorders: dyspnea, palpitation, tachycardia
Ear and labyrinth disorders: vertigo
Eye disorders: vision blurred, visual disturbances
Gastrointestinal disorders: abdominal distension, abdominal pain, constipation, diarrhea
General disorders and administration site conditions: chest discomfort, fatigue, irritability, malaise
Immune system disorders: hypersensitivity
Nervous system disorders: dizziness, headache, migraines, paresthesia, psychomotor hyperactivity
Psychiatric disorders: anxiety, disorientation, insomnia, nightmares
Renal and urinary disorders: dysuria, urinary retention
Skin and subcutaneous tissue disorders: hyperhidrosis, pruritus, rash, rash maculo-papular
• 6- DRUG INTERACTIONS
6.1 Drug Interactions
Use of **MORNIGAG** is contraindicated in women who are taking monoamine oxidase inhibitors (MAOIs), which prolong and intensify the anticholinergic (drying) effects of antihistamines. Concurrent use of alcohol and other CNS depressants (such as hypnotic sedatives and tranquilizers) with **MORNIGAG** is not recommended.
6.2 Drug-Food Interactions
A food-effect study demonstrated that the delay in the onset of action of **MORNIGAG** may be further delayed, and a reduction in absorption may occur when tablets are taken with food [see Dosage and Administration (2), Clinical Pharmacology (12.3)]. Therefore, **MORNIGAG** should be taken on an empty stomach with a glass of water [see Dosage and Administration (2)].
6.3 False Positive Urine Tests for Methadone, Opiates and PCP
False positive drug screens for methadone, opiates, and PCP can occur with doxylamine succinate/pyridoxine hydrochloride use. Confirmatory tests, such as Gas Chromatography Mass Spectrometry (GC-MS), should be used to confirm the identity of the substance in the event of a positive immunoassay result.
• 7- USE IN SPECIFIC POPULATIONS
7.1 Pregnancy
Risk Summary
MORNIGAG is intended for the treatment of nausea and vomiting of pregnancy in women who do not respond to conservative management. Maternal risks are discussed throughout the labeling. No increased risk for congenital malformations has been reported in epidemiologic studies in pregnant women.
In the U.S. general population, the estimated background risks for major birth defects and miscarriage in clinically recognized pregnancies are 2-4% and 15-20%, respectively.
7.2 Lactation
Women should not breastfeed while using **MORNIGAG**.
The molecular weight of doxylamine succinate is low enough that passage into breast milk can be expected. Excitement, irritability and sedation have been reported in nursing infants presumably exposed to doxylamine succinate through breast milk. Infants with apnea or other respiratory syndromes may be particularly vulnerable to the sedative effects of **MORNIGAG** resulting in worsening of their apnea or respiratory conditions.
Pyridoxine hydrochloride is excreted into breast milk. There have been no reports of adverse events in infants presumably exposed to pyridoxine hydrochloride through breast milk.
• 8- Pediatric Use
The safety and effectiveness of **MORNIGAG** in children under 18 years of age have not been established.
Fatalities have been reported from doxylamine overdose in children. The overdose cases have been characterized by coma, grand mal seizures and cardiorespiratory arrest. Children appear to be at a high risk for cardiorespiratory arrest. A toxic dose for children of more than 1.8 mg/kg has been reported. A 3 year old child died 18 hours after ingesting 1,000 mg doxylamine succinate. However, there is no correlation between the amount of doxylamine ingested, the doxylamine plasma level and clinical symptomatology.
• 9- OVERDOSAGE
9.1 Signs and Symptoms of Overdose
MORNIGAG is a delayed-release formulation, therefore, signs and symptoms of intoxication may not be apparent immediately. Signs and symptoms of overdose may include restlessness, dryness of mouth, dilated pupils, sleepiness, vertigo, mental confusion and tachycardia. At toxic doses, doxylamine exhibits anticholinergic effects, including seizures, rhabdomyolysis, acute renal failure and death.
9.2 Management of Overdose
If treatment is needed, it consists of gastric lavage or activated charcoal, whole bowel irrigation and symptomatic treatment.
•10- DESCRIPTION

MORNIGAG (doxylamine succinate 10 mg and pyridoxine hydrochloride 10 mg) delayed-release tablets are Blue enteric coated biconvex rounded tablet
Inactive ingredients are as follows: Avicel PH 200 (Microcrystalline cellulose), Aerosil 200 (Colloidal Silicon Dioxide), Croscarmellose sodium, Lactose Monohydrate, Sodium steraryl fumarate, Talc.
Enteric coat: Acryl EZE Blue, Triethyl citrate, Dimethicone 350
•11- CLINICAL PHARMACOLOGY
11.1 Mechanism of Action
The mechanism of action of **MORNIGAG** is unknown.
11.2 Pharmacokinetics
The pharmacokinetics of Doxylamine succinate and pyridoxine hydrochloride has been characterized in healthy non-pregnant adult women. Pharmacokinetic results for doxylamine and pyridoxine, including its vitamin B6 metabolites, pyridoxal, pyridoxal 5'-phosphate, pyridoxamine and pyridoxamine 5'-phosphate, are summarized in Tables 2 to 5.
Absorption
A single-dose (two tablets) and multiple-dose (four tablets daily), open-label study was conducted to assess the safety and pharmacokinetic profile of Doxylamine succinate and pyridoxine hydrochloride administered in healthy non-pregnant adult women. Single-doses (two tablets at bedtime) were administered on Days 1 and 2. Multiple-doses (one tablet in the morning, one tablet in the afternoon and two tablets at bedtime) were administered on Days 3–18.
Doxylamine and pyridoxine are absorbed in the gastrointestinal tract, mainly in the jejunum.
The Cmax of doxylamine and pyridoxine are achieved within 2.5 and 5.5 hours, respectively (see Table 2).

Table 2 – Single-Dose and Multiple-Dose Pharmacokinetics of Doxylamine succinate and pyridoxine hydrochloride in Healthy Non-Pregnant Adult Women

	Single Dose			Multiple Dose		
	AUC0-inf (ng•h/mL)	Cmax (ng/mL)	Tmax (h)	AUC0-inf (ng•h/mL)	Cmax (ng/mL)	Tmax (h)
Doxylamine	1280.9 ± 369.3	83.3 ± 20.6	7.2 ± 1.9	3721.5 ± 1318.5	168.6 ± 38.5	7.8 ± 1.6
Pyridoxine	43.4 ± 16.5	52.6 ± 15.0	5.7 ± 1.5	64.5 ± 36.4	46.1 ± 28.3	5.6 ± 1.3
Pyridoxal	211.6 ± 46.1	74.3 ± 21.8	6.5 ± 1.4	1587.2 ± 550.0	210.0 ± 54.4	6.8 ± 1.2
Pyridoxal 5'Phosphate	1536.4 ± 721.5	50.0 ± 10.0	11.7 ± 5.3	6099.7 ± 1383.7	84.9 ± 16.9	6.3 ± 6.6
Pyridoxamine	4.1 ± 2.7	0.5 ± 0.7	5.9 ± 2.1	2.6 ± 0.8	0.5 ± 0.2	6.6 ± 1.4
Pyridoxamine 5'-phosphate	5.2 ± 3.8	0.7 ± 0.5	14.8 ± 6.6	58.0	2.3 ± 1.7	12.4 ± 11.2

Multiple-dose administration of Doxylamine succinate and pyridoxine hydrochloride results in increased concentrations of doxylamine as well as increases in doxylamine Cmax and AUC0-last of absorption. The time to reach the maximum concentration is not affected by multiple doses. The mean accumulation index is more than 1.0 suggesting that doxylamine accumulates following multiple dosing (see Table 3). Although no accumulation was observed for pyridoxine, the mean accumulation index for each metabolite (pyridoxal, pyridoxal 5'-phosphate, and pyridoxamine 5'-phosphate) is more than 1.0 following multiple-dose administration of Doxylamine succinate and pyridoxine hydrochloride. The time to reach the maximum concentration is not affected by multiple doses (see Table 2).

Table 3 – Pharmacokinetics of Doxylamine and Pyridoxine Following Single Dose and Multiple Dose Administration of Doxylamine succinate and pyridoxine hydrochloride to Healthy Non-Pregnant Adult Women

		AUC0-last (ng•h/mL)	AUC0-inf (ng•h/mL)	Cmax (ng/mL)	Tmax (h)	T1/2el (h)
Doxylamine Mean±SD N=18	Single	911.4 ± 205.6	1280.9 ± 369.3	83.3 ± 20.6	7.2 ± 1.9	10.1 ± 2.1
	Multiple	3661.3 ± 1279.2	3721.5 ± 1318.5	168.6 ± 38.5	7.8 ± 1.6	11.9 ± 3.3
Pyridoxine Mean±SD N=18	Single	39.3 ± 16.5	43.4 ± 16.5	32.6 ± 15.0	5.7 ± 1.5	0.5 ± 0.2
	Multiple	59.3 ± 33.9	64.5 ± 36.4	46.1 ± 28.3	5.6 ± 1.3	0.5 ± 0.1

Food Effect
The administration of food delays the absorption of both doxylamine and pyridoxine. This delay is associated with a lower peak concentration of doxylamine, but the extent of absorption is not affected (see Table 4). The effect of food on the peak concentration and the extent of absorption of the pyridoxine component is more complex because the pyridoxal, pyridoxamine, pyridoxal 5'-phosphate and pyridoxamine 5'-phosphate metabolites also contribute to the biological activity. Food significantly reduces the bioavailability of pyridoxine, lowering its Cmax and AUC by approximately 50% compared to fasting conditions. Similarly, food significantly reduces pyridoxal AUC and reduces its Cmax by 50% compared to fasting conditions. In contrast, food slightly increases pyridoxal 5'-phosphate Cmax and extent of absorption. As for pyridoxamine and pyridoxamine 5'-phosphate, the rate and extent of absorption seem to decrease under fed conditions.

Table 4 – Pharmacokinetics of Doxylamine and Pyridoxine Following Administration of Doxylamine succinate and pyridoxine hydrochloride Under Fed and Fasted Conditions in Healthy Non-Pregnant Adult Women

		AUC0-t (ng•h/mL)	AUC0-inf (ng•h/mL)	Cmax (ng/mL)	Tmax (h)	T1/2el (h)
Doxylamine Mean±SD N=42	Fasted	1407.2 ± 336.9	1447.9 ± 332.2	94.9 ± 18.4	5.1 ± 3.4	12.6 ± 3.4
	Fed	1488.0 ± 463.2	1579.0 ± 422.7‡	75.7 ± 16.6	14.9 ± 7.4	12.5 ± 2.9‡
Pyridoxine Mean±SD N=42	Fasted	33.8 ± 13.7	39.5 ± 12.9†	35.5 ± 21.4	2.5 ± 0.9	0.4 ± 0.2†
	Fed	18.3 ± 14.5	24.2 ±14.0‡	13.7 ± 10.8	9.3 ± 4.0	0.5 ± 0.2‡

† N=37
‡ N=51
‡ N=18
Distribution
Pyridoxine is highly protein bound, primarily to albumin. Its main active metabolite, pyridoxal 5'-phosphate (PLP) accounts for at least 60% of circulating vitamin B6 concentrations.
Metabolism
Doxylamine is biotransformed in the liver by N-dealkylation to its principle metabolites N-desmethyl-doxylamine and N, N-didesmethyldoxylamine.
Pyridoxine is a prodrug primarily metabolized in the liver.
Excretion
The principle metabolites of doxylamine, N-desmethyl-doxylamine and N, N-didesmethyldoxylamine, are excreted by the kidney.
The terminal elimination half-life of doxylamine and pyridoxine are 12.5 hours and 0.5 hours, respectively (see Table 5)

Table 5 – Terminal Elimination Half-Life (T1/2el) for Doxylamine succinate and pyridoxine hydrochloride Administered as a Single Dose of Two Tablets under Fasting Conditions in Healthy Non-Pregnant Adult Women

	T1/2el (h)
Doxylamine	12.6 ± 3.4
Pyridoxine	0.4 ± 0.2
Pyridoxal	2.1 ± 2.2
Pyridoxal 5'-Phosphate	81.6 ± 42.2
Pyridoxamine	3.1 ± 2.5
Pyridoxamine 5'-Phosphate	66.5 ± 51.3

Use in Specific Populations
Race: No pharmacokinetic studies have been conducted related to race.
Hepatic Impairment: No pharmacokinetic studies have been conducted in hepatic impaired patients.
Renal Impairment: No pharmacokinetic studies have been conducted in renal impaired patients.
•12- HOW SUPPLIED/STORAGE AND HANDLING
12.1 How supplied
Carton box containing 1,2,3 (AL/Colorless transparent Aclar) strips each of 10 delayed release tablet + Pamphlet
12.2 Storage and Handling
Shelf Life: 2 years
Storage condition: Store at temperature not exceeding 25 °C, In dry place.

Keep all medicaments out of reach of children

Product of:
AMOUN PHARMACEUTICAL CO. S.A.E.
El-Obour City, Al Qalyubia, Egypt.

مورنيجاج ١٠ / ١٠ مجم

اقراص متأخرة الأنطلاق
دوكسيلامين ساكسينات وبيريدوكسين هيدروكلوريد.

ما هو مورنيجاج؟

مورنيجاج هو دواء يصرف عن طريق الروشتة يستخدم لعلاج الغثيان والقئ في الحمل في السيدات اللواتي لم تتحسن عن طريق تغيير الطعام او العلاج بغير ادوية.

من غير المعروف إذا كان **مورنيجاج** امن وفعال في السيدات الذين يعانون قيء وغثيان شديد اثناء الحمل، الذي يسمى التقيؤ الحملي. السيدات اللواتي تعاني من هذه الحالة قد تحتاج لدخول المستشفى.

من غير المعروف إذا كان **مورنيجاج** امن وفعال في الأطفال تحت سن ١٨ سنه.

من يجب عليه عدم تناول مورنيجاج؟

لا تتناول مورنيجاج:

إذا كانت لديك حساسية من دوكسيلامين ساكسينات، وادوية الحساسية الأخرى التي تحتوي على ايثانول امين، بيريدوكسين هيدروكلوريد او أي من المواد الغير فعالة الأخرى في **مورنيجاج**. انظر نهاية النشرة لمعرفة المواد الغير فعالة المستخدمة في **مورنيجاج**.

إذا كنت تتناول مثبطات مونوامين اوكسيداز. اسال طبيبك او الصيدلي إذا لم تكن متأكد إذا كنت تأخذ الادوية التي تحتوي على مثبطات مونوامين اوكسيداز.

المرضى المصابون بأمراض وراثية نادرة مثل عدم تحمل الجالاكتوز، نقص انزيم اللاكتوز، سوء امتصاص جلوكوز – جالاكتوز، يجب عليهم عدم تناول هذا الدواء

قبل تناول مورنيجاج، أخبر طبيبك او الصيدلي عن حالتك الصحية، شاملا إذا كنت تعاني من:

• حساسية بالصدر.
• مشاكل بالعين تدعى زيادة ضغط العين او مياه زرقاء ضيقة الزاوية.
• مشاكل بالمعدة مثل ضيق مصاحب لقرحة الاثني عشر او انسداد فتحة البواب بالاثني عشر.
• إذا كان لديك مشاكل بالمثانة تدعى انسداد عنق المثانة.
• إذا كنت تقومين بالرضاعة او تخططين للرضاعة – يفرز **مورنيجاج** في لبن الام وقد يؤذى طفلك.
• يجب ان لا تقومي بإرضاع طفلك اثناء تناول **مورنيجاج**.
• أخبر طبيبك عن كل الادوية التي تتناولها، شاملا التي بروشته او التي بدون روشتة، الفيتامينات، والاعشاب.

كيف يمكن تناول مورنيجاج؟

• تكلم مع مقدم الخدمة الصحية عن كيفية تناول **مورنيجاج** ومتى يمكن تناوله.
• تناول **مورنيجاج** كل يوم كما هو موصوف لك من مقدم الخدمة الصحية. لا تتوقف عن تناول **مورنيجاج** بدون التحدث مع مقدم الخدمة الصحية أولا.
• **انظر التعليمات الاتية عن كيفية البدء في تناول مورنيجاج:**
• اليوم الأول تناول ٢ قرص عن طريق الفم عند النوم.
• اليوم الثاني تناول ٢ قرص عند النوم. إذا حدث تحسن في الغثيان والقيء او توقف على اليوم الثاني استمر في تناول ٢ قرص كل مساءاً يوميا عند النوم. سوف تكون هذه جرعتك المعتادة الا اذا اخبرك طبيبك بشئ آخر
• اليوم الثالث إذا استمر لديك الغثيان والقيء فى اليوم الثاني، ابدا في تناول ٣ أقراص في اليوم الثالث (١ قرص فى الصباح و٢ قرص عند النوم كل يوم).
• اليوم الرابع إذا حدث تحسن في الغثيان والقيء او توقف على اليوم الثالث استمر في تناول ٣ أقراص كل يوم. إذا استمر لديك الغثيان والقيء فى اليوم الثالث، ابدا في تناول ٤ أقراص كل يوم (١ قرص الصباح و ١ قرص في الظهر و٢قرص عند النوم).
• لا تتناول أكثر من ٤ أقراص (١ قرص الصباح و ١ قرص في الظهر و٢قرص عند النوم) في اليوم الواحد.
• تناول **مورنيجاج** على معدة فارغة يكوب من الماء.
• تناول قرص **مورنيجاج** كاملا لا تكسره او تمضغه. إذا لم تكن تستطيع تناول قرص **مورنيجاج** كاملا أخبر مقدم الخدمة الصحية.
• إذا تناولت كمية زائده من **مورنيجاج** (جرعة زائده)، قد تحدث لك هذه الأعراض الأرق، جفاف الفم، كبر الحدقة (توسيع الحدقة)، نعاس، دوخه، أرتباك، سرعة ضربات القلب، تشنجات، آلام العضلات او ضعف، مشاكل مفاجئه و شديده في الكلي.
• إذا كان لديك هذه الأعراض، إذا كانت شديدة، قد تؤدى الى الوفاة. إذا تناولت كمية زائده من **مورنيجاج** اتصل بقسم السموم بوزارة الصحة.

ما هي الاعراض الجانبية المحتملة مع مورنيجاج؟

• **قد يسبب مورنيجاج أعراض جانبية خطيرة تشمل النعاس.**
• النعاس هو عرض جانبي شائع من **مورنيجاج** قد يكون شديد:
• لا تقوم بقيادة السيارات، تشغيل الآلات الثقيلة، او القيام ببعض الأنشطة التي تحتاج الى أنتباه تام. الا إذا سمح لك مقدم الخدمة الصحية بالقيام بها.
• لا تتناول الكحوليات، او أي من الادوية التي تثبط الجهاز العصبي المركزي مثل أدوية الكحة والبرد، وبعض أدوية الألم، والأدوية التي تساعد على النوم وانت تتناول **مورنيجاج**. قد يحدث نعاس شديد او يصبح اسوا مما يسبب سقوط او حوادث.
• **قد يسبب مورنيجاج نتائج ايجابية غير صحيحة اثناء عمل اختبارات الفحص للميثادون و المخدرات فينيلسيكليدين.**
• هذه هي ليست كل الأعراض الجانبية مع **مورنيجاج** اتصل بطبيبك للنصيحة إذا حدثت لك أي اعراض جانبية.
• يمكن تسجيل حدوث أعراض جانبية على موقع وزارة الصحة.

• ماهي المواد الفعالة؟

دوكسيلامين ساكسينات١٠ مجم وبيريدوكسين هيدروكلوريد ١٠ مجم.

• ما هي المواد الغير فعالة؟

افيسيل ٢٠٠ PH، ايروسيل ٢٠٠، كروسكاراميللوز الصوديوم، لاكتوزاحادي التميؤ، ستيرات الفيومارات الصوديوم، تلك.
الغطاء: اكريل ايز ازرق، تراي ايثيل سيترات، داي ميثيكون ٣٥٠.

• ظروف التخزين

يحفظ في درجه حراره لا تزيد عن٢٥ درجه مئويه في مكان جاف

• العبوه

علبه كرتون تحتوي علي ٣،٢،١ (الومنيوم / اكلار عديم اللون شفاف) شرائط يحتوي كل منها علي ١٠ اقراص متأخرة الأنطلاق + نشره داخليه.

تحفظ جميع الأدوية بعيداً عن متناول الأطفال

إنتاج **شركة آمون للأدوية** ش.م.م
مدينة العبور، القليوبية، مصر.

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