*נובמבר 2019*

**רופא /ה, רוקח/ת נכבד/ה**

**חברת טבע מודיעה על העדכונים הבאים בעלון לצרכן ובעלון לרופא של התכשיר:**

# NAXYN® 500 mg Tablets

# נקסין® 500 מ"ג טבליות

## Contains: Naproxen 500 mg

## עדכונים בעלון לצרכן ובעלון לרופא

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**<u>התוויה כפי שאושרה בתעודת הרישום:</u>**

- Relief of the signs and symptoms of rheumatic diseases including osteoarthritis ankylosing spondylitis of rheumatoid arthritis both in the treatment of acute flares and in the long-term management of the disease.
- Juvenile Rheumatoid Arthritis.
- Periarticular and musculoskeletal disorders
- Relief of pain in bursitis tendinitis synovitis tenosynovitis and lumbago.
- Relief of pain, swelling, tenderness and fever in acute gouty Arthritis.
- Relief of symptoms of primary dysmenorrhea.

**<u>ברצוננו להודיע שהעלון לצרכן עודכן, בפירוט שלהלן כלולים העדכונים העיקריים בלבד (תוספות מסומנות באדום והסרות מידע כטקסט מחוק):</u>**

## עדכונים בעלון לצרכן

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### 2. לפני השימוש בתרופה

[...]

**תגובות בין תרופתיות**

- חומסי הקולטן (רצפטור) לאנגיוטנסין 2, כמו קאנדסרטאן, אפרוסרטאן או לוסרטאן.

[...]

**היריון, הנקה ופוריות**

- אל תטלי נקסין 500 מ"ג אם את בשלושת החודשים האחרונים להיריון, כיוון שזה עלול להזיק לתינוקך.

- אם את בהיריון או מניקה, חושבת שאת בהיריון או מתכננת היריון היוועצי ברופא או ברוקח לפני נטילת תרופה זו.
- נקסין 500 מ"ג עלול לגרום לקשיים בכניסה להיריון. יש לספר לרופא אם את מתכננת להיכנס להיריון או אם את נתקלת בקשיים בכניסה להיריון.

[...]

**מידע חשוב על חלק מהמרכיבים של התרופה**

- התרופה מכילה חומר צבע הנקרא FD&C Yellow No. 6 (Sunset yellow FCF (E 110)) העלול לגרום לתגובות אלרגיות.

[...]

**3. כיצד תשתמש בתרופה?**

[...]

יש להקפיד על שתייה מספקת במהלך הטיפול בנקסין 500 מ"ג. הדבר חשוב במיוחד עבור מטופלים שיש להם בעיות כליות.

במהלך הטיפול בנקסין 500 מ"ג ייתכן שהרופא יבקש לראות אותך על מנת לבדוק שאתה מקבל את המינון המתאים עבורך ולבחון אם ישנן תופעות לוואי. הדבר חשוב במיוחד במטופלים קשישים.

[...]

**עדכונים בעלון לרופא**

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**4.3 Contraindications**

Active or history of peptic ulceration or active gastrointestinal bleeding (two or more distinct episodes of proven ulceration or bleeding). History of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy.

Naproxen is contraindicated during the last trimester of pregnancy (see Section 4.6).

[...]

**4.4 Special warnings and precautions for use**

[...]

***Renal Effects***

There have been reports of impaired renal function, renal failure, acute interstitial nephritis, haematuria, proteinuria, renal papillary necrosis and occasionally nephrotic syndrome associated with naproxen.

***Renal failure linked to reduced prostaglandin production***

The administration of an NSAID may cause a dose dependent reduction in prostaglandin formation and precipitate renal failure. Patients at greatest risk of this reaction are those with impaired renal function, cardiac impairment, liver dysfunction, those taking diuretics,

angiotensin converting enzyme inhibitors, angiotensin-II receptor antagonists and older people. Renal function should be monitored in these patients (see also Section 4.3).

***SLE and mixed connective tissue disease***
In patients with systemic lupus erythematosus (SLE) and mixed connective tissue disorders there may be an increased risk of aseptic meningitis (see Section 4.8).
[...]

***Excipients with known effect***
Naxyn 500 mg contains colouring agent called FD&C yellow No. 6 (Sunset yellow FCF (E 110)) which may cause allergic reactions.

Naxyn 500 mg contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

**4.5 Interaction with other medicinal products and other forms of interaction**

Concomitant administration of antacid or colestyramine can delay the absorption of naproxen but does not affect its extent. Concomitant administration of food can delay the absorption of naproxen, but does not affect its extent.

It is considered unsafe to take NSAIDs in combination with anti-coagulants such as warfarin or heparin unless under direct medical supervision, as NSAIDs may enhance the effects of anti-coagulants (see Section 4.4).

Caution is advised when Naxyn is co-administered with diuretics as there can be a decreased diuretic effect. The natriuretic effect of furosemide has been reported to be inhibited by some drugs of this class. Diuretics can increase the risk of nephrotoxicity of NSAIDs.

Inhibition of renal lithium clearance leading to increases in plasma lithium concentrations has also been reported.

Naproxen and other non-steroidal anti-inflammatory drugs can reduce the antihypertensive effect of anti-hypertensives. Concomitant use of NSAIDs with ACE inhibitors or angiotensin-II receptor antagonists may increase the risk of renal impairment, especially in patients with pre-existing poor renal function (See Section 4.4).

[...]

It is suggested that Naxyn therapy be temporarily discontinued 48 hours before adrenal function tests are performed, because naproxen may artifactually interfere with some tests for 17-ketogenic steroids. Similarly, naproxen may interfere with some assays of urinary 5-hydroxyindoleacetic acid.

**4.6 Fertility, Pregnancy and lactation**

***Pregnancy***
Congenital abnormalities have been reported in association with NSAID administration in man; however, these are low in frequency and do not appear to follow any discernible pattern. As with other drugs of this type, naproxen produces delay in parturition in animals and also affects the human foetal cardiovascular system (closure of ductus arteriosus). Use of Naxyn in the last trimester of pregnancy is contraindicated (see Section 4.3). NSAIDs should not be used during the first two trimesters of pregnancy, unless the potential benefit to the patient outweighs the potential risk to the foetus.

***Labour and delivery***
Naproxen containing products are not recommended in labour and delivery because, through its prostaglandin synthesis inhibitory effect, naproxen may adversely affect foetal circulation and inhibit contractions, with an increased bleeding tendency in both mother and child.
[...]

**4.8 Undesirable effects**

The following adverse events have been reported with NSAIDs and with naproxen.

*Gastrointestinal disorders:* The most commonly observed adverse events are gastrointestinal in nature. Heartburn, nausea, vomiting, constipation, diarrhoea, flatulence, dyspepsia, abdominal discomfort and epigastric distress.
More serious reactions which may occur are gastro-intestinal bleeding, which is sometimes fatal, particularly in older people (see section 4.4), inflammation, ulceration, perforation, and obstruction of the upper and lower gastrointestinal tract, melaena, haematemesis, stomatitis, exacerbation of ulcerative colitis and Crohn's disease (see section 4.4), oesophagitis, gastritis and pancreatitis.

*Immune system disorders*: Hypersensitivity reactions have been reported following treatment with NSAIDs in patients with, or without, a history of previous hypersensitivity reactions to NSAIDs. These may consist of (a) nonspecific allergic reactions and anaphylaxis (b) respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or

dyspnoea, or (c) assorted skin disorders, including rashes of various types, pruritus, urticaria, purpura, angio-oedema and more rarely exfoliative and bullous dermatoses (including epidermal necrolysis and erythema multiforme).

*Nervous system disorders:* Convulsions, dizziness, headache, lightheadedness, drowsiness, paraesthesia, retrobulbar optic neuritis, inability to concentrate and cognitive dysfunction have been reported. Aseptic meningitis (especially in patients with existing auto-immune disorders, such as systemic lupus erythematosus, mixed connective tissue disease), with symptoms such as stiff neck, headache, nausea, vomiting, fever or disorientation (see section 4.4).

*Eye Disorders:* Visual disturbances, corneal opacity, papillitis and papilloedema.

*Cardiac disorders:* Oedema, palpitations, cardiac failure and congestive heart failure have been reported.

*Vascular disorders:* Hypertension, vasculitis.

*Respiratory, thoracic and mediastinal disorders:* Dyspnoea, asthma, eosinophilic pneumonitis and pulmonary oedema.

*Hepatobiliary disorders*: Jaundice, fatal hepatitis and abnormal liver function tests.

*Skin and subcutaneous tissue disorders:* Skin rashes including fixed drug eruption, itching (pruritus), urticaria, ecchymoses, purpura, sweating.
Alopecia, erythema multiforme, Stevens Johnson syndrome, erythema nodosum, lichen planus, pustular reaction, SLE, epidermal necrolysis, very rarely toxic epidermal necrolysis, photosensitivity reactions (including cases in which skin resembles porphyria cutanea tarda "pseudoporphyria") or epidermolysis bullosa-like reactions which may occur rarely.

If skin fragility, blistering or other symptoms suggestive of pseudoporphyria occur, treatment should be discontinued and the patient monitored.

*Musculoskeletal and connective tissue disorders*: Myalgia and muscle weakness.

*Renal and urinary disorders:* Including, but not limited to, glomerular nephritis, interstitial nephritis, nephrotic syndrome, haematuria, raised serum creatinine, renal papillary necrosis and renal failure.

*Reproductive system and breast disorders:* Female infertility.

*General disorders and administration site conditions:* Thirst, pyrexia, fatigue and malaise.

[...]

**4.9 Overdose**

Symptoms

Symptoms include headache, heartburn, nausea, vomiting, epigastric pain, gastrointestinal bleeding, rarely diarrhoea, disorientation, excitation, drowsiness, dizziness, tinnitus, fainting. In cases of significant poisoning acute renal failure and liver damage are possible.

Respiratory depression and coma may occur after the ingestion of NSAIDs but are rare.

[...]

Management

Patients should be treated symptomatically as required. Within one hour of ingestion of a potentially toxic amount activated charcoal should be considered. Alternatively in adults gastric lavage should be considered within one hour of ingestion of a potentially life-threatening overdose.

Good urine output should be ensured.

Renal and liver function should be closely monitored.

Patients should be observed for at least four hours after ingestion of potentially toxic amounts.

Frequent or prolonged convulsions should be treated with intravenous diazepam.

[...]