רופא/ה, רוקח/ת נכבד/ה
חברת טבע מודיעה על העדכונים הבאים בעלון לרופא של התכשיר

Optalgin® Drops New אופטלגין® טיפות חדש

Contains Dipyrone 500 mg/ml
Each 1 ml contains 20 drops

תכשיר בהרכב חדש
עלון לרופא מעודכן

התוויה כפי שאושרה בתעודת הרישום:

Relief of moderate to severe pain as in headache, toothache, dysmenorrhea and for high fever that does not respond to other measures.

ברצוננו להודיע שהעלון לצרכן עודכן, בפירוט שלהלן כלולים העדכונים העיקריים בלבד
(תוספות /החמרות/שינוי משמעותי מסומנים על רקע צהוב והסרות מידע כטקסט מחוק):

1. NAME OF THE MEDICINAL PRODUCT

OPTALGIN® DROPS NEW
Oral drops, solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml (**20 drops**) contains 500 mg Dipyrone
For the full list of excipients, see Section 6.1.

3. PHARMACEUTICAL FORM

Oral drops, solution.
Clear, slightly yellow to yellow-green solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Relief of moderate to severe pain as in headache, toothache, dysmenorrhea and for high fever that does not respond to other measures.

4.2 Posology and method of administration

Posology

טבע ישראל בע"מ.
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Dosage is determined by the intensity of the pain or fever and individual sensitivity of response to *Optalgin Drops New*. It is essential to use the lowest dose that effectively relieves pain and reduces fever.

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Adults and Adolescents from 15 Years Old (over 53 kg body weight) :
~~**25-50**~~ 20-40 drops up to 3 times daily.

Infants and Children
For all age groups except babies, 8-16 mg of dipyrone per kg body weight can be administered as a single dose. The table below shows the recommended single dose and the maximum daily dose as a function of body weight or age.

Age	**Body weight (kg)**	**Dose in Number of drops (Dose in mg)**
3-11 months	5-8 kg	2-4 drops, up to 3 times daily (50 – 100 mg)
1-3 years	9-15 kg	3-10 drops, up to 3 times daily (75 – 250 mg)
4-6 years	16-23 kg	5-15 drops, up to 3 times daily (125 – 375 mg)
7-9 years	24-30 kg	8-20 drops, up to 3 times daily (200 – 500 mg)
10-12 years	31-45 kg	10-30 drops, up to 3 times daily (250 – 750 mg)
13-14 years	46-53 kg	15-35 drops, up to 3 times daily (375 – 875 mg)

Special patient populations
Elderly patients, patients in reduced general health, and patients with impaired creatinine clearance

In elderly patients, patients in reduced general health and patients with impaired creatinine clearance, the dose should be reduced as the elimination of metamizole metabolites may be prolonged.

Impaired kidney and liver function
Since the elimination rate is reduced when renal or hepatic function is impaired, multiple high doses should be avoided. No dose reduction is required when only used for a short time. There is no adequate experience with long-term use of metamizole in patients with severe renal and/or hepatic impairment.

Duration of use
The duration of use depends upon the type and severity of the disease.

In the event of longer-term treatment with Optalgin Drops New, regular monitoring of blood count is required, including differential blood count.

4.3 Contraindications

- Hypersensitivity to the active substance, other pyrazolones or pyrazolidines (this also includes patients who have developed agranulocytosis following use of such substances), or to any of the excipients listed in section 6.1.
- Patients diagnosed with analgesic-asthma-syndrome or analgesic-intolerance of urticaria-angioedema type, i.e. patients who react to salicylates, paracetamol or other non-narcotic analgesics (e.g., diclofenac, ibuprofen, indomethacin, naproxen) with bronchospasm or other anaphylactoid symptoms (e.g., urticaria, rhinitis, angioedema).
- Bone marrow failure (e.g., after treatment with cytostatics) or hematopoietic disorders.
- Acute intermittent hepatic porphyria (risk of triggering an attack of porphyria).
- In patients with a body, weight less than 5 kg.

4.4 Special warnings and precautions for use

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Pancytopenia

If pancytopenia occurs, treatment must be discontinued immediately and complete blood count must be monitored until it normalizes (see section 4.8). All patients should be instructed to consult their doctor immediately if signs and symptoms occur during treatment which may indicate blood dyscrasia (e.g., malaise, infection, persistent fever, bruising, bleeding, pallor).

Anaphylactic/anaphylactoid reactions

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Severe skin reactions

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Patients should be advised of the signs and symptoms and should be monitored closely for skin reactions, especially in the first few weeks of treatment.

Isolated hypotensive reactions

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Patients should be asked relevant questions prior to administration of *Optalgin*. *Optalgin* should only be used after carefully weighing the potential risks against the anticipated benefits in patients at increased risk of anaphylactoid reactions. If *Optalgin Drops* are administered in such cases, patients should be placed under close medical supervision, with emergency facilities available.

Important information about some of the excipients:

- This medicinal product contains 37.5 mg sodium per 1 ml, equivalent to 1.87% of the WHO recommended maximum daily intake of 2 g sodium for an adult.
- This medicine contains benzyl alcohol. Benzyl alcohol may cause allergic reactions. Benzyl alcohol has been linked with the risk of severe side effects including breathing problems (called “gasping syndrome”) in young children. Do not give to newborn baby (up to 4 weeks old), unless recommended by the doctor. Do not use for more than a week in young children (less than 3 years old), unless advised by the doctor.Ask your doctor or pharmacist for advice if you have a liver or kidney disease. This is because large amounts of benzyl alcohol can build-up in your body and may cause side effects (called “metabolic acidosis”). High volumes

should be used with caution and only if necessary, especially in subjects with liver or kidney impairment because of the risk of accumulation and toxicity (metabolic acidosis).

- This medicine contains propylene glycol

4.5 Interaction with other medicinal products and other forms of interaction

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- Co-administration of Dipyrone and methotrexate may increase the hematotoxicity of methotrexate, especially in elderly patients. This combination should therefore be avoided.

- When used concomitantly, Dipyrone may reduce the effects of acetylsalicylic acid on platelet aggregation. Dipyrone should therefore be used with caution in patients taking low-dose aspirin for cardioprotection.

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Effect on assay methods

There have been reports of Dipyrone interference with Trinder and Trinder-like reaction assays (e.g., determination of serum levels of creatinine, triglyceride, HDL cholesterol or uric acid). Therefore, In cases of these tests the patient should take Optalgin only after giving a blood sample.

4.6 Pregnancy and breast-feeding

Pregnancy

There are no adequate data from the use of Dipyrone in pregnant women. Dipyrone crosses the placental barrier. Dipyrone has not been associated with teratogenic effects in animal studies (see section 5.3).

Although Dipyrone is a weak inhibitor of prostaglandin synthesis, the possibility of premature closure of the ductus arteriosus (Botalli) and perinatal complications due to a reduction in platelet aggregability in the mother and child cannot be excluded.
The use of Dipyrone in the third trimester (after week 28) should be used at the lowest effective dose. The daily dose should be up to 3 grams, for only 3-4 days. Longer treatment needs close medical supervision.

Breast-feeding

The metabolites of Dipyrone are excreted in breast milk. The use of Dipyrone should be limited to cases which do not respond to the use of paracetamol or ibuprofen

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4.8 Undesirable effects

The frequency of adverse reactions is defined using the following convention:

Very common	≥ 1/10
Common	≥ 1/100, < 1/10
Uncommon	≥ 1/1,000, < 1/100
Rare	≥ 1/10,000, < 1/1,000
Very rare	< 1/10,000
Not known	Frequency cannot be estimated from available data

Blood and lymphatic system disorders

Rare:	Leukocytopenia.
Very rare:	Agranulocytosis (including fatal cases), thrombocytopenia.
Frequency not known:	Aplastic anemia, pancytopenia (including fatal cases).

These reactions can occur even if Dipyrone was previously administered without complications.

There is isolated evidence that the risk of agranulocytosis may increase if Dipyrone is used for more than one week.

This reaction is not dose-dependent and can occur at any time during treatment. It is manifested by high fever, chills, sore throat, dysphagia and inflammation of the mouth, nose, throat and genital or anal area. These signs may be minimal, however, in patients receiving antibiotics.
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Immune system disorders

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Frequency not known:	Anaphylactic shock*.

*These reactions may occur in particular following parenteral application and may be severe and life-threatening, in some cases even fatal. They can also occur if Dipyrone was previously administered without complications.

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Milder reactions are typically manifested in the form of skin and mucosal reactions (e.g., itching, burning sensation, redness, urticaria, swelling), dyspnea, and (in rarer cases) gastrointestinal complaints. Such milder reactions may become more severe, progressing to generalized urticaria, severe angioedema (also in the laryngeal region), severe bronchospasm, cardiac arrhythmias, hypotension (sometimes with preceding hypertension) and circulatory shock.

Optalgin Drops should therefore be discontinued immediately in the event of skin reactions.

Cardiac disorders

Frequency not known:	Kounis syndrome.

Vascular disorders

Uncommon:	Hypotensive reactions during or after administration, which may be pharmacologically induced and may not be accompanied by other signs of anaphylactoid or anaphylactic reaction. Such reactions can lead to severe hypotension. Rapid intravenous injection increases the risk of hypotensive reactions.

Dose-dependent critical hypotension may also occur in the event of hyperpyrexia, without further signs of hypersensitivity.

Gastrointestinal disorders

Frequency not known: There have been reports of cases of gastrointestinal bleeding.

Skin and subcutaneous tissue disorders

Uncommon:	Fixed drug eruption.
Rare:	Rash (e.g., maculopapular exanthema).
Very rare:	Stevens-Johnson syndrome or toxic epidermal necrolysis (discontinue treatment, see section 4.4).

Renal and urinary disorders

Very rare: Acute deterioration of renal function, which may progress in very rare cases to proteinuria, oliguria or anuria, or acute renal failure, acute interstitial nephritis.

4.9 Overdose

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Therapeutic measures following overdose:

No specific antidote is known for Dipyrone. If the Dipyrone was only recently taken, attempts can be made to limit systemic absorption using primary detoxification measures (e.g., gastric lavage) or absorption-reducing measures (e.g., activated charcoal). The main metabolite (4-N-methylaminoantipyrine) can be eliminated by hemodialysis, hemofiltration, hemoperfusion or plasma filtration.

Treatment of intoxication and prevention of severe complications may require general and specialist intensive care monitoring and treatment.

Emergency measures in the event of severe hypersensitivity reactions (shock):

Stop administration at the first sign of hypersensitivity (e.g., cutaneous reactions such as urticaria and flushing, agitation, headache, sweating, nausea). In addition to standard emergency measures such as Trendelenburg positioning, maintenance of patent airways and administration of oxygen, the administration of sympathomimetics, volume expanders or glucocorticoids may be necessary.

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6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Saccharin sodium, Sodium cyclamate, Flavor Raspberry (contains nature-identical flavoring substances, benzyl alcohol, flavoring preparations, propylene glycol); Flavor cream (contains nature-identical flavoring substances, triacetin, propylene glycol, benzyl alcohol); Citric acid monohydrate, sodium hydroxide, Purified water.

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.

Shelf life after first opening: 6 months

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6.5 Nature and contents of container

Amber glass dropper bottle (type III glass) with a (polyethylene) drop dispenser and (polypropylene) child-resistant closure.

Pack containing 20 ml oral drops, solution

Pack containing 50 ml oral drops, solution

Pack containing 100 ml oral drops, solution

Not all pack sizes may be marketed.

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