רופא/ה נכבד/ה,
רוקח/ת נכבד/ת,

דצמבר 2021

חברת רז רוקחות מבקשת להודיעכם כי העלון לרופא של התכשיר:
PARACETAMOL S.A.L.F 10 MG/ML עודכן.

בהודעה זו מצוינים רק הסעיפים בהם נעשו שינויים מהותיים בעלון לרופא או החלק הרלוונטי שבו נעשה השינוי מתוך הסעיף.
התוספות סומנו בצבע סגול, החמרות סומנו בצבע צהוב והמחיקות סומנו בצבע כחול עם קו מחיקה.
העלון המעודכן נשלח למשרד הבריאות לצורך פרסומו במאגר התרופות שבאתר משרד הבריאות: www.health.gov.il וניתן לקבלו מודפס על ידי פנייה לבעל הרישום:
רז רוקחות בע"מ, רחוב המתכת 6, א.ת. קדימה.

בברכה,
אריאל מימון
רוקחת ממונה

PARACETAMOL S.A.L.F 10 MG/ML

מרכיב פעיל וחוזק:

Paracetamol 10 mg/ml

התוויה מאושרת:

Paracetamol is indicated for the short-term treatment of moderate pain, especially following surgery and for the short-term treatment of fever, when intravenous administration is clinically justified by an urgent need to treat pain or hyperthermia and/or when other routes of administration are not possible.

העדכונים בעלון לרופא:

4.3 Contraindications

- Hypersensitivity to paracetamol, propacetamol hydrochloride (prodrug of paracetamol) or to any of the excipients listed in section 6.1.
- Cases of severe hepatocellular insufficiency.
- ~~In patients with hepatic failure or decompensated active liver disease.~~

4.4 Special warnings and precautions for use

RISK OF MEDICATION ERRORS
Take care to avoid dosing errors due to confusion between milligram (mg) and ~~millilitre~~milliliter (ml), which could result in accidental overdose and death (see section 4.2).

Prolonged or frequent use is discouraged. It is recommended that a suitable analgesic oral treatment will be used as soon as this route of administration is possible.

In order to avoid the risk of overdose, check that other medicines administered do not contain either paracetamol or propacetamol. The dose may require adjustment (see section 4.2).

Doses higher than those recommended entail the risk of very serious liver damage. Clinical signs and

symptoms of liver damage (including fulminant hepatitis, hepatic failure, cholestatic hepatitis, cytolytic hepatitis) are usually first seen after two days of drug administration with a peak seen, usually after 4 – 6 days. Treatment with antidote should be given as soon as possible (See section 4.9).

This product contains less than 1 mmol sodium (23 mg) per 100 ml of solution, i.e. it is essentially "sodium-free".

This product contains 33 mg/ml of glucose monohydrate. To be taken into account in patients with diabetes mellitus.

Paracetamol should be used with caution in cases of:

- hepatocellular insufficiency
- severe renal insufficiency (creatinine clearance ≤ 30 ml/min) (see sections 4.2 and 5.2)
- chronic alcoholism
- chronic malnutrition (low reserves of hepatic glutathione)
- dehydration
- patients suffering from a genetically caused G-6-PD deficiency (favism), the occurrence of a haemolytic anaemia is possible due to the reduced allocation of glutathione following the administration of paracetamol.

~~As common practice in infusion therapy it is advisable to observe the patient for the occurrence of allergic reactions to the active ingredient or to the excipients (e.g. hydroxyethyl starch) (see also section 4.8).~~

~~Paracetamol can cause serious skin reactions such as acute generalized exanthematous pustulosis (AGEP), Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. Patients should be informed about the signs of serious skin reactions, and use of the drug should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.~~

4.6 Fertility, pregnancy and lactation

Pregnancy:

A large amount of data on pregnant women indicate neither malformative, nor feto/neonatal toxicity. Epidemiological studies on neurodevelopment in children exposed to paracetamol in utero show inconclusive results.

If clinically needed, paracetamol can be used during pregnancy. however, it should be used at the lowest effective dose for the shortest possible time and at the lowest possible frequency.

~~Clinical experience of the intravenous administration of paracetamol is limited. However, epidemiological data from the use of oral therapeutic doses of paracetamol indicate no undesirable effects in pregnancy or on the health of the foetus / newborn infant.~~

~~Prospective data on pregnancies exposed to overdoses did not show any increase in the risk of malformation.~~

~~No reproductive studies with the intravenous form of paracetamol have been performed in animals. However, studies with the oral route did not show any malformation or foetotoxic effects.~~

~~Nevertheless, PARACETAMOL S.A.L.F 10 MG/ML should only be used during pregnancy after a careful benefit-risk assessment. In this case, the recommended posology and duration must be strictly observed.~~

Lactation:
After oral administration, paracetamol is excreted into breast milk in small quantities. No undesirable effects on nursing infants have been reported. Consequently, PARACETAMOL S.A.L.F 10 MG/ML may be used in breast-feeding women.

4.8 Undesirable effects

As all paracetamol products, adverse drug reactions are rare (≥~~>~~1/10000~~,~~ to <1/1000) or very rare (<1/10000~~),~~). T~~t~~hey are described below:

~~Organ system~~	~~Rare >1/10000, <1/1000~~	~~Very rare <1/10000~~	~~Isolated reports~~[2]
~~General~~	~~Malaise~~	~~Hypersensitivity reaction~~	
~~Cardiovascular~~	~~Hypotension~~	~~Shock~~[2]	
~~Liver~~	~~Increased levels of hepatic transaminases~~		
~~Blood and the lymphatic system disorders~~[2]	~~Agranulocytosis, neutropenia~~[2]	~~Leucopenia Thrombocytopenia~~	
~~Neurological~~ [2]		~~Neurological disorders~~[2]	~~Coma~~[2]
~~Renal/Genitourinary~~[2]		~~Acute renal failure~~[2]	
~~Skin and subcutaneous tissue disorders~~[2]	~~Macular rash, injection site reaction~~[2]	~~Maculo-papular rash, pemphigoid reaction, pustular rash~~[2]	~~Lyell Syndrome~~[2]

System Organ Class	**Rare** (≥1/10000 to <1/1000)	**Very rare** (<1/10000)	**Not known** (cannot be estimated from the available data)
General disorders and administration site conditions	Malaise	-	-
Vascular disorders	Hypotension	-	Flushing (2)
Hepatobiliary disorders	Increased levels of hepatic transaminases	-	-
Blood and the lymphatic system disorders	-	Thrombocytopenia, Leucopenia, Neutropenia	-
Immune system disorders	-	Hypersensitivity reaction (1, 3)	-
Cardiac disorders	-	-	Tachycardia (2)
Skin and subcutaneous tissue disorders	-	serious skin reactions (3)	Pruritus (2), Erythema (2)

(1) Very rare cases of hypersensitivity reactions ranging from simple skin rash or urticaria to an aphylactic shock have been reported and require discontinuation of treatment.
(2) Isolated cases
(3) Very rare cases of serious skin reactions have been reported.

Frequent adverse reactions at injection site have been reported during clinical trials (pain and burning sensation).

~~Very rare cases of hypersensitivity reactions ranging from simple skin rash or urticaria to anaphylactic~~

~~shock have been reported and require discontinuation of treatment.~~

~~Post Market Adverse Effects for Propacetamol/Paracetamol~~

~~The following adverse events have also been reported during postmarketing surveillance, but incidence rate (frequency) is not known.~~

~~Organ System~~	**~~Adverse Event~~**
~~*Blood and the lymphatic system disorders*~~	~~Thrombocytopenia~~
~~*Cardiac disorders*~~	~~Tachycardia~~
~~*Gastrointestinal disorders*~~	~~Nausea~~ ~~Vomiting~~
~~*General disorders and administration site conditions*~~	~~Administration site reaction~~
~~*Hepatobiliary disorders*~~	~~Fulminant hepatitis~~ ~~Hepatic necrosis~~ ~~Hepatic failure~~ ~~Hepatic enzymes increased~~
~~*Immune system disorders*~~	~~Angioneurotic (Quincke's) edema~~ ~~Anaphylactic shock~~ ~~Anaphylaxis~~ ~~Hypersensitivity reactions (ranging from simple skin rash or urticaria to anaphylactic shock) have been reported and require the discontinuation of treatment~~
~~*Skin and subcutaneous tissue disorders*~~	~~Erythema~~ ~~Flushing~~ ~~Pruritus~~ ~~Rash~~ ~~Urticaria~~ ~~Acute generalised exanthematous pustulosis~~ ~~Toxic epidermal necrolysis~~ ~~Stevens-Johnson syndrome~~

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il

5.2 Pharmacokinetic properties

Table - Age related pharmacokinetic values (standardised clearance, *CL_{std}/F_{oral}×(l×h^{-1}×70 kg^{-1})

Age	Weight (kg)	CL_{std}/F_{oral}×(l×h^{-1}×70 kg^{-1})
40 weeks post-conception	3.3	5.9
3 months postnatal	6	8.8
6 months postnatal	7.5	11.1

1 year postnatal 2 years postnatal	10 12	13.6 15.6
5 years postnatal	20	16.3
8 years postnatal	25	16.3

*CL_{std} is the population estimate for CL

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans beyond the information included in other sec—tions of the SmPC.

Studies on local tolerance of paracetamol in rats and rabbits showed good tolerability. Absence of delayed contact hypersensitivity has been tested in guinea pigs.

Conventional studies using the currently accepted standards for the evaluation of toxicity to reproduction and development are not available.

6.3 Shelf life

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

After first opening
The infusion should commence immediately after connecting the container to the giving set.

After dilution:
See solutions listed in section 6.6.
~~The solution diluted with 0.9% sodium chloride or 5% glucose should be used immediately.~~

From a microbiological point of view, the product ~~drug~~ should be used immediately. If not used immediately, in-use storage times and conditions prior to use ~~time and storage conditions~~ are the responsibility of the user.
~~Also the solution diluted with 0.9% sodium chloride or 5% glucose should be used immediately.~~