נספח 16 טפסים להגשת החמרות בעלונים

הודעה על החמרה (מידע בטיחות) בעלון לצרכן במתכונת עלון לרופא

תאריך: 12.2020

שם תכשיר באנגלית: **Ketamine Panpharma 50 mg/ml**

מספר רישום: **159-85-34830-00**

שם בעל הרישום: **Pharmalogic Ltd**

ההחמרות המבוקשות		
טקסט חדש	טקסט נוכחי	פרק בעלון
Ketamine Panpharma 50 mg/ml Solution for injection/infusion	Ketamine Rotexmedica 50 mg/ml Solution for injection	1. Name of the Medicinal Product
Solution for I.M, I.V use	Solution for injection/infusion	2. Pharmaceutical Form
		4. Clinical Particulars
Long-Term Use Cases of cystitis including hemorrhagic cystitis, acute kidney injury, hydronephrosis, and ureteral disorders have been reported in patients being given ketamine on a long-term basis, especially in the setting of ketamine abuse. This adverse reaction develops in patients receiving long-term ketamine treatment after a time ranging from 1 month to several years. **Ketamine is not indicated nor recommended for long-term use.** Hepatotoxicity has also been reported in patients with extended use (> 3 days).	Long-Term Use Cases of cystitis including hemorrhagic cystitis have been reported in patients being given ketamine on a long-term basis. This adverse reaction develops in patients receiving long-term ketamine treatment after a time ranging from 1 month to several years. **Ketamine is not indicated nor recommended for long-term use.** Hepatotoxicity has also been reported in patients with extended use (> 3 days).	4.4 Special warnings and precautions for use
Prolonged recovery time may occur if barbiturates and/or narcotics are used concurrently with Ketamine. Ketamine is chemically incompatible with barbiturates and diazepam because of precipitate formation. Therefore, these should not be mixed in the same syringe or infusion fluid. Ketamine may potentiate the neuromuscular blocking effects of atracurium and tubocurarine including respiratory depression with apnea.	Prolonged recovery time may occur if barbiturates and/or narcotics are used concurrently with Ketamine. Ketamine is chemically incompatible with barbiturates and diazepam because of precipitate formation. Therefore, these should not be mixed in the same syringe or infusion fluid. Ketamine may potentiate the neuromuscular blocking effects of atracurium and tubocurarine including respiratory depression with apnea.	4.5. Interaction with other medicinal products and other forms of interaction

Diazepam is known to increase the half-life of ketamine and prolongs its pharmacodynamic effects. Dose adjustments may therefore be needed. The use of halogenated anesthetics concomitantly with ketamine can lengthen the elimination half-life of ketamine and delay recovery from anesthesia. Concurrent use of ketamine (especially in high doses or when rapidly administered) with halogenated anesthetics can increase the risk of developing bradycardia, hypotension or decreased cardiac output. The use of ketamine with other central nervous system (CNS) depressants (e.g. ethanol, phenothiazines, sedating H1 – blockers or skeletal muscle relaxants) can potentiate CNS depression and/or increase risk of developing respiratory depression. Reduced doses of ketamine may be required with concurrent administration of other anxiolytics, sedatives and hypnotics. Ketamine has been reported to antagonize the hypnotic effect of thiopental. Patients taking thyroid hormones have an increased risk of developing hypertension and tachycardia when given ketamine. Concomitant use of antihypertensive agents and ketamine increases the risk of developing hypotension. Sympathomimetics (directely or indirectely acting) and vasopressin may enhance the sympathomimetic effects of ketamine. Concomitant use with ergometrine may lead to an increase in blood pressure. When ketamine and theophylline or aminophylline are given concurrently, a clinically significant reduction in the seizure threshold may be observed. Unpredictable extensor-type seizures have been reported with concurrent administration of these agents. Drugs that inhibit CYP3A4 enzyme activity generally decrease hepatic clearance, resulting in increased plasma concentration of CYP3A4 substrate medications, such as ketamine. Coadministration of ketamine with drugs that inhibit CYP3A4 enzyme may require a decrease in ketamine dosage to achieve the desired clinical outcome. Drugs that induce CYP3A4 enzyme activity generally increase hepatic	The use of halogenated anesthetics concomitantly with ketamine can lengthen the elimination half-life of ketamine and delay recovery from anesthesia. Concurrent use of ketamine (especially in high doses or when rapidly administered) with halogenated anesthetics can increase the risk of developing bradycardia, hypotension or decreased cardiac output. The use of ketamine with other central nervous system (CNS) depressants (e.g. ethanol, phenothiazines, sedating H1 – blockers or skeletal muscle relaxants) can potentiate CNS depression and/or increase risk of developing respiratory depression. Reduced doses of ketamine may be required with concurrent administration of other anxiolytics, sedatives and hypnotics. Ketamine has been reported to antagonize the hypnotic effect of thiopental. Patients taking thyroid hormones have an increased risk of developing hypertension and tachycardia when given ketamine. Concomitant use of antihypertensive agents and ketamine increases the risk of developing hypotension. When ketamine and theophylline are given concurrently, a clinically significant reduction in the seizure threshold is observed. Unpredictable extensor-type seizures have been reported with concurrent administration of these agents. Drugs that inhibit CYP3A4 enzyme activity generally decrease hepatic clearance, resulting in increased plasma concentration of CYP3A4 substrate medications, such as ketamine. Coadministration of ketamine with drugs that inhibit CYP3A4 enzyme may require a decrease in ketamine dosage to achieve the desired clinical outcome. Drugs that induce CYP3A4 enzyme activity generally increase hepatic	

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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/	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 http://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffect Medic@moh.health.gov.il	4.8. Undesirable effects
		6. Pharmaceutical properties
Benzethonium chloride, water for injection, nitrogen.	Benzethonium chloride, water for injection	6.1 List of Excipients
The expiry date of the product is indicated on the packaging materials After first opening can used within 4 weeks, below 25℃, protected from light. Shelf life of prepared solutions for infusion: The chemical and physical stability of the drug product diluted in 5% glucose or isotonic sodium chloride solution at a concentration of 1mg/ml, has been demonstrated for 24 hours at 25℃.	The expiry date of the product is indicated on the packaging materials After first opening can be stored for 4 weeks, below 25℃, protected from light. Shelf life of prepared solutions for infusion: The chemical and physical stability of the drug product diluted in 5% glucose or isotonic sodium chloride solution at a concentration of 1mg/ml, has been demonstrated for 24 h. at 25℃.	6.3 Shelf Life
Store below 30°C. Protect from light in the original pack. For storage, conditions after reconstitution/dilution of the medicinal product see section 6.3.	Store below 30°C. Protect from light. For storage, conditions after reconstitution/dilution of the medicinal product see section 6.3.	6.4 Special Precautions for storage
Panpharma GmbH, Germany Bunsenstrasse 4, D-22946 Trittau, Germany	Rotexmedica GmbH Arzneimittelwerk Bunsenstrasse 4, Trittau 22946, Germany	7. Manufacturer
8. Importer and License Holder: Pharmalogic Ltd. P.OB. 3838, Petah Tikva 49511	Importer and License Holder: Pharmalogic Ltd. P.OB. 3838, Petah Tikva 49511 **Tel: 1-800-071-277**	
Registration Number 159-85-34830	**Registration Number**	

מצ"ב העלון, שבו מסומנות ההחמרות על רקע צהוב והטקסט למחיקה מסומן בצבע אדום.
שינויים שאינם בגדר ההחמרות סומנו בטקסט ירוק.
העלון הועבר בדואר אלקטרוני בתאריך: 22.12.2020

☒ כל השינויים עולים בקנה אחד עם תנאי הרישום (תעודת רישום, תעודת איכות, וטופס פרטי התכשיר העדכני).

☒ כל הכתוב בהצעת עלון, תואם לתנאי הרישום.

☒ קיים עלון לצרכן והוא מעודכן בהתאם.

☒ אסמכתא לבקשה: **Ketalar 50 mg/ml injection-PFIZER PFE PHARMACEUTICALS ISRAEL LTD**

האסמכתא מצ"ב

☒ השינוי הנ"ל אושר על ידי משרד הבריאות ב: 03.2020

☒ אני רוקחת הממונה של חברת פארמלוגיק בע"מ מצהירה בזה כי אין שינויים נוספים, מלבד אלה שסומנו בהצעת העלון.

☒ אני מצהירה כי השינויים אינם יוצרים סתירה פנימית במידע בעלון.

עלון זה לא מטופל במקביל במסגרת אחרת (כגון: עדכון עלון במסגרת בקשה לתוספת התוויה, החמרה וכו')

במידה וקיים טיפול במקביל במסגרת אחרת – יש לציין זאת.

חתימת הרוקחת הממונה: Frida Shud
