הודעה על החמרה (מידע בטיחות) בעלון לרופא
(מעודכן 05.2013)

תאריך: ***13/03/17***

שם תכשיר באנגלית ומספר הרישום: **Propofol Lipuro 1%** **127-87-30672-11/127-87-30672-10**

שם בעל הרישום : **Lapidot medical import and marketing LTD**

טופס זה מפרט ההחמרות בלבד !

ההחמרות המבוקשות

טקסט חדש	טקסט נוכחי	פרק בעלון
Method and duration of administration ● *Method of administration* Intravenous use Propofol-Lipuro 1% is administered intravenously by injection or continuous infusion either undiluted or diluted with 5 % w/v glucose solution or 0.9 % w/v sodium chloride solution as well as in a 0.18 % w/v sodium chloride and 4 % w/v glucose (see also section 6.6). Containers should be shaken before use. Before use, the neck of the ampoule or the surface of the rubber stopper of the vial should be cleaned with medicinal alcohol (spray or swabs). After use, tapped containers must be discarded. Propofol-Lipuro 10 mg/ml contains no antimicrobial preservatives and supports growth of microorganisms. Therefore, Propofol-Lipuro 10 mg/ml is to be drawn up aseptically into a sterile syringe or an infusion set immediately after opening the ampoule or breaking the vial seal. Administration must commence without delay. Asepsis must be maintained for both Propofol-Lipuro 10 mg/ml and the infusion equipment throughout the infusion period. Any medicinal products or fluids added to a running Propofol-Lipuro 10 mg/ml infusion must be administered close to the cannula siteIf infusion sets with filters are to be used, these must be lipid-permeable. The contents of one ampoule or one vial of	***Method and duration of administration*** ● *Method of administration* Intravenous use Propofol-Lipuro 1% is administered intravenously by injection or continuous infusion either undiluted or diluted with 5 % w/v glucose solution or 0.9 % w/v sodium chloride solution as well as in a 0.18 % w/v sodium chloride and 4 % w/v glucose (see also section 6.6). Containers should be shaken before use. Before use, the neck of the ampoule or the surface of the rubber stopper of the vial should be cleaned with medicinal alcohol (spray or swabs). After use, tapped containers must be discarded. Infusion of undiluted Propofol-Lipuro 1% When administering Propofol-Lipuro 1% by continuous infusion, it is recommended that burettes, drop counters, syringe pumps or volumetric infusion pumps, should always be used to control the infusion rates.	**4.2 Posology and Method of Administration**

Propofol-Lipuro 10 mg/ml and any syringe containing Propofol-Lipuro 10 mg/ml are for **single use** in **one** patient. Infusion of undiluted Propofol-Lipuro 1% When administering Propofol-Lipuro 1% by continuous infusion, it is recommended that burettes, drop counters, syringe pumps or volumetric infusion pumps, should always be used to control the infusion rates. As established for the parenteral administration of all kinds of fat emulsions, the duration of continuous infusion of Propofol-Lipuro 1 % (10 mg/ml) from **one** infusion system must not exceed 12 hours. The infusion line and the reservoir of Propofol-Lipuro 1 % (10 mg/ml) must be discarded and replaced after 12 hours at the latest. Any portion of Propofol-Lipuro 1 % (10 mg/ml) remaining after the end of infusion or after replacement of the infusion system must be discarded.		
The abuse of and dependence on propofol, predominantly by health care professionals, have been reported. As with other general anaesthetics, the administration of propofol without airway care may result in fatal respiratory complications. ……. Appropriate care should be applied in patients with disorders of fat metabolism and in other conditions where lipid emulsions must be used cautiously. **Paediatric population** The use of propofol is not recommended in newborn infants as this patient population has not been fully investigated. Pharmacokinetic data (see section 5.2) indicate that clearance is considerably reduced in neonates and has a very high inter-individual variability. Relative overdose could occur on administering doses recommended for older children and result in severe cardiovascular depression. Propofol must not be used in patients of 16 years of age or younger for sedation for intensive care as the safety and efficacy of propofol for sedation in this age group have not been demonstrated (see section 4.3). **Advisory statements concerning Intensive**	The abuse propofol, predominantly by health care professionals, has been reported. As with other general anaesthetics, the administration of propofol without airway care may result in fatal respiratory complications. ……. Appropriate care should be applied in patients with disorders of fat metabolism and in other conditions where lipid emulsions must be used cautiously. It is recommended that blood lipid levels should be monitored if propofol is administered to patients thought to be at particular risk of fat overload. Administration of propofol should be adjusted appropriately if the monitoring indicates that fat is being inadequately cleared from the body. If the patient is receiving other intravenous lipid concurrently, a reduction in quantity should be made in order to take account of the amount of lipid infused as part of the propofol formulation; 1.0 ml of Propofol-Lipuro 10 mg/ml contains 0.1 g of fat. The use of propofol is not recommended in newborn infants as this patient population has not been fully investigated. Pharmacokinetic data (see section 5.2) indicate that clearance is considerably reduced in neonates and has a very high inter-individual variability. Relative overdose could occur on administering doses recommended for older	**4.4 Special Warnings and Precautions for Use**

Care Unit management Use of propofol for ICU sedation has been associated with a constellation of metabolic disturbances and system organ failures that may result in death. Reports have been received of combinations of the following: Metabolic acidosis, Rhabdomyolysis, Hyperkalaemia, Hepatomegaly, Renal failure, Hyperlipidaemia, Cardiac arrhythmia, Brugada-type ECG (elevated ST-segment and coved T-wave) and rapidly progressive Cardiac failure usually unresponsive to inotropic supportive treatment. Combinations of these events have been referred to as the **Propofol infusion syndrome**. These events were mostly seen in patients with serious head injuries and children with respiratory tract infections who received dosages in excess of those advised in adults for sedation in the intensive care unit. The following appear to be the major risk factors for the development of these events: decreased oxygen delivery to tissues; serious neurological injury and/or sepsis; high dosages of one or more of the following pharmacological agents - vasoconstrictors, steroids, inotropes and/or propofol at dose rates greater than 4 mg/kg/h for more than 48 hours). Prescribers should be alert to these events in patients with the above risk factors and promptly consider decreasing or stopping the propofol dosage when the above signs develop. All sedative and therapeutic agents used in the intensive care unit (ICU)-should be titrated to maintain optimal oxygen delivery and haemodynamic parameters. Patients with raised intra-cranial pressure (ICP) should be given appropriate treatment to support the cerebral perfusion pressure during these treatment modifications. Treating physicians are reminded if possible not to exceed the dosage of 4 mg/kg/h. Appropriate care should be applied in patients with disorders of fat metabolism and in other conditions where lipid emulsions must be used cautiously. It is recommended that blood lipid levels should be monitored if propofol is administered to patients thought to be at particular risk of fat overload.	children and result in severe cardiovascular depression. **Advisory statements concerning Intensive Care Unit management** The safety and efficacy of propofol for (background) sedation in children younger than 16 years of age have not been demonstrated. Although no causal relationship has been established, serious undesirable effects with (background) sedation in patients younger than 16 years of age (including cases with fatal outcome) have been reported during unlicensed use. In particular these effects concerned occurrence of metabolic acidosis, hyperlipidemia, rhabdomyolysis and/or cardiac failure. These effects were most frequently seen in children with respiratory tract infections who received dosages in excess of those advised in adults for sedation in the intensive care unit. Reports have been received of combinations of the following: Metabolic acidosis, Rhabdomyolysis, Hyperkalaemia, Hepatomegaly, Renal failure, Hyperlipidaemia, Cardiac arrhythmia, Brugada-type ECG (elevated ST-segment and coved T-wave) and rapidly progressive Cardiac failure usually unresponsive to inotropic supportive treatment.(in some cases with fatal outcome) in adults Combinations of these events have been referred to as the **Propofol infusion syndrome**. The following appear to be the major risk factors for the development of these events: decreased oxygen delivery to tissues; serious neurological injury and/or sepsis; high dosages of one or more of the following pharmacological agents - vasoconstrictors, steroids, inotropes and/or propofol (usually following extended dosing at dose rates greater than 4 mg/kg/h). Prescribers should be alert to these events and consider decreasing the propofol dosage or switching to an alternative sedative at the first sign of occurrence of symptoms. All sedative and therapeutic agents used in the intensive care unit (ICU), including propofol,-should be titrated to maintain optimal oxygen delivery and haemodynamic parameters. Patients with raised intra-cranial pressure (ICP) should be given appropriate treatment to support the cerebral perfusion pressure during these treatment modifications. Treating physicians are reminded if possible not to exceed the dosage of 4 mg/kg/h. **Additional precautions**	

Administration of propofol should be adjusted appropriately if the monitoring indicates that fat is being inadequately cleared from the body. If the patient is receiving other intravenous lipid concurrently, a reduction in quantity should be made in order to take account of the amount of lipid infused as part of the propofol formulation; 1.0 ml of Propofol-Lipuro 10 mg/ml contains 0.1 g of fat. **Additional precautions** Caution should be taken when treating patients with mitochondrial disease. These patients may be susceptible to exacerbations of their disorder when undergoing anaesthesia, surgery and ICU care. Maintenance of normothermia, provision of carbohydrates and good hydration are recommended for such patients. The early presentations of mitochondrial disease exacerbation and of the 'propofol infusion syndrome' may be similar. Propofol-Lipuro 1% contains no antimicrobial preservatives and supports growth of micro-organisms. When propofol is to be aspirated, it must be drawn aseptically into a sterile syringe or giving set immediately after opening the ampoule or breaking the vial seal. Administration must commence without delay. Asepsis must be maintained for both propofol and infusion equipment throughout the infusion period. Any infusion fluids added to the propofol line must be administered close to the cannula site. If infusion sets with filters are to be used, these must be lipid-permeable. Propofol and any syringe containing propofol are for single use in an individual patient. In accordance with established guidelines for other lipid emulsions, a single infusion of propofol must not exceed 12 hours. At the end of the procedure or at 12 hours, whichever is the sooner, both the reservoir of propofol and the infusion line must be discarded and replaced as appropriate. This medicinal product contains less than 1 mmol (23 mg) sodium in 100 ml, i.e. essentially 'sodium free'.	Propofol-Lipuro 1% contains no antimicrobial preservatives and supports growth of micro-organisms. When propofol is to be aspirated, it must be drawn aseptically into a sterile syringe or giving set immediately after opening the ampoule or breaking the vial seal. Administration must commence without delay. Asepsis must be maintained for both propofol and infusion equipment throughout the infusion period. Any infusion fluids added to the propofol line must be administered close to the cannula site. Propofol must not be administered via a microbiological filter. Propofol and any syringe containing propofol are for single use in an individual patient. In accordance with established guidelines for other lipid emulsions, a single infusion of propofol must not exceed 12 hours. At the end of the procedure or at 12 hours, whichever is the sooner, both the reservoir of propofol and the infusion line must be discarded and replaced as appropriate. This medicinal product contains less than 1 mmol (23 mg) sodium in 100 ml, i.e. essentially 'sodium free'.	
Propofol has been used in association with spinal and epidural anaesthesia and with	Propofol has been used in association with spinal and epidural anaesthesia and with commonly used	**4.5 Interaction with Other**

commonly used premedicants, neuromuscular blocking drugs, inhalational agents and analgesic agents; no pharmacological incompatibility has been encountered. Lower doses of propofol may be required where general anaesthesia or sedation is used as an adjunct to regional anaesthetic techniques. Profound hypotension has been reported following anaesthetic induction with propofol in patients treated with rifampicin.	premedicants, neuromuscular blocking drugs, inhalational agents and analgesic agents; no pharmacological incompatibility has been encountered. Lower doses of propofol may be required where general anaesthesia or sedation is used as an adjunct to regional anaesthetic techniques.	**Medicinal Products and Other Forms of Interaction**

System Organ Class	**Frequency**	**Undesirable Effects**
Immune system disorders:	Very rare (<1/10 000)	Anaphylaxis – may include angioedema, bronchospasm, erythema and hypotension
Metabolism and Nutritional disorder:	Frequency not known (9)	Metabolic acidosis (5), hyperkalaemia (5), hyperlipidaemia (5)
Psychiatric disorders:	Frequency not known (9)	Euphoric mood, drug abuse and drug dependence (8)
Nervous system disorders:	Common (>1/100, <1/10)	Headache during recovery phase
	Rare (>1/10 000, <1/1000)	Epileptiform movements, including convulsions and opisthotonus during induction, maintenance and recovery
	Very rare (<1/10 000)	Postoperative unconsciousness
	Frequency not known (9)	Involuntary movements
Cardiac disorders:	Common (>1/100, <1/10)	Bradycardia (1)
	Very rare (<1/10 000)	Pulmonary oedema
	Frequency not known (9)	Cardiac arrhythmia (5), cardiac failure (5), (7)
Vascular disorders:	Common (>1/100, <1/10)	Hypotension (2)
	Uncommon (>1/1000, <1/100)	Thrombosis and phlebitis
Respiratory, thoracic and mediastinal disorders:	Common (>1/100, <1/10)	Transient apnoea during induction
	Frequency not known (9)	Respiratory depression (dose dependent)
Gastrointestinal disorders:	Common (>1/100, <1/10)	Nausea and vomiting during recovery phase

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Psychiatric disorders:	Frequency not known (9)	Euphoric mood, drug abuse (8)
Nervous system disorders:	Common (>1/100, <1/10)	Headache during recovery phase
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Gastrointestinal disorders:	Common (>1/100, <1/10)	Nausea and vomiting during recovery phase
	Very rare (<1/10 000)	Pancreatitis

4.8 Undesirable Effects

	Very rare (<1/10 000)	Pancreatitis
Hepatobiliary disorders	Frequency not known (9)	Hepatomegaly (5)
Musculoskeletal and connective tissue disorders:	Frequency not known (9)	Rhabdomyolysis (3), (5)
Renal and urinary disorders	Very rare (<1/10 000)	Discolouration of urine following prolonged administration
	Frequency not known (9)	Renal failure(5)
Reproductive system and breast	Very rare (<1/10 000)	Sexual disinhibition
General disorders and administration site conditions:	Very common (>1/10)	Local pain on induction (4)
	Very rare	Tissue necrosis (10) following accidental extravascular administration (11)
	Frequency not known (9)	Local pain, swelling following accidental extravascular administration
Investigations	Frequency not known (9)	Brugada type ECG (5), (6)
Injury, poisoning and procedural complications:	Very rare (<1/10 000)	Postoperative fever

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8) Abuse of and drug dependence on propofol, predominantly by health care professionals.

(9) Not known as it cannot be estimated from the available clinical trial data.

(10) Necrosis has been reported where tissue viability has been impaired.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation 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=AdversEffectMedic@moh.gov.il

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Injury, poisoning and procedural complications:	Very rare (<1/10 000)	Postoperative fever

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8) Drug abuse, predominantly by health care professionals.

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…….. Pack sizes: glass ampoules : 5 x 20 ml glass vials: 10 x 20 ml, 1 x 50 ml, 10 x 50 ml, 1 x 100 ml, 10 x 100 ml ……..	…….. Pack sizes: glass ampoules : 5 x 20 ml glass vials: 1 x 50 ml, 10 x 50 ml, 1 x 100 ml, 10 x 100 ml ……..	**6.5 Nature and Contents of Container**