מרץ 2019

רופא/ה נכבד/ה,

רוקח/ת נכבד/ה,

הנדון: **MEPACT®, Powder for concentrate for dispersion for infusion, I.V.**
מפקט, אבקה להכנת תרכיז לפיזור ולעירוי, מתן תוך-ורידי

חברת טקדה ישראל בע"מ מבקשת להודיעכם כי העלון לרופא של התכשיר שבנדון, התעדכן במרץ 2019.

העדכונים המהותיים ביותר מופיעים במכתב זה, אך קיימים עדכונים נוספים.

למידע נוסף, יש לעיין בעלון לרופא המעודכן אשר נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות:

https://www.old.health.gov.il/units/pharmacy/trufot/PerutTrufa.asp?Reg_Number=147 07 33425 00&safa=
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כמו כן, ניתן לקבלו מודפס על-ידי פנייה לבעל הרישום:

טקדה ישראל בע"מ, רח' אפעל 25, פתח-תקווה, טל': 03-3733140.

ההתוויה המאושרת לתכשיר בישראל:

Mepact is indicated in children, adolescents and young adults for the treatment of high grade resectable non-metastatic osteosarcoma after macroscopically complete surgical resection.

It is used in combination with post-operative multi-agent chemotherapy.

Safety and efficacy have been assessed in studies of patients 2 to 30 years of age at initial diagnosis.

מרכיב פעיל:

MIFAMURTIDE 4 MG/VIAL

בברכה,

יהב ורדי
רוקחת ממונה
טקדה ישראל בע"מ

IL/MEP/0319/0001

Takeda Israel Ltd.
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העדכונים בעלון לרופא הינם (טקסט שהושמט מסומן באדום עם קו חוצה, טקסט שהוסף מסומן כטקסט כחול):

4.2 Posology and method of administration

Method of administration

~~MEPACT must be reconstituted, filtered using the filter provided and further diluted prior to administration. The reconstituted, filtered and diluted suspension for infusion is a homogenous, white to off-white, opaque liposomal suspension, free of visible particles and free of foam and lipid lumps.~~

~~After reconstitution, filtering using the filter provided and further dilution,~~ MEPACT is administered by intravenous infusion over a period of 1 hour.

…

For further instructions on reconstitution, filtering using the filter provided and dilution of the medicinal product before ~~prior to~~ administration, see section 6.6.

4.4 Special warnings and precautions for use

…

MEPACT contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per dosage unit.

4.7 Effects on ability to drive and use machines

MEPACT has a moderate influence on the ability to drive and use machines. Dizziness, vertigo, fatigue and blurred vision have shown as ~~No studies of the effects on the ability to drive and use machines have been performed. The~~ very common or common undesirable effects of mifamurtide treatment ~~(such as dizziness, vertigo, fatigue and blurred vision) may have an effect on the ability to drive and use machines~~.

4.8 Undesirable effects

Summary of the safety profile

…

The most frequent adverse reactions~~, occurring in >50% of patients, were~~ are chills, pyrexia, fatigue, nausea, tachyc~~h~~ardia and headache. Many of the very commonly reported adverse reactions as shown in the following summary table are thought to be related to the mechanism of action of mifamurtide (see ~~Table~~ table 1). The majority of these events were reported as either mild or moderate. ~~This profile is consistent whether summarising all early studies (n=248) or only those studies in osteosarcoma (n=51). It is likely that these adverse reactions also occurred in the large randomised study, but they were not recorded because only serious and life-threatening adverse reactions were collected in that study.~~

…

Table 1. Adverse reactions ~~associated with MEPACT in ≥ 1/100 patients~~

…

4.9 Overdose

~~No case of overdose has been reported within the approved indication.~~ The maximum tolerated dose in phase I studies was 4-6 mg/m^2 with a high variability of adverse reactions.

…

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5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

…

Mechanism of action

…It has similar immunostimulatory effects as natural MDP ~~with the additional advantage of a longer half-life in plasma~~.

…

Clinical safety and efficacy

…

~~Mifamurtide significantly increased the overall survival of patients with newly-diagnosed resectable high-grade osteosarcoma when used in conjunction with combination chemotherapy when compared to chemotherapy alone.~~ In a randomised phase III study of 678 patients (age range from 1.4 to 30.6 years) with newly-diagnosed resectable high-grade oseteosarcoma, the addition of adjuvant mifamurtide to chemotherapy (either doxorubicin cisplatin and methotrexate with or without ifosfamide), significantly increased the 6-year overall survival and resulted in a relative reduction in the risk of death ~~of~~ by 28% (p = 0.0313, hazard ratio (HR) = 0.72 [95% confidence interval (CI): 0.53, 0.97]).

Paediatric population

Based on the prevalence of the disease, children and young adults were studied in the pivotal trial. However, no specific subset analyses for efficacy are available in patients < 18 years of age and ≥ 18 years of age.

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6.3 Shelf life

Unopened vial of powder*:*

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

~~30 months~~

…

6.6 Special precautions for disposal and other handling

MEPACT must be reconstituted, filtered using the filter provided and further diluted using aseptic technique, prior to administration.

…

The reconstituted, filtered and diluted suspension for infusion is a homogenous, white to off-white, opaque liposomal suspension, free of visible particles and free of foam and lipid lumps.

Instructions for preparation of MEPACT for intravenous infusion

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16. Based on the liposomal nature of the product, use of an infusion set with an in-line filter during administration is not recommended.

…

~~*Disposal*~~

No special requirements for disposal.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

…

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