פברואר 2024

רופא/ה נכבד/ה,

רוקח/ת נכבד/ה,

הנדון: הלאבן- HALAVEN, eribulin as mesilate 0.44 mg/ml, Solution for injection

חברת אסאיי ישראל בע"מ (Eisai Israel Ltd.) מבקשת להודיעכם כי העלון לרופא של התכשיר שבנדון התעדכן בינואר 2024.

פרטי העדכון העיקריים מופיעים בהמשך (טקסט שנוסף מסומן באדום, טקסט שהושמט מסומן בטקסט ~~אדום עם קו חוצה~~).

ההתוויות המאושרות לתכשיר בישראל:

HALAVEN is indicated for the treatment of adult patients with locally advanced or metastatic breast cancer who have progressed after at least one chemotherapeutic regimen for advanced disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting unless patients were not suitable for these treatments.
HALAVEN is indicated for the treatment of adult patients with unresectable liposarcoma who have received prior anthracycline containing therapy (unless unsuitable) for advanced or metastatic disease.

העלון המעודכן נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות ומצורף לפרסום זה. כמו כן, ניתן לקבל העתק מודפס שלו באמצעות פנייה לבעל הרישום: אסאיי ישראל בע"מ, ת.ד. 8049 כפר סבא, 4418001.

להלן העדכונים בעלון לרופא:

4.2 Posology and method of administration

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Paediatric population

There is no relevant use of HALAVEN in children and adolescents for the indication of breast cancer.
There is no relevant use of HALAVEN in the paediatric population for the indication of soft tissue sarcoma (see section 5.1).
~~The safety and efficacy of HALAVEN in children from birth to 18 years of age have not yet been established in soft tissue sarcoma. No data are available.~~

4.8 Undesirable effects

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Paediatric population

Three open-label studies, Studies 113, 213 and 223, were conducted in paediatric patients with refractory or recurrent solid tumours and lymphomas, but excluding central nervous system (CNS) tumours (see section 5.1).

The safety of eribulin monotherapy was evaluated in 43 paediatric patients who received up to

1.58 mg/m2 on Days 1 and 8 of a 21-day cycle (Studies 113 and 223). The safety of eribulin

combination with irinotecan was also evaluated in 40 paediatric patients who received eribulin 1.23 mg/m2 on Days 1 and 8 and irinotecan 20 or 40 mg/m2 on Days 1 to 5 of a 21-day cycle, or 100 or 125 mg/m2 on Days 1 and 8 of a 21-day cycle (Study 213).

In Study 113 (Phase 1), the most frequently reported adverse drug reactions were white blood cell count decreased, lymphocyte count decreased, anaemia and neutrophil count decreased.

In Study 213 (Phase 1/2), the most frequently reported adverse drug reactions were neutropenia (Phase 1) and diarrhoea and neutrophil count decreased (Phase 2).

In Study 223 (Phase 2), the most frequently reported adverse drug reactions were neutrophil count decreased, anaemia, and white blood cell count decreased.

The safety profile of eribulin as monotherapy or in combination with irinotecan hydrochloride in this paediatric population was consistent with the known safety profile of either study drug in the adult population.

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5.1 Pharmacodynamic properties

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Paediatric population

Soft Tissue Sarcoma

Efficacy of eribulin was assessed but not established in three open-label studies:
Study 113 was a Phase 1, open-label, multicentre, dose-finding study that assessed eribulin in paediatric patients with refractory or recurrent solid tumours and lymphomas but excluding CNS tumours. A total of 22 paediatric patients (age range: 3 to 17 years) were enrolled and treated. The patients were administered eribulin intravenously on Days 1 and 8 of a 21-day cycle at three dose levels (0.97, 1.23 and 1.58 mg/m2). The maximum tolerated dose (MTD)/recommended Phase 2 dose (RP2D) of eribulin was determined as 1.23 mg/m2 on Days 1 and 8 of a 21-day cycle.

Study 223 was a Phase 2, open-label, multicentre study that assessed the safety and preliminary activity of eribulin in paediatric patients with refractory or recurrent rhabdomyosarcoma (RMS), non-rhabdomyosarcoma soft tissue sarcoma (NRSTS) or Ewing sarcoma (EWS). Twenty-one paediatric patients (age range: 2 to 17 years) were enrolled and treated with eribulin at a dose of 1.23 mg/m2 intravenously on Days 1 and 8 of a 21-day cycle (the RP2D from Study 113). No patient achieved confirmed partial response (PR) or complete response (CR).

Study 213 was a Phase 1/2, open-label, multicentre study to evaluate the safety and efficacy of eribulin in combination with irinotecan hydrochloride in paediatric patients with relapsed/refractory solid tumours and lymphomas but excluding CNS tumours (Phase 1), and to assess the efficacy of the combination treatment in paediatric patients with relapsed/refractory RMS, NRSTS and EWS (Phase 2). A total of 40 paediatric patients were enrolled and treated in this study. In Phase 1, 13 paediatric patients (age range: 4 to 17 years) were enrolled and treated; the RP2D was determined as eribulin 1.23 mg/m2 on Days 1 and 8 with irinotecan hydrochloride 40 mg/m2 on Days 1 to 5 of a 21-day cycle. In Phase 2, 27 paediatric patients (age range: 4 to 17 years) were enrolled and treated at the RP2D. Three patients had confirmed PR (1 patient in each of the RMS, NRSTS, and EWS histology cohorts). The objective response rate (ORR) was 11.1%.

No new safety signals were observed in the three paediatric studies (see section 4.8); however, due to the small patient populations no firm conclusions can be made.

5.2 Pharmacokinetic properties

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Paediatric population

Eribulin plasma concentrations were collected from 83 paediatric patients (age range: 2 to 17 years), with refractory/relapsed and recurrent solid tumours and lymphomas, who received eribulin in Studies 113, 213 and 223. Eribulin PK in paediatric patients was comparable to adult patients with STS and patients with other types of tumour. Eribulin exposure in paediatric patients was similar to exposure in adult patients. Concomitant irinotecan did not have an effect on eribulin PK in paediatric patients with refractory/relapsed and recurrent solid tumours.

6.3 Shelf life

In-use shelf life

From a microbiological point of view ~~unless the method of opening precludes the risk of microbial contamination~~ the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user and would normally not be longer than 24 hours at 2°C - 8°C, unless dilution has taken place in controlled and validated aseptic conditions.

Chemical and physical in-use stability of ~~If not used immediately~~ HALAVEN as an undiluted solution in a syringe has been demonstrated for up to ~~should not normally be stored longer than~~ 4 hours at 15-25°C and ambient lighting, or up to 24 hours at 2°C - 8°C.

Chemical and physical in-use stability of HALAVEN as a diluted solution (0.018 mg/ml to 0.18 mg/ml eribulin in sodium chloride 9 mg/ml (0.9%)) has been demonstrated for up to 72 ~~solution for injection should not be stored longer than 24~~ hours at 2°C - 8°C, ~~unless dilution has taken place in controlled and validated aseptic conditions~~.

6.6 Special precautions for disposal and other handling

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If using a spike to administer the product refer to the instructions provided from the device manufacturer. HALAVEN vials have a 13mm stopper. The device selected should be compatible with small vial stoppers.

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בברכה,
אלינה ורמן, רוקחת ממונה
אסאיי ישראל בע"מ