

חברת תרו מבקשת להודיעכם על עדכון העלון לצרכן של התכשיר:

**Bortezomib Taro 3.5 mg
Powder for Solution for
Injection****בורטזומיב תרו 3.5 מ"ג
אבקה להכנת תמיסה להזרקה****מרכיבים פעילים:**

Bortezomib 3.5 mg/vial

התוויה מאושרת:

Bortezomib is indicated for the treatment of patients with multiple myeloma.
Bortezomib is indicated for the treatment of patients with mantle cell lymphoma who have received at least one prior therapy.
Bortezomib in combination with rituximab, cyclophosphamide, doxorubicin and prednisone is indicated for the treatment of adult patients with previously untreated mantle cell lymphoma who are unsuitable for haematopoietic stem cell transplantation.

שינויים בעלונים המהווים החמרה מודגשים ברקע **צהוב**, תוספות מסומנות בצבע **אדום** והשמטות מסומנות בקו אופקי. כמו כן, בעלונים בוצעו שינויים נוספים הכוללים תוספת מידע, השמטת מידע ועדכוני נוסח שאינם מהווים החמרה.

העלון המעודכן נשלח למשרד הבריאות לצורך פרסומו במאגר התרופות שבאתר משרד הבריאות וניתן לקבלו מודפס על ידי פנייה לבעל הרישום: תרו אינטרנשיונל בע"מ, רחוב הקיטור 14, מפרץ חיפה 2624761, טל. 04-8475700.

עדכונים עיקריים בעלון לרופא:

[...]

13. CLINICAL PHARMACOLOGY

[...]

Drug Interaction Studies*Clinical Studies*

No clinically significant differences in bortezomib pharmacokinetics were observed when coadministered with dexamethasone (weak CYP3A4 inducer), omeprazole (strong CYP2C19 inhibitor), or melphalan in combination with prednisone.

In vitro studies indicate that bortezomib is a weak inhibitor of the cytochrome P450 (CYP) isozymes 1A2, 2C9, 2C19, 2D6 and 3A4. Based on the limited contribution (7%) of CYP2D6 to the metabolism of bortezomib, the CYP2D6 poor metaboliser phenotype is not expected to affect the overall disposition of bortezomib.

A drug-drug interaction study assessing the effect of ketoconazole, a potent CYP3A4 inhibitor, on the pharmacokinetics of bortezomib (injected intravenously), showed a mean

bortezomib AUC increase of 35% (CI90% [1.032 to 1.772]) based on data from 12 patients. Therefore, patients should be closely monitored when given bortezomib in combination with potent CYP3A4 inhibitors (e.g. ketoconazole, ritonavir).

In a drug-drug interaction study assessing the effect of omeprazole, a potent CYP2C19 inhibitor, on the pharmacokinetics of bortezomib (injected intravenously), there was no significant effect on the pharmacokinetics of bortezomib based on data from 17 patients.

A drug-drug interaction study assessing the effect of rifampicin, a potent CYP3A4 inducer, on the pharmacokinetics of bortezomib (injected intravenously), showed a mean bortezomib AUC reduction of 45% based on data from six patients. Therefore, the concomitant use of bortezomib with strong CYP3A4 inducers (e.g., rifampicin, carbamazepine, phenytoin, phenobarbital and St. John's Wort) is not recommended, as efficacy may be reduced.

In the same drug-drug interaction study assessing the effect of dexamethasone, a weaker CYP3A4 inducer, on the pharmacokinetics of bortezomib (injected intravenously), there was no significant effect on the pharmacokinetics of bortezomib based on data from seven patients.

Strong CYP3A4 Inhibitor

Coadministration with ketoconazole (strong CYP3A4 inhibitor) increased bortezomib exposure by 35%.

Strong CYP3A4 Inducer

Coadministration with rifampin (strong CYP3A4 inducer) decreased bortezomib exposure by approximately 45%.

[...]