דצמבר 2022

רופא/ה נכבד/ה,
רוקח/ת נכבד/ה,

הנדון:
Vitrakvi 25mg, Vitrakvi 100mg,
ויטראקבי 25 מ"ג, ויטראקבי 100 מ"ג
Capsules
Larotrectinib (as sulfate) 25mg, 100mg

Vitrakvi 20 mg/ml oral solution
Solution
Larotrectinib (as sulfate) 20mg/ml

אנו מבקשים להודיעכם שהעלון לרופא של התכשירים שבנדון עודכן.

ההתוויה המאושרת לתכשיר:
Vitrakvi as monotherapy is indicated for the treatment of adult and paediatric patients with solid tumours that display a Neurotrophic Tyrosine Receptor Kinase (NTRK) gene fusion,
• Who have a disease that is locally advanced, metastatic or where surgical resection is likely to result in severe morbidity, and
• Who have no satisfactory treatment options

בהודעה זו כלולים העידכונים המהותיים בלבד, בפירוט שלהלן מופיע, רק המידע שהתעדכן. תוספת טקסט מודגש בצבע אדום ומסומן בקו תחתון.

המידע במלואו מופיע בעלון לרופא אשר נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות:
https://israeldrugs.health.gov.il/#!/byDrug
כמו כן, ניתן לקבלו מודפס ע"י פניה לחברת באייר ישראל, רח' החרש 36 הוד השרון, טלפון: 09-7626700

העדכונים בעלון לרופא:

4.8 Undesirable effects

Additional information on special populations

Paediatric patients

Of the 248 patients treated with VITRAKVI, 98 (40%) patients were from ~~28 days~~birth to ≤ 18 years of age~~. Of these 98 patients, 36~~ (n=9% from ~~were 28 days~~birth to < 3~~2 years~~ months~~(n=35)~~, n=46% ~~were~~ ≥ 3 months to < 6 months ~~2 years to < 12 years (~~n=415~~), and 18% were~~ ≥ 6 months to < 12 months, n=7 ≥ 12 months to < 2 years, n=22 ≥ 2 years to <6 years, n=23≥ 6 years to < 12 years, n=18 ≥ 12 years to < 18 years)~~12 years to < 18 years (n=18). The safety profile in the paediatric population (< 18 years) was consistent in types of reported adverse reactions to those observed in the adult population.~~ The majority of adverse reactions were Grade 1 or 2 in severity (see Table 3) and were resolved without VITRAKVI dose modification or discontinuation. Adverse reactions of Grade 3 or 4 in severity were generally observed more frequently in patients < 6 years of age. They were reported in 67% of patients from birth to < 3 months and in 44% of patients ≥ 3 months to < 6 years.~~The adverse reactions of vomiting (48% versus 16% in adults), leucocyte count decrease (17% versus 9% in adults), neutrophil count decrease (31% versus 6% in adults), and blood alkaline phosphatase increased (13% versus 5% in adults) were more frequent in paediatric patients compared to adults.~~ Decreased neutrophil count has been reported to have led to study drug discontinuation, dose modification and dose interruption.

5.2 Pharmacokinetic properties

Special populations

Paediatric patients

Based on population pharmacokinetic analyses exposure (C_{max} and AUC) in paediatric patients ~~(1 month to <3 months of age)~~ at the recommended dose of 100 mg/m^2 with a maximum of 100 mg BID was ~~3-fold~~ higher than in adults (≥18 years of age) given the dose of 100 mg BID~~. At the recommended dose, the C_{max}~~ (see Table 7)~~.in paediatric patients (≥3 months to <12 years of age) was higher than in adults, but the AUC was similar to that in adults. For paediatric patients older than 12 years of age, the recommended dose is likely to give similar C_{max} and AUC as observed in adults.~~ Data defining exposure in small children (1 month to <~~6~~2 years of age) at the recommended dose is limited (n=~~33~~40).

Table 7: Exposure (C_{max} and AUC on day 1[a]) in patients grouped by age group at the recommended dose of 100 mg/m^2 with a maximum of 100 mg BID

Age group	n=348[b]	Fold difference compared to patients ≥ 18 years of age[c]	
		C_{max}	AUC[a]
1 to < 3 months	9	4.2	4.5
3 to < 6 months	4	2.6	2.5
6 to < 12 months	18	2.5	1.9
1 to < 2 years	9	2.0	1.4
2 to < 6 years	31	2.0	1.4
6 to < 12 years	26	1.5	1.2
12 to < 18 years	27	1.2	1.0
≥ 18 years	224	1.0	1.0

[a] area under the plasma concentration-time curve for 24 hours on day 1

[b] number of patients from 26 November 2020 data cut-off

[c] fold difference is the ratio of stated age group to ≥18 years group. A fold-difference of 1 equates to no difference.

בברכה,

באייר ישראל