הודעה על החמרה (מידע בטיחות) בעלון לרופא

(מעודכן 05.2013)

אושר – 6.16

תאריך 20.06.2016

שם תכשיר באנגלית ומספר הרישום

SUTENT CAPSULES 12.5MG 136.89.31430.00
SUTENT CAPSULES 25MG 136.90.31431.00
SUTENT CAPSULES 50MG 136.91.31432.00

שם בעל הרישום: פייזר פרמצבטיקה בע"מ

טופס זה מיועד לפרוט ההחמרות בלבד !

ההחמרות המבוקשות		
טקסט חדש	**טקסט נוכחי**	**פרק בעלון**
Paediatric population A phase I dose-escalation study of oral sunitinib was conducted in 35 paediatric and young adult patients (aged 2-21) with refractory solid tumours, the majority of whom had a primary diagnosis of brain tumour. All study participants experienced adverse drug reactions and in those patients with previous exposure to anthracyclines or cardiac radiation most of these were severe (toxicity grade ≥3) and included cardiac toxicity. The risk of cardiac adverse drug reactions appears higher in paediatric patients with previous exposure to cardiac radiation and anthracycline, compared to those paediatric patients without previous exposure. No maximum tolerated dose of sunitinib has been identified for this patient population due to dose limiting toxicities (see section 5.1). In paediatric patients without previous exposure to anthracyclines or cardiac radiation, the most common adverse reactions were GI toxicity, neutropenia, fatigue and ALT elevation. Based on a population pharmacokinetics (PK) and pharmacokinetic	**N/A**	**4.8 Undesirable effects**

pharmacodynamic (PK/PD) analysis, sunitinib at doses of 25 mg/m^2/day on schedule 4/2 in paediatric patients (ages 6-11 and 12-17 years) with GIST is predicted to provide comparable plasma drug exposures, and subsequently safety and efficacy profiles, to those in adult patients with GIST treated at 50 mg/day on schedule 4/2.		
Experience on the use of sunitinib in paediatric patients is limited (see section 4.2 Paediatric population). A phase I dose-escalation study of oral sunitinib was conducted in paediatric and young adult patients (aged 2-21) with refractory solid tumours, the majority of whom were enrolled with a primary diagnosis of brain tumour. Dose-limiting cardiotoxicity was observed in the first part of the study which was therefore amended to exclude patients with previous exposure to potentially cardiotoxic therapies (including anthracyclines) or cardiac radiation. In the second part of the study including patients with prior anticancer therapy but without risk factors for cardiac toxicity, sunitinib was generally tolerable and clinically manageable at the dose of 15 mg/m^2/day on schedule 4/2. None of the subjects achieved complete response or partial response. Stable disease was observed in 6 patients (17%). One GIST patient was enrolled at the 15 mg/m^2 dose level with no evidence of benefit. The observed adverse drug reactions were overall similar to those seen in adults (see section 4.8). A population PK and PK/PD analysis was conducted with the scope to extrapolate the PK and key safety and efficacy endpoints of sunitinib in paediatric patients with GIST (age group 6-17 years). This analysis was based on data collected from adults with GIST or solid tumours, and from paediatric patients with solid tumours. Based on the modelling analyses, the younger age and lower body size did not appear to affect negatively the safety and efficacy responses to plasma drug exposure.	**N/A**	**Pharmacodynamic properties**

Sunitinib benefit/risk did not appear to be negatively affected by younger age or lower body size, and was mainly driven by plasma drug exposure. Based on the PK, safety, and efficacy trial simulation results, a starting dose of approximately 25 mg/m^2/day on schedule 4/2 in paediatric patients with GIST (ages 6-11 and 12-17 years) is predicted to provide comparable plasma drug exposures, and subsequently safety and efficacy to those in adult patients with GIST treated at 50 mg/day on schedule 4/2.		
Paediatric population: Experience on the use of sunitinib in paediatric patients is limited (see section 4.2 Paediatric population). Population PK analyses of a pooled dataset from adult patients with GIST and solid tumours and paediatric patients with solid tumours were completed. Stepwise covariate modelling analyses were performed to evaluate the effect of age and body size (total body weight or body surface area) as well as other covariates on important PK parameters for sunitinib and its active metabolite. Among age and body-size related covariates tested, age was a significant covariate on apparent clearance of sunitinib (the younger the age of the paediatric patient, the lower the apparent clearance). Similarly, body surface area was a significant covariate on the apparent clearance of the active metabolite (the lower the body surface area, the lower the apparent clearance). Based on the final PK model trial simulation results, taking into account all the covariates effects, a sunitinib dose of 25 mg/m^2/day in paediatric patients (ages 6-11 and 12-17 years) with GIST is predicted to achieve comparable plasma drug exposures to those in adult patients with GIST treated at 50 mg/day, on Schedule 4/2.	**N/A**	**Pharmacokinetic properties**

מצ"ב העלון, שבו מסומנות ההחמרות המבוקשות על רקע צהוב.
שינויים שאינם בגדר החמרות סומנו (בעלון) בצבע שונה. יש לסמן רק תוכן מהותי ולא שינויים במיקום הטקסט.

הועבר בדואר אלקטרוני בתאריך 20.06.2016