Pharmacokinetics of secnidazole in healthy volunteers after single oral dose

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Résumé en anglais	**Introduction:** Secnidazole is an anti infective agent which belongs to the 5-nitroimidazole class. **Method:** The objective of the trial was to characterize the pharmacokinetics of secnidazole after oral administration of a 2g dose, as microgranules formulation in healthy subjects. Blood samples were collected before, 1, 2, 3, 6, 9, 12, 24, 36, 48, 72, 96, 120, 168 and 240 h after dosing. Urines were collected in 24-h-fractions for the first five days and in 48 h-fraction for the last sample. The cumulative urinary excretion was captured for each subject from urine concentration (lg/L). Pharmacokinetic parameters were obtained by a non-compartmental approach (WinNonlin Pharsight). The assay was performed by ultra-performance liquid chromatography coupled with mass spectrometry detection (UPLC-MS/MS, Quattro Premier, Waters) after simple protein precipitation of 50 lL plasma sample. Chromatographic separation was done on a C18 Acquity column (50 mm · 2.1 mm, id 1.7 lm, Waters), in isocratic mode (80% water/0.1% formic acid and 20% acetonitrile). Ornidazole was used as internal standard. The detection was operated in positive mode and multiple reaction monitoring was used for quantification (186 > 128 ion transition for secnidazole). The lower limit of quantification was 10 and 100 lg/L for plasma and urine samples respectively. **Results:** Sixteen subjects (8 female, 8 male) were included. Population characteristics such as: age ranged from 23 to 50 years (mean ± SD: 38 ± 9.2 years), weight ranged from 51 to 90 Kg (mean ± SD = 64.6 ± 10.1 Kg) and body mass index (BMI) ranged from 19.9 to 24.2 Kg/m 2 (mean ± SD = 21.9 ± 1.5 Kg/m 2 ;). Secnidazole exposure achieved a maximal concentration (Cmax) with a mean of 37.9 ± 8.5 mg/L (range 20–56 mg/L) and at a median time associated with the Cmax (Tmax) of 6 h (range 3–6 h). The area under the curve to the last measurable time (AUC0_t) and the total area under the curve (AUC0_¥) were 1281.9 ± 416.4 mg h/L and 1304.2 ± 444.1 mg h/L (mean ± SD) respectively. The Cl/F and V/F were 1.7 ± 0.5 L/h and 40.2 ± 9.2 L respectively and the elimination half-life (t1/2) was 17.5 ± 4.3 h (mean ± SD). The mean amount of secnidazole excreted in the 168-h urine collection was 310.47 mg (15.5% of the administered dose). For example, for the subject number 5, the observed parameters are: Cmax 37.3 mg/L, Tmax 3 h, AUC0_¥ 1029.5 mg h/L and t1/2 15.6 h. **Conclusion:** After a 2 g single oral dose, secnidazole presents a good absorption profile and relatively long elimination half life ensuring probable sufficient exposure with once a day administration.
Notes	Résumé publié dans : *Fundamental & Clinical Pharmacology*, avril 2010, 24(Suppl. 1): p. 55-56. doi:10.1111/j.1472-8206.2010.00819.x [6]
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