

Ref	Highest single dose	Max. freq.	Max. number of doses	Maximum total dose (period)	Population	Sample by dose	AEs
Awadzi et al 1995 [1]	800 mcg/kg	Single	Single	800 mcg/kg (once)	Males with moderate to heavy Onchocerca infection	600 mcg/kg x 1: 24 patients 800 mcg/kg x 1: 17 patients	No difference with controls taking the 150 mcg/kg dose
Awadzi et al 1999 [2]	800 mcg/kg	Days 1 and 4	2	1.600 mcg/kg (4 days)	Adult males infected with Onchocerca	400-550 mcg/kg x 2: 25 patients 600-750 mcg/kg x 2: 23 patients 800-950 mcg/kg x 2: 24 patients 1600 mcg/kg x 2: 12 patients	No difference with controls taking the 150 mcg/kg dose
Guzzo et al 2002 [3]	2.000 mcg/kg	Days 1, 4 and 7	3	3.273 mcg/kg (one week)	68 male and female healthy, adult volunteers	347-594 mcg/kg x 3: 15 volunteers 713-1091 mcg/kg x 3: 12 volunteers 1031-1466 mcg/kg x 1: 12 volunteers 1404-2000 mcg/kg x 1: 12 volunteers 347-541 mcg/kg x 1 (fed): 11 volunteers	No difference with controls
Kamgno et al 2002 [4]	800 mcg/kg	3-monthly	13	8.950 mcg/kg (3 years)	657 adult males infected with Onchocerca	150 mcg/kg yearly: 166 participants 400 then 800 mcg/kg yearly: 161 participants 150 mcg/kg 3-monthly: 161 participants 400 then 800 mcg/kg 3-monthly: 158 participants	The high dose group reported a statistically higher rate of transitory mild and subjective visual side effects. (No structural explanation). For all other AE comparable rates reported in all groups.
Munoz et al 2018 [5]	705 mcg/kg (single 36 mg dose)	Single	Single	705 mcg/kg (once)	54 male and female healthy adult volunteers	276-352 mcg/kg x 1: 18 volunteers 227-272 mcg/kg x 1: 19 volunteers 157-225 mcg/kg x 1: 20 volunteers 553-705 mcg/kg x 1: 18 volunteers 455-545 mcg/kg x 1: 19 volunteers 315-450 mcg/kg x 1: 20 volunteers	No significant difference compared to weight-adjusted dose of 200 mcg/kg
Smit et al 2018 [6]	600 mcg/kg	Days 1, 2 and 3	3	1.800 mcg/kg (3 days)	141 male and female adults with uncomplicated malaria	300 mcg/kg x 3: 48 participants 600 mcg/kg x 3: 47 participants	No difference in SAE. Ivermectin 600 x 3 had 15% more AEs predominantly reflecting transient minor visual disturbances. One case of anaphylaxis was reported in the trial

Table. Ivermectin studies assessing the safety of doses above 400 mcg/kg

14. REFERENCES

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3. Guzzo CA, Furtek CI, Porras AG, Chen C, Tipping R, Clineschmidt CM et al: Safety, tolerability, and pharmacokinetics of escalating high doses of ivermectin in healthy adult subjects. *J Clin Pharmacol* 2002, 42:1122-33.
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