

**14 Day Oral (Gavage Administration) Toxicity Study in the Female Rat
using Five Test Articles; M546152, M529556, M528099, M544201 and
M550822. Covance Study Number 88/350.
Sponsor Reference Number TDR/3194.**

AstraZeneca UK Limited
Alderley Park
Macclesfield
Cheshire
SK10 4TG

Study Director R P Jones MIBiol CBiol
Test facility Covance, Otley Road, Harrogate, North Yorkshire, HG3 1PY, ENGLAND

Study dates

Protocol approved : 30 November 2000
First dose : 6 December 2000
Last necropsy : 20 December 2000
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5 CONCLUSION

Oral administration of M546152, M529556, M528099, M544201 and M550822 for 14 days to the female rat at 100 mg/kg/day was generally well tolerated, the only observed effect being a reduction in bodyweight gain in animals receiving M529556, M528099 and M550822.

Similarly, administration of M528099, M544201 and M550822 at 500 mg/kg/day (reduced from Day 7 to 400, 250 & 250 mg/kg/day respectively) was reasonably well tolerated, resulting only in reduced bodyweight gain and a slight increase in liver weight.

However, three animals were found dead following administration of 500 mg/kg/day M529556 and both M546152 and M529556 at dose levels of 500 mg/kg/day resulted in a reduction in food consumption, accompanied by bodyweight loss, substantial enough to warrant the early termination of these groups and a significant increase in liver weight.