

TOXICITY PROFILE OF PARENTERAL ARTESUNATE FOLLOWING SUBACUTE TREATMENT IN RATS AND DOGS

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January 30, 2024

Abstract

OBJECTIVES The objectives of these studies were to investigate the toxicity, safety and toxicokinetics of single and multiple doses of artesunate for injection in rats and dogs. **METHODS** Sprague-Dawley rats and Beagle dogs were treated intravenously or intramuscularly for 28 consecutive days with doses of up to 30 mg/kg artesunate, evaluating toxicity, kinetics, genotoxicity, and cardiovascular and central nervous safety parameters after single and 4-week repeated administrations. Furthermore, respiratory parameters were evaluated after a single intravenous administration in rats. **RESULTS** Artesunate was well tolerated with no mortality and only minor effects on clinical pathology parameters. Following repeated intramuscular administration, local reactions at the injection site became evident. Signs of regenerative anaemia were evident in both rats and dogs and are attributed to the pharmacological effect of artesunate (effective against blood stages of malaria parasites). No severe toxicity or any effects on safety measures were noticed. **CONCLUSIONS** The results obtained in these studies support the safe use of intravenous and intramuscular artesunate for a period beyond the commonly used three (to maximum seven) days in humans. Cardiovascular, central nervous and respiratory safety measures indicate no risk at clinically used doses.

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