



Pharmacokinetic and Pharmacodynamic Variability of Fluindione in Octogenarians

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Résumé en anglais In the PREPA observational study, we investigated the factors influencing pharmacokinetic and pharmacodynamic variability in the responses to fluindione, an oral anticoagulant drug, in a general population of octogenarian inpatients. Measurements of fluindione concentrations and international normalized ratio (INR) were obtained for 131 inpatients in whom fluindione treatment was initiated. Treatment was adjusted according to routine clinical practice. The data were analyzed using nonlinear mixed-effects modeling, and the parameters were estimated using MONOLIX 3.2. The pharmacokinetics (PK) of fluindione was monocompartmental, whereas the evolution of INR was modeled in accordance with a turnover model (inhibition of vitamin K recycling). Interindividual variability (IIV) was very large. Clearance decreased with age and with prior administration of cordarone. Patients who had undergone surgery before the study had lower IC50 values, leading to an increased sensitivity to fluindione. Pharmacokinetic exposure is substantially increased in elderly patients, warranting a lower dose of fluindione.

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