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Tolerance and kinetic behaviour after single and repeated vaginal administration of sertaconazole cream and tablets in healthy volunteers

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Sertaconazole is a new imidazole derivative which has demonstrated to have a wide "in vitro" activity, particularly in front of dermatophytes and C. albicans. Experimental studies inducing vaginal candidiasis in mice have shown that sertaconazole 2% cream is more active than miconazole 2% cream. The aim of our study was to evaluate vaginal and systemic tolerance of sertaconazole administered in two formulations (cream 2% and vaginal tablets 500 mg). The cream was applied in a single dose followed by a multiple administration twice daily during seven days. Vaginal tablets were given in a single dose. All studies were performed in a double-blind, cross-over, randomized and placebo-controlled design. Twelve subjects were involved in the study during 3 consecutive menstrual cycles leaving appropriate wash-out periods between treatments. The variables assessed at various times were: Subjective evaluations of vaginal discomfort by means of ten visual analogue scales (VAS-100 mm) and a questionnaire with eighteen suggested side effects, a pharmacological safety including blood pressure, heart rate, ECG, body temperature, biochemical and heamatological analysis and systematic ginecological examinations including vaginal mucous and flux evaluation, pH, Papanicolau and colposcopy. Additionally, blood, vaginal flux and urine samples were collected to determine drug levels by means of an HPLC method with UV detection.

The clinical parameters measured showed no differences between cream or tablets and placebo. Overall results indicate that sertaconazole in both formulations displays a good local and systemic tolerance. Sertaconazole in plasma was not detected. Erratic levels were found in urine probably due to contamination. Sertaconazole levels in high concentrations persisted in vaginal flux for over 72 h, supporting the potential clinical usefulness of this new drug in antifungal therapy.

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Non-haemopoietic reactions to dipyrone containing compounds

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Drugs containing Dipyrone are banned in some countries but are widely used as analgesics, antipyretics and anti spasmodics in others. Much publicity is given to the bone marrow suppressant effects of these drugs but the average practitioner does not readily recognise it and hence is not reported. Many of the non-haemopoietic reactions of Dipyrone containing compounds are dramatic and severe enough to cause death and are easily picked up by the practitioners.

This study is based on the reports to the ADR monitoring centre from general practitioners. Analysis of a year's drug reaction reports under this voluntary reporting scheme showed that Dipyrone containing drugs were the single most commonly used agent producing ADR of a moderately severe to severe nature.

7.5% (n = 35) of all the reports were related to this. Of these, 23 were moderately severe and severe reactions. The causal relationship between the administration of the drug and the development of ADR shows that in 74% of cases Dipyrone was the only drug in use. The reactions occurred within a few minutes to 24 hours of drug use. 53% of reactions followed oral administration and 90% after parenteral use. The incidence of reactions was more following parenteral use and more than half of these were severe. The reactions reported were angioneurotic edema, severe