

- Nevertheless, the steady-state is reached by the third administration and the mean elimination half-life is then around 7 to 8 hours.
- Taking diacerein with a standard meal delays systemic absorption, but is associated with a 25% increase in the amount absorbed.
- Mild-to-severe (Child Pugh's grade B to C) liver cirrhosis does not change the kinetics of diacerein, whereas mild-to-severe renal insufficiency (creatinine clearance < 2.4 L/h) is followed by accumulation of rhein which justifies a 50% reduction of the standard daily dosage.
- Rhein is highly bound to plasma proteins (about 99%), but this binding is not saturable so that no drug interactions are likely to occur, in contrast to those widely reported with nonsteroidal anti-inflammatory drugs.
- Except for moderate and transient digestive disturbances (soft stools, diarrhoea), diacerein is well tolerated and seems neither responsible for gastrointestinal bleeding nor for renal, liver nor haematological toxicity.

In the light of literature data, it is well accepted that molecules which essentially rely on conjugation processes mediated by glucuronic acid do not exhibit modified pharmacokinetics in patients with cirrhotic-type hepatic failure (Shull et al., 1976; Kraus et al., 1978).

The active metabolite of diacerein, rhein, reaches the targeted tissues and does not accumulate within the organism, even after repeated use therapeutic doses.