DX-9065a, a Direct Inhibitor of Factor Xa

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ABSTRACT

The synthetic compound DX-9065a represents a low molecular weight, direct, competitive inhibitor of factor Xa (FXa) with a high affinity and selectivity for the enzyme. Under experimental conditions DX-9065a exerts strong anticoagulant actions in vitro and in vivo and is antithrombotically effective in various thrombosis models. It inhibits proliferation of vascular smooth muscle cells in cell culture systems as well as in in vivo models. As a small molecule inhibitor, DX-9065a inactivates both free and fibrin-bound FXa. By this mechanism it effectively affects the clot-associated procoagulant activity which might be responsible for the propagation of intravascular thrombi as well as for recurrent thrombosis and thrombotic reocclusion after lysis. Although DX-9065a is effective after oral administration, its oral bioavailability is relatively low and seems not to be sufficient for a long-term therapeutic use of the drug. However, first clinical trials in healthy volunteers and in patients with cardiovascular diseases demonstrated a predictable pharmacokinetic and pharmacodynamic behavior of DX-9065a after either intravenous bolus injection or constant infusion, as well as its high safety, especially a lower bleeding risk compared with other commonly used drugs. Further experimental studies and ongoing clinical trials will evaluate the inhibitory profile of the drug, its effectiveness and its possible superiority over other drug regimens in various cardiovascular indications.