

## Fondaparinux, a Synthetic Pentasaccharide: The First in a New Class of Antithrombotic Agents — The Selective Factor Xa Inhibitors

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### ABSTRACT

Despite currently available antithrombotic therapies, venous thromboembolism (VTE) remains a major cause of morbidity and mortality. Fondaparinux sodium (pentasaccharide), the first in a new class of antithrombotic agents developed for the prevention and treatment of VTE, inhibits thrombin generation by selectively inhibiting factor Xa. Fondaparinux exhibits complete bioavailability by the subcutaneous route and is rapidly absorbed, reaching its maximum concentration approximately 2 h post dosing. It has a terminal half-life of 13 to 21 h, permitting once-daily dosing. Fondaparinux's reproducible linear pharmacokinetic profile exhibits minimal intrasubject and intersubject variability, suggesting that individual dose adjustments will not be required for the vast majority of the population and that there will be no need for routine hemostatic monitoring. At therapeutic concentrations (<2 mg/L), fondaparinux exhibits >94% binding to its target protein, antithrombin. Within this same concentration range there is no specific binding by fondaparinux to plasma proteins commonly involved in drug binding, indicating a low potential for drug-drug interactions by protein displacement. Unlike antithrombotic agents prepared from animal extracts (heparins), fondaparinux is chemically synthesized; this leads to batch-to-batch consistency and the absence of potential risk of contamination problems. In recently completed phase III clinical trials in VTE prevention in major orthopedic surgery, fondaparinux showed significant superiority over the low-molecular-weight heparin enoxaparin, providing an overall >50% ( $P < 0.001$ ) reduction in VTE risk without increasing clinically important bleeding. Additional clinical data support its potential benefits in other venous and arterial thrombotic disorders. In view of these collective findings, fondaparinux is expected to play a major role in the prevention and treatment of venous and arterial thrombotic disease.