

Chemical Formula

Not Available

Drugs

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IUPAC Name

Not Available

Not Available

SMILES

InChl

Not Available

PHARMACOLOGY

Indication

Indicated for the prophylaxis of post-operative deep venous thrombosis (DVT), which may lead to pulmonary embolism (PE), in patients undergoing elective hip replacement surgery [Label].

Associated Conditions

Deep Vein Thrombosis caused by Major Abdominal Surgery

Deep Vein Thrombosis caused by Orthopedic Surgery

Deep Vein Thrombosis caused by Thoracic Surgery

Cardiac surgery, heparin-induced thrombocytopenia and thrombosis syndrome

Non-hemorrhagic stroke

Pharmacodynamics

Danaparoid contains a mixture of heparan sulfate, dermatan sulfate and chondroitin sulfate in amounts of approximately 84%, 12% and 4%, respectively [3]. Danaparoid is as an antithrombotic agent that prevents the formation of fibrin in the coagulation pathway. It has a high antifactor Xa to antifactor IIa (thrombin) activity that primarily works via antithrombin III-mediated inhibition of factor Xa [3]. The ratio of antifactor Xa to antifactor II activity is $\geq 20:1$ [3]. Danaparoid has a minor effect on platelet function and aggregation [Label]. In a worldwide compassionate-use programme involving a total of 667 patients with heparin-induced thrombocytopenia (HIT), treatment with danaparoid resulted in 93% of successful outcomes in resolving HIT [3].

In healthy volunteers, danaparoid caused significantly less prolongation of the activated partial thromboplastin time (APTT) and was associated with a significantly lower thrombin time than unfractionated heparin (UFH) and low molecular weight heparins (LMWHs) [3]. Danaparoid displays lower lipolytic activity than UFH *in vitro* and in healthy individuals, leading to lower plasma levels of free fatty acids [3]. Danaparoid has been associated with the cross-reactivity with pathogenic heparin-induced platelet-factor 4 (PF4) antibodies, which occurs in about 10 % or more by *in vitro* testing ^[1]. The clinical relevance of this effect is not fully understood ^[1].

Mechanism of action

In the coagulation cascade leading to clot formation, factor X and factor II requires activation to promote subsequent conversion of fibrinogen to fibrin. The mechanism of action of danaparoid resulting in anticoagulant and antithrombic effects involves a complex interaction between 2 components, factor IIa and in particular, factor Xa [3]. Via binding to antithrombin and inducing a conformational change [A32579], danaparoid enhances and catalyzes the the binding of factor Xa to antithrombin, which induces antithrombin-mediated inactivation of factor Xa. This leads to inhibition of thrombin generation and subsequently, thrombus formation [2]. Danaparoid also weakly enhances antithrombin III and heparin cofactor II inactivation of factor IIa [2]. There is evidence that danaparoid also suppresses the activation of factor IX which, in conjunction with simultaneous inhibition of factor X, may lead to antithrombic effects [3].

TARGET	ACTIONS	ORGANISM
Antithrombin-III	positive allosteric modulator	Humans

Absorption

Pharmacokinetic studies on danaparoid are based on the kinetics of its anticoagulant activities, which are mostly antifactor Xa and antifactor IIa activities. The bioavailability of danaparoid is 100% following subcutaneous administration [Label]. Following administration of single subcutaneous doses of 750, 1500, 2250, and 3250 anti-Xa units of danaparoid, the peak plasma anti-Xa activities were 102.4, 206.1, 283.9, and 403.4 mU/mL, respectively [Label]. The time to reach maximum anti-Xa activity is approximately 2-5 hours [Label].

Danaparaid DrugBank

Volume of distribution Pharmacokinetic studies on danaparoid are based on the kinetics of its anticoagulant activities, which are mostly anti factor Xa and anti factor IIa activities. The volumes of distribution of anti-Xa

Drugs

Protein binding

Not Available

Metabolism

There is no evidence of hepatic metabolism and danaparoid is unlikely to undergo cellular metabolism [3].

Route of elimination

Renal excretion is the main route of elimination, accounting for approximately 40-50% of the total clearance of antifactor Xa activity following intravenous administration of danaparoid [3]. Therefore in patients with severe renal impairment, the elimination half-life of anti-Xa activity may be prolonged [Label].

Half life

Pharmacokinetic studies on danaparoid are based on the kinetics of its anticoagulant activities, which are mostly anti factor Xa and anti factor IIa activities. The elimination half-life ranges from 19.2 to 24.5 hours during anti-Xa activity and ranges from 1.8 to 4.3 hours during anti-Ila activity <u>3</u>]

Clearance

Pharmacokinetic studies on danaparoid are based on the kinetics of its anticoagulant activities, which are mostly anti factor Xa and anti factor IIa activities. Total plasma clearance is about 0.36 L/h during anti-Xa activity, which may be accelerated with higher body surface area [Label]. Total plasma clearance during anti-IIa activity ranges from 2.3 to 3 L 3.

Toxicity

Subcutaneous administration of a single dose at 3800 anti-Xa units/kg, which is 20.5 times the recommended dose for humans based on body surface area, was found to be lethal to female rats. Lethal effects were seen in male rats when administering a single subcutaneous dose at 15200 anti-Xa units/kg, which is approximately 82 times the recommended human dose based on body surface area [Label]. In rats, the symptoms of acute toxicity following intravenous administration included respiratory depression, prostration and twitching [Label].

Accidental overdosage of danaparoid may lead to severe bleeding complications. While protamine sulfate may partially neutralize the anti-Xa actions of danaparoid, there is no evidence that it is capable of reducing severe non-surgical bleeding during treatment of danaparoid. In case of serious bleeding, danaparoid should be discontinued and blood transfusions should be administered if necessary. Withdrawal of danaparoid is expected to restore the coaquiation balance without rebound phenomenon [Label].

There is no evidence of danaparoid to have a potential to induce carcinogenesis, mutagenesis and impairment of fertility [Label].

Affected organisms Not Available

Pathways

Not Available

Pharmacogenomic Effects/ADRs ①

Not Available

Drug Interactions

ALL DRUGS NUTRACEUTICAL <u>ILLICIT</u> WITHDRAWN **APPROVED VET APPROVED**

combination with (1,2,6,7-3H)Testosterone.

INVESTIGATIONAL **EXPERIMENTAL**

entries

10 DRUG

Show

↑ INTERACTION

The therapeutic efficacy of Danaparoid can be increased when used in

Search

(1,2,6,7-3H)Testosterone

https://www.aragoanmoararago/DD00701

3/6

DRUG	↑ INTERACTION	₩
(R)-warfarin	The risk or severity of bleeding can be increased when Danap	aroid is
	(Drugs)	

combined with (S)-Warfarin.

1-(3-Mercapto-2-Methyl-Propionyl)Pyrrolidine-2-Carboxylic Acid

1-Testosterone

combined with (S)-Warfarin.

The risk or severity of hyperkalemia can be increased when 1-(3-Mercapto-2-Methyl-Propionyl)-Pyrrolidine-2-Carboxylic Acid is combined with Danaparoid.

1-Testosterone

The therapeutic efficacy of Danaparoid can be increased when used in combination with 1-Testosterone.

combination with 1-Testosterone.

18-methyl-19-nortestosterone

The therapeutic efficacy of Danaparoid can be increased when used in combination with 18-methyl-19-nortestosterone.

3,5-diiodothyropropionic acid

3,5-diiodothyropropionic acid may increase the anticoagulant activities of Danaparoid.

4-hydroxycoumarin

The risk or severity of bleeding can be increased when Danaparoid is combined with 4-hydroxycoumarin.

4-Hydroxytestosterone

The therapeutic efficacy of Danaparoid can be increased when used in

<u>4-Hydroxytestosterone</u>
The therapeutic efficacy of Danaparoid can be increased when used in combination with 4-Hydroxytestosterone.

<u>5beta-dihydrotestosterone</u>
The therapeutic efficacy of Danaparoid can be increased when used in

<u>Sbeta-dihydrotestosterone</u>
The therapeutic efficacy of Danaparoid can be increased when used in combination with 5beta-dihydrotestosterone.

Showing 1 to 10 of 866 entries

Search

Food Interactions

Not Available

REFERENCES

General References

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- 2. Ibbotson T, Perry CM: Danaparoid: a review of its use in thromboembolic and coagulation disorders. Drugs. 2002;62(15):2283-314. [PubMed:12381232]
- 3. Wilde MI, Markham A: Danaparoid. A review of its pharmacology and clinical use in the management of heparininduced thrombocytopenia. Drugs. 1997 Dec;54(6):903-24. [PubMed:9421696]
- 4. 24. (2012). In Rang and Dale's Pharmacology (7th ed., pp. 299-300). Edinburgh: Elsevier/Churchill Livingstone. [ISBN:978-0-7020-3471-8]

External Links PubChem Substance 347910366

Wikipedia <u>Danaparoid</u>

ATC Codes

B01AB09 — Danaparoid

- B01AB Heparin group
- B01A ANTITHROMBOTIC AGENTS
- B01 ANTITHROMBOTIC AGENTS

entries

• B — BLOOD AND BLOOD FORMING ORGANS

AHFS Codes

20:12.04.16 — Heparins

FDA label

<u>Download</u> (566 KB)

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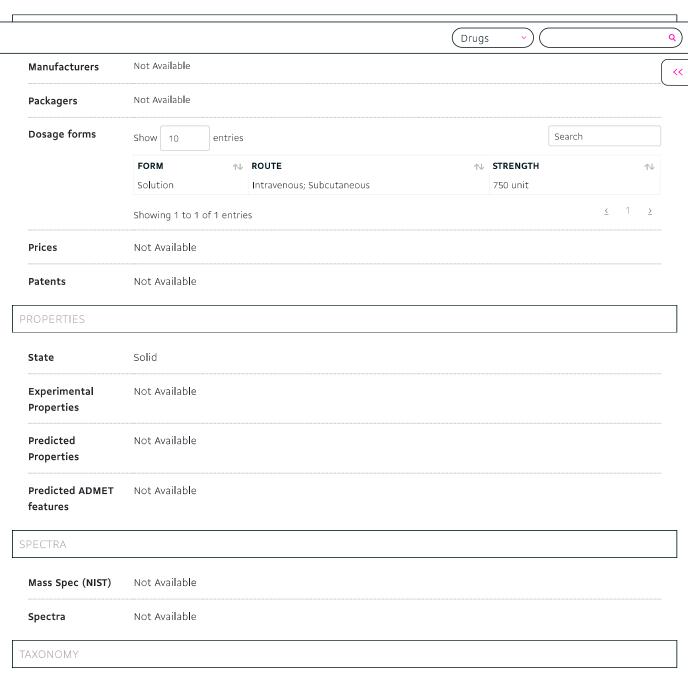
CLINICAL TRIALS

Clinical Trials ①

PHASE ↑↓	STATUS ↑↓	PURPOSE \wedge	$ \text{conditions} \qquad \qquad \uparrow \lor$	COUNT 1	₩
3	Not Yet Recruiting	Treatment	<u>Cardiac surgery, heparin-induced thrombocytopenia</u> and thrombosis <u>syndrome</u>	1	
Not Available	Completed	Not Available	Acute HIT II (Heparin-induced Thrombocytopenia Type II).	1	

Danasaraid DevaBask

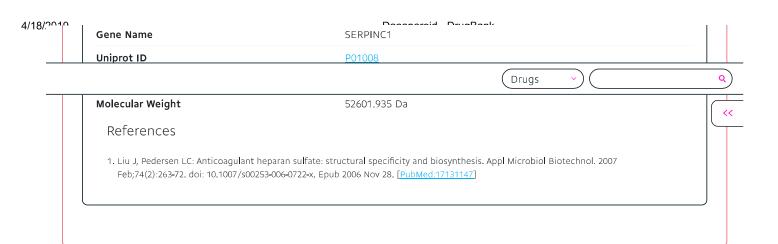
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Classification Not classified

TARGETS

1. Antithrombin-III	Details
Kind	Protein
Organism	Humans
Pharmacological action	Yes
Actions General Function	Positive allosteric modulator Serine-type endopeptidase inhibitor activity
Specific Function	Most important serine protease inhibitor in plasma that regulates the blood coagulation cascade. AT-III inhibits thrombin, matriptase-3/TMPRSS7, as well as factors IXa, Xa and XIa. Its inhibitory a



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