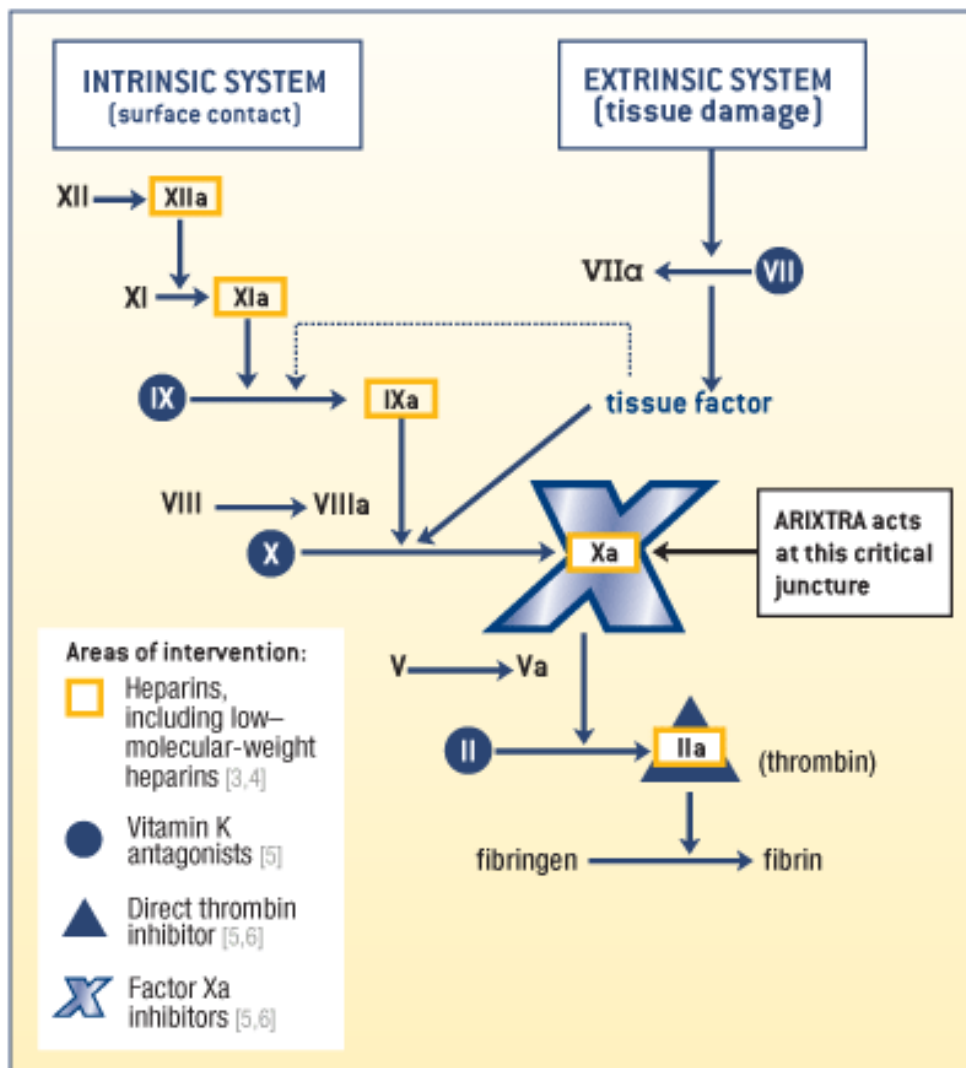


Factor/Component	Also called	Target
I	Fibrinogen	
II	Prothrombin	Heparin (IIa), Warfarin
IIa	Thrombin	Common Pathway
III	Tissue Thromboplastic	
IV	Calcium	
V	Proaccelerin	
VII	Proconvertin	Heparin (VIIa), Warfarin
VIII	Antihemophilic globulin (AHG)	
IX	Christmas Factor, plasma thromboplastin component (PTC)	Heparin (IXa), Warfarin
X	Smart-Prower	Heparin (IXa), Warfarin
XI	Plasma thromboplastic antecedent (PTA)	
XII	Hageman factor	
XIII	Fibrin-stabilizing factor	
Protein C & S		Warfarin (synthesis)
Plasminogen		Thrombolytic enzymes, aminocaproic acid





## Factor X a Inhibitors

### Indirect

#### Subcutaneous

- Fondaparinux, SQ, approved in 2001
- Idraparinux, once weekly SQ (Sanofi-Aventis) Phase III
- Idrabiotaparinux Sodium, SQ, REVERSIBLE (Sanofi-Aventis) Phase III

### Direct

#### Parenteral:

- Otimixaban (direct selective inhibitor) for ACS (Sanofi-Aventis)

#### Oral: (as presented in order of slides)

- Rivaroxaban [Xarelto®] Bayer w/ J & J
- Apixaban [?] (BMS, Pfizer)
- YM-150 (Astellas)
- Edoxaban [DU-176B] (Daiichi Sankyo)
- LY517717 (Lilly)
- Betrixaban PRT-054021 (Portola)
- Eribaxaban (PD0348292) (Pfizer)
- TAK-442 (Takeda)
- DX-9065a, (Daiichi)

#### Not presented but in literature

- SAR 377142 (Sanofi-Aventis) Preclinical Stages
- KFA-1982 (Kissei Pharmaceutical Co.)
- JTV-803 (Akros) Terminated 3Q2005
- DPC-602 (BMS)
- DPC423 (BMS)
- Razaxaban (BMS) Withdrawn P3
- GW813893 (GSK) Terminated p P1

## Oral Direct Thrombin Inhibitors (DTIs)

- Dabigatran [Pradax™] Reversible
- AZD0837 (AstraZeneca) 2012?
- MCC-977 (Mitsubishi Pharma)
- SSR-182289A (Sanofi) Phase 1 General Thrombosis
- Ximelagatran [Exanta] (D/Cd 2006)
- YM222714 (Astellas) Metabolite of YM150 being studied

## VKOR inhibitor

Tecarfarin ATI-5923

- Selective inhibitor of the vitamin K epoxide reductase enzyme, or a VKOR inhibitor
- ARYx Therapeutics
- Completed Phase 2/3 trial, EmbraceAC (CLN-505)

## ULMWH

AVE5026

is a new hemisynthetic ultra-low-molecular-weight heparin (ULMWH)

Sanofi-Aventis

TREK study: VTE prophylaxis with TKR.

[J Thromb Haemost.](#) 2009 Apr;7(4):566-72. Epub 2009 Jan 24.

SAVE-ONCO: VTE prevention in cancer patients. Phase III. Ends Dec 2010

Dose of between 20 and 40 mg **SQ**

\* The most studied and w most advanced phases w FDA  
Presented In Alphabetical Order by drug name (not class categorized)

### **ARC183**

Class: **Oral Direct Factor Xa inhibitor / Aptamer**  
Current Names:  
US Trade Names:  
Company: Archemix-Nuvelo  
Studies:  
Indications (Prop.)  
Doseage:

### **AZD0837**

Class: **Oral Direct Thrombin Inhibitor (DTI)**  
Current Names: None  
US Trade Names: None  
Company: AstraZeneca  
Studies: *Eur Heart J (2009) doi: 10.1093/eurheartj/ehp318*. First published online: August 18, 2009  
Indications (Prop.) SPAF  
Doseage: 150, 300, or 450 mg once-daily, or 200 mg twice-daily

### **APIXABAN \***

Class: **Oral Direct Factor Xa inhibitor**  
Current Names: None  
US Trade Names: None  
Company: BMS, Pfizer  
Studies: ADVANCE 1, 2, EXPANSE, ADOPT, APPRAISE-2, ARISTOTLE AVERROES  
Indications (Prop.) VTE prophylaxis post TKR and Acute Medical Illness, preventing CV death, non-fatal MI, or ischemic stroke in pts with recent ACS, SPAF (stroke prevention in patients with atrial fibrillation)  
Doseage: 2.5 mg BID or 10 mg QD

### **Bertrixaban**

Class: **Oral Direct Factor Xa inhibitor**  
Current Names: PRT-054021, (MLN-1021)  
US Trade Names:  
Company: Portola (licensed from Millennium Pharmaceuticals) and Merk  
Studies: EXPERT, EXPLORE-Xa  
Indications (Prop.) Any VTE, SPAF  
Doseage: 15 mg or 40 mg BID and 40 mg, 60 mg, and 80 mg QD

\* The most studied and w most advanced phases w FDA  
Presented In Alphabetical Order by drug name (not class categorized)

### **DABIGATRAN ETEXILATE \***

Class: **Oral Direct Thrombin Inhibitor (DTI)**  
Current Names: Pradaxa ® (Europe) or Pradax ® (Canada)  
US Trade Names: Rendix® and Pradaxa® (planned)  
Company: Boehringer Ingelheim  
Studies: RE-LY, BISTRO I and II, RE-MODEL, RE-MOBILIZE, RE-NOVATE, REVOLUTION (RE-MEDY, RE-COVER, RE-SONATE, RE-DEEM)  
Indications (Prop.) Total Knee and Hip Replacement  
Doseage: 150 mg or 220 mg

### **DX-9065a**

Class: **Oral Direct Factor Xa inhibitor**  
Current Names:  
US Trade Names:  
Company: Daiichi  
Studies:  
Indications (Prop.) ACS (IV) and Oral tested. Not active.  
Doseage: Not available

### **Endoxaban**

Class: **Oral Direct Factor Xa inhibitor**  
Current Names: DU-176B  
US Trade Names:  
Company: Daiichi Sankyo  
Studies: STARTS II, EXPLORE-Xa, ENGAGE-AFTIMI-48  
Indications (Prop.) VTE prevention, SPAF, and prevention of thromboembolic events in patients with acute coronary syndrome (ACS) are planned or have been initiated.  
Doseage: 15, 30, 60, 90 mg

### **Eribaxaban**

Class: **Oral Direct Factor Xa inhibitor**  
Current Names: PD0348292  
US Trade Names:  
Company: Pfizer  
Studies:  
Indications (Prop.) TKA,  
Doseage:

\* The most studied and w most advanced phases w FDA  
Presented In Alphabetical Order by drug name (not class categorized)

**LY517717**

Class: **Oral Direct Factor Xa inhibitor**  
Current Names:  
US Trade Names:  
Company: Lilly  
Studies:  
Indications (Prop.) Total Knee and Hip Replacement  
Doseage: 50, 75, 100, 125, 150 mg QD

**MCC-977**

Class: **Oral Direct Thrombin Inhibitor (DTI)**  
Current Names;  
US Trade Names:  
Company: Mitsubishi Pharma  
Studies: Phase II, In house  
Indications (Prop.) DVT  
Doseage:

**RIVAROXABAN** \* (Sentinel in this category)

Class: **Oral Direct Factor Xa inhibitor**  
Current Names: Xarelto  
US Trade Names: None  
Company: Developed by Bayer HealthCare AG and Johnson & Johnson Pharmaceutical Research & Development. In the US, to be commercialized by Scios Inc. and Ortho-McNeil, Inc., both of which are wholly-owned subsidiaries of Johnson & Johnson  
Studies: OdiXa-Knee, OdiXa-Hip, RECORD 1, 2, 3, 4, ROCKET-AF, EINSTEIN-DVT, PE, EXT, ATLAS, MAGELLAN  
Indications (Prop.) VTE Prophylaxis and SPAF, ACS  
Doseage: 10 mg daily

**TAK-442**

Class: **Oral Direct Factor Xa inhibitor**  
Current Names:  
US Trade Names:  
Company: Takeda  
Studies: AXIOM-ACS  
Indications (Prop.) Acute Coronary Syndromes, TKA  
Doseage: 60 mg BID, 40 to 160 Total Daily (QD or BID)

\* The most studied and w most advanced phases w FDA  
Presented In Alphabetical Order by drug name (not class categorized)

**Tecarfarin**

Class: Selective inhibitor of the vitamin K epoxide reductase enzyme,  
**VKOR inhibitor**  
Current Names: ATI-5923  
US Trade Names:  
Company: ARYx Therapeutics  
Studies: Completed Phase 2/3 trial, EmbraceAC (CLN-505)  
Indications (Prop.)  
Doseage:

**YM 150**

Class: **Oral Direct Factor Xa inhibitor**  
Current Names:  
US Trade Names:  
Company: Astellas  
Studies: ONYX 1, 2, PEARL 1, 2  
Indications (Prop.) Total Knee and Hip Replacement, AF, major abdominal surgery  
Doseage: 30, 60, 120 mg daily dose in QD and BID dosing

**ttt**

Class:  
Current Names:  
US Trade Names:  
Company:  
Studies:  
Indications (Prop.)  
Doseage:

**ttt**

Class:  
Current Names:  
US Trade Names:  
Company:  
Studies:  
Indications (Prop.)  
Doseage:

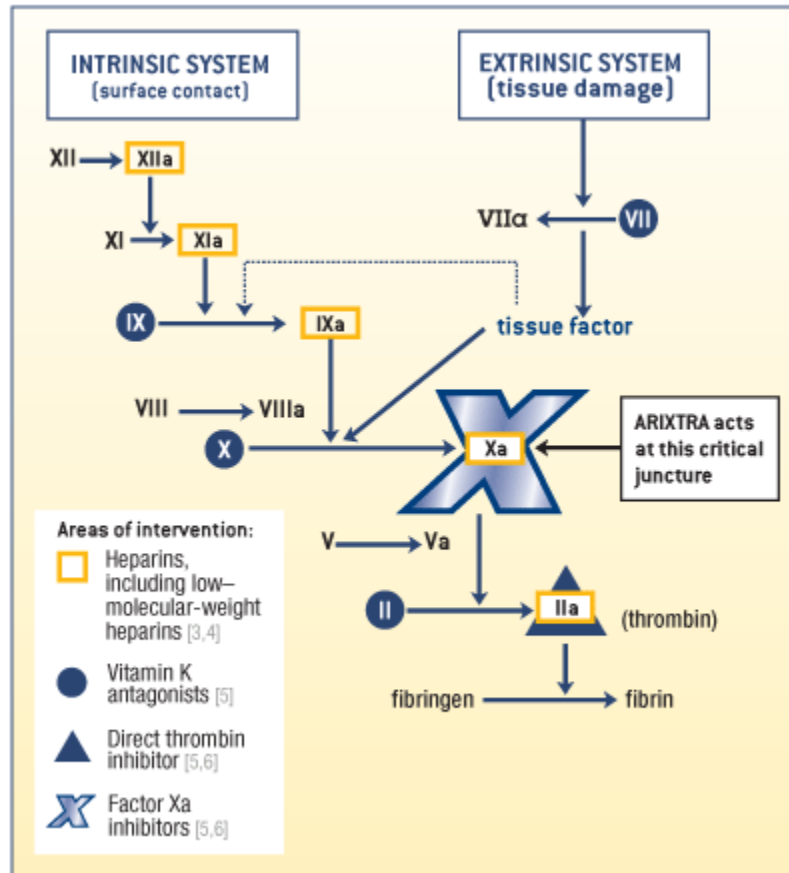
**ttt**

Class:

Current Names:  
US Trade Names:  
Company:  
Studies:  
Indications (Prop.)  
Doseage:

Exanta (ximelagatran)  
France, 2003 Approved  
Withdrawn 2006  
Oral DTI  
AstraZeneca  
EXTEND  
severe liver injury in a patient  
occurred after a long-term (35-day) study, once the patient had stopped treatment.

Lilly Amgen PMD-3112  
Oral  
Factor Xa inhibitor  
D/C 2008



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IIa	Thrombin	Common Pathway
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X	Smart-Prower	Heparin (IXa), Warfarin
XI	Plasma thromboplastic antecedent (PTA)	
XII	Hageman factor	
XIII	Fibrin-stabilizing factor	
Protein C & S		Warfarin (synthesis)
Plasminogen		Thrombolytic enzymes, aminocaproic acid