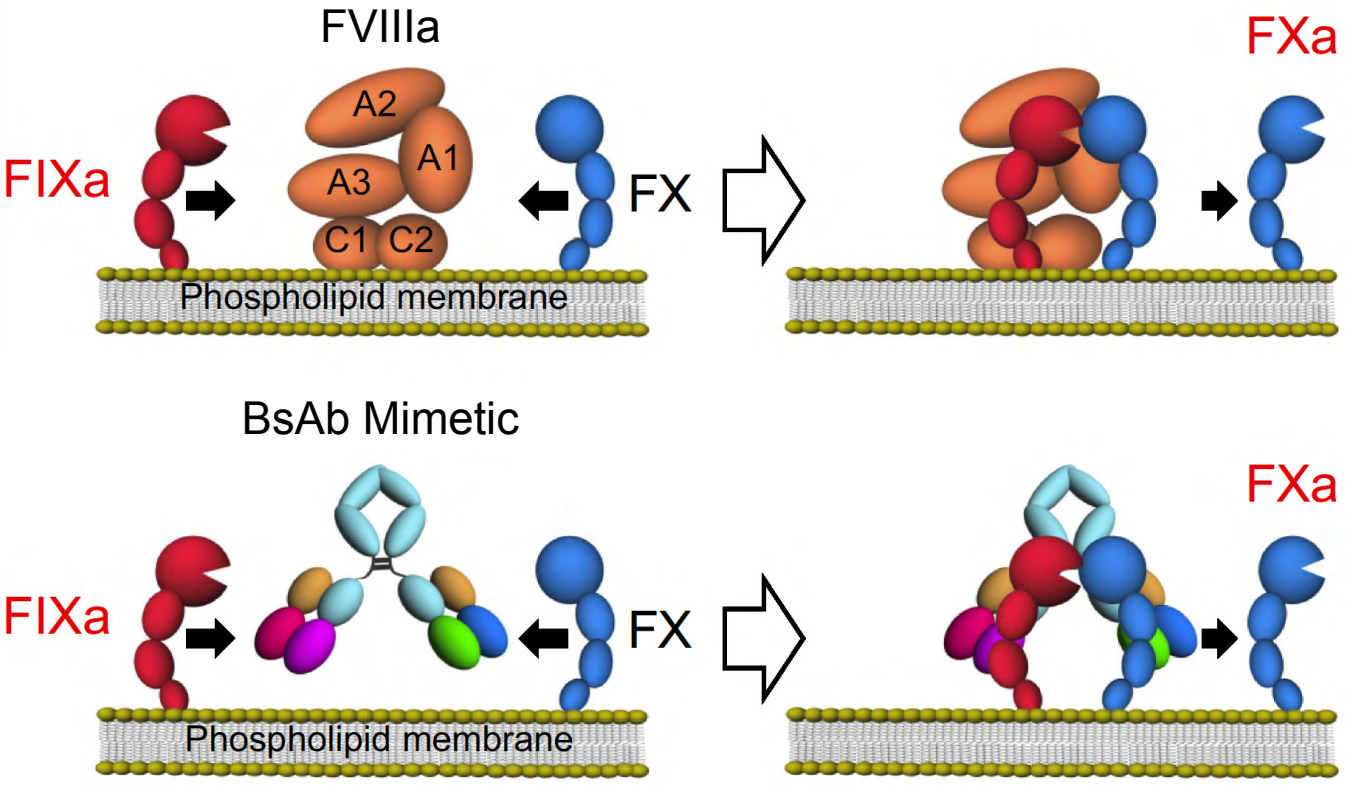
Updates in

FVIIIa MIMETICS

Advancing HEMOPHILIA Treatment Today and Tomorrow

RAPID RECAP

MECHANISM OF ACTION OF FACTOR MIMETICS[1,2]



Factor mimetics are engineered molecules that mimic the function of clotting FVIII. Instead of replacing FVIII, they bridge the gap in the clotting process between FIXa and FXa using a bispecific antibody.[1,2]

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APPROVED AND INVESTIGATIONAL THERAPIES[3-9]

Drug Name	Status	Half-Life	Administration	Rate of FX Activation	Epitope	Binding Affinity to FIX/FIXa	Binding Affinity to FX/FXa
Emicizumab[3,4]	Approved	Absorption: 1.7 days Elimination: 28 days	SC	2.88	EGF1 on FIX/FIXa EGF2 on FX/FXa	1.52 μM	1.58 μM
Mim8 (dencecimig)[5,6]	Phase 3	Terminal: 1 month	SC	31-fold compared to emicizumab	162CT-helix on FIX/FIXa EGF2 and series protease domain on FX/FXa	2.3 μM	1.5 μM
NXT007[7,8]	Phase 1/2	Plasma elimination: 22.1 days post IV 19.6-24.4 days post subcutaneous	SC	Similar to emicizumab	EGF1 on FIX/FIXa using a non-common light chain EGF2 on FX/FXa using a non-common light change	~1 μM	30-40 fold reduced relative to emicizumab
Inno8[9-,10]	Phase 1	Plasma: 115 hours	Oral	~90x higher than emicizumab	FX activation peptide FIXa serine protease domain	Not reported	Not reported

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CONSIDERATIONS FOR TRANSITIONING PATIENTS[3,4,11]

Considerations	Patient Selection	Patient Education	Transition Planning	Safety	Lab Monitoring	Emergency Planning	Psycho-Social Support
Details	Inhibitor status, age, comorbidities, treatment history	Mechanism, administration, expectations	Washout/ overlap period, dosing, monitoring	Thrombotic risk, drug interactions	Assay interference, bleed assessment	Bleed management, medical alerts	Quality of life, support resources

LABORATORY MONITORING CONSIDERATIONS[4,12-14]

aPTT will be artificially shortened in patients on factor mimetics, even if there is no improvement in clinical hemostasis

- aPTT cannot be used to monitor therapy effectiveness or to detect bleeding risk

One-stage clotting assays and chromogenic assays using **human reagents are unreliable**, as they are affected by the presence of the mimetic

- Chromogenic FVIII assays using bovine reagents are not affected by emicizumab and are preferred if FVIII activity needs to be measured

Inhibitor testing (Bethesda assay) is also affected; use **bovine-based reagents** for accurate results

Routine monitoring for thrombosis is not required, but vigilance is needed if patients receive **concomitant activated prothrombin complex concentrates (aPCC)**

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KEY TAKEAWAYS

- Factor mimetics overcome limitations of FVIII replacement therapy and reduce bleeding rates in hemophilia patients, including those with inhibitors
- Factor mimetics are not a monotherapy, and alternative therapies should be considered for these patients to maintain hemostasis
- These therapies have favorable safety profiles, with most adverse events being mild and serious complications rare
- Long-term safety and rare risks still require ongoing monitoring as these treatments become more widely used

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