**Factor Concentrates and Non-factor Therapeutics**

Basics of Factor Concentrates

* Dosing
	+ Varying half-life depending upon the product.
	+ One unit/kg raises Factor VIII levels by 2%; one unit/kg raises Factor IX levels by 1%.
* Highlighted product on the following charts are the brands on par level at VCUHS
* All VCUHS factor assays are one-stage. Factor level from products using other assays may underestimate the factor level.
* Factor assays are not run after hours or on weekends; need path resident approval for exception.
* Generations of the product refer to the presence of blood product in recombinant products.

**Factor VIII Concentrates**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Product | FVIII | Host cell line | Half-life | Product names | Approved |
| Plasma derived | FVIII only | Full length | Pooled human plasma | 14.8-17.5 hours | Hemofil-MKoate DVIMonarc-MMonoclate-P | 1966-1974 |
| Plasma derived/VWF | FVIII/VWF complex | Full length | Pooled human plasma | 12/3-17.9 hours | AlphanateHumate-PWilate | 1978-2009 |
| First | FVIII only | Full length | CHO with albumin | 14.6+/4.9- | Recombinate | 1992 |
| Second | Generation | Full length | CHO with albumin in culture | 13.74 hours | Kogenate | 2000 |
| Third | FVIII | Full length | CHO | 12.0 | Advate | 2003 |
| Third | FVIII | B-domain deleted | CHO | 11.2 | Xyntha | 2008 |
| Third | FVIII | B-domain truncated | CHO | 11 | Novoeight | 2013 |
| Third | FVIII | Full length | BHK | 14.3 | Kovaltry | 2016 |

**Factor VIII Concentrates: Extended half-life agent**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Assay needed | Product | FVIII | Host cell  | Half-life | Product name | Approved |
| One stage | FVIII with increased VWF affinity | Full length | HEK | 17.1 | Nuwiq | 2015 |
| Chromogenic | FVIII single chain | Extended half life | CHO | 14.2 | Afstyla | 2016 |
| One-stage | FVIII | B domain deleted | CHO | 14.69+/-3.79 hours | Adynovate | 2016 |
| One-stage | FVIII | B domain deleted; Fc domain fusion protein | HEK | 19.7+/2.3 hours | Eloctate | 2014 |
| Chromogenic | FVIII | B domain deleted; pegylated | CHO | 18.6 | Jivi | 2018 |
| One-stage | FVIII | pegylated | CHO | 21.6 (↓ <21) | Esperoct | 2019 |

**Factor IX Concentrates: Plasma Derived**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Generation | Product | Host cell | Half-life | Product name | Approval date |
| Plasma-derived | FIX | Pooled human plasma | 21 hours | Alphanine | 1987 |
| Plasma-derived | FIX | Pooled human plasma | 22.6 hours | Mononine | 1992 |
| Plasma-derived | FIX | Pooled human plasma | 24.6 hours | Profilnine | Rev. 2018 |

**Factor IX Recombinant**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Assay | Product | Host cell | Half-life | Product name | Approval date |
| One-stage | Full IX | CHO | 18.8+/- 5.424 +/- 7 hrs25-27 hrs | BenefixIxinityRixubis | 1998 (?); 200720152013 |
| One-stage | Full IX Albumin fusion EHL | CHO | 104-118 hours | Idelvion | 2016 |
| One-stage | Full IX; Fc fusion | HEK | 83-97 hours | Alprolix | 2014 |
| Chromogenic | Full IX; pedgylated;Not for routine prophy. ped in Choroid plexis in animals | CHO | 83 hours | Rebinyn | 2017 |

**Von Willebrand Factor Concentrates: Plasma Derived**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Generation | Product | Host cell | Half-life | Ratio VWF: FVIII | Product name | Approval date |
| Plasma derived | VIII and VWF | Pooled human plasma: SD | 17.9 +/- 9.6 | 1.3:1 | Alphanate | 1978, 2007 |
| Plasma derived | VIII and VWF | Pooled human plasma: pasteurized | 8.4 to 17.4 hours  | 1.8-2.4:1 | Humate P | 1986 |
| Plasma derived | VIII and VWF | Pooled human plasma: SD | VWF: RCo: 15.8 ± 11 hours FVIII:C: 19.6 ± 6.9 hrs | 1:1 | Wilate | 2009 |

Von Willebrand Factor Concentrates: Recombinant

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Generation | Product | Host cell | Half-life | Product name | Approval date |
| Third | VWF | CHO | 19.1 +/- 4.9\*\*Must have FVIII>40% or give FVIII | VonVendi | 2015 |

**Products for patients with inhibitors**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Product | Host cell | Half-life | Product name | Dosing | Approval date |
| Recombinant | Activated Factor VII (7) |  | 2-3 hours | Novoseven | 90-270 mcg/kg | 1978, 2007 |
| Plasma derived | Activated and non-activatedfactors | Pooled human plasma: pasteurized | Dose every 6-12 hours  | **FEIBA\*\*\*\*caution Hemlibra** | **100 units/kg; no more than 200 units/kg/24 hours** | Revised 2013 |

**Emicizumab: Key Points**

* Bispecific antibody to FIXa and X
* Use with only Factor VIII Deficiency (not IX)
* Used prophylactically; may still need treatment doses of standard medications
	+ Patients on Emicizumab are similar in clotting capacity to mild Factor VIII patients.
	+ If factor levels are needed higher than ~15%, factor VIII must be used to supplement.
* Considerations for monitoring: All routine aPTT clotting assays will be inaccurate.
* For patients with inhibitors, DO NOT USE FEIBA to treat bleeds when on Emicizumab due to TMA and thrombosis. Novoseven is a safer alternative.
* Emicizumab has a very long half-life and remains bioavailable for up to six months. Stopping the drug will not stop the effect of the drug.
* VCUHS does not have on formulary.