# Hematopoietic Growth Factors

<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Administration</th>
<th>Uses</th>
<th>Side Effects</th>
<th>Notes</th>
</tr>
</thead>
</table>
| **Recombinant Human Erythropoietin (epoetin-α)** | - Stimulates erythroid proliferation and differentiation by interacting with JAK/STAT cytokine receptor on red cell progenitor  
- Releases reticulocytes from the bone marrow | - IV & subcutaneous injection  
- In anemia of chronic failure: 50-150 IU/kg three times a week  
- In primary bone marrow disorders and secondary anemias: patients require higher doses (100-500 IU/kg) | 1. Anemia of chronic renal failure (most likely to benefit): failure to respond is usually due to iron or folic acid deficiency  
2. Primary bone marrow disorders and secondary anemias: plastic anemia, myeloproliferative and myelodysplastic disorders, multiple myeloma and bone marrow malignancies, anemia of chronic inflammation, AIDS and cancer  
*Response is generally incomplete, better with low baseline erythropoietin levels  
3. Anemia of zidovudine treatment  
4. Anemia of prematurity  
5. Iron overload  
6. Unethically, used by athletes | *Toxicity:  
- Due to rapid increases in hematocrit and hemoglobin: hypertension and thrombotic complications  
- Allergic reactions are infrequent and mild | -34-39 kDa glycoprotein  
- Was the first isolated growth factor  
- Originally purified from urine of patients with severe anemia → elevated in most anemias but lowered in anemia of renal failure  
- Produced in a mammalian cell expression system  
- Half-life after IV administration is 4-13 hours  
- Darbepoetin α has longer half life  
- It is not cleared by dialysis |
| **Megakaryocyte GFs**                      |                                                                    |                     |                                                                                           |                                                                              |                                                                      |
| IL-11                                      | - Acts through a specific receptor  
→ Stimulates the growth of lymphoid and myeloid cells and primitive megakaryocytic progenitors  
→ Increases the number of peripheral platelets and neutrophils | IV & S.C injection  | - Thrombocytopenia: for the secondary prevention of thrombocytopenia in patients receiving cytotoxic chemotherapy for nonmyeloid cancers (Platelets transfusion is an alternative) | - Toxicity: Fatigue, headache, dizziness, anemia, dyspnea, transient atrial arrhythmias and hypokalemia | - 65-85 kDa protein  
- Produced by fibroblasts and stromal cells in the bone marrow  
- Half-life is 7-8 hours after s.c injection.  
- Recombinant form of IL-11 → Produced by expression in E.coli |
| Oprelvekin                                 | IV & S.C injection                                                 |                     |                                                                                           |                                                                              |                                                                      |
# Hematopoietic Growth Factors

<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Administration</th>
<th>Uses</th>
<th>Side Effects</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Megakaryocyte GFs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Thrombopoietin              | - Independently stimulates the growth of primitive megakaryocytic progenitors  
- Stimulates mature megakaryocytes. 
- Activates mature platelets to respond to aggregation-inducing stimuli |                |                                                                      | - Toxicity: Fatigue, headache, dizziness, anemia, dyspnea, transient atrial arrhythmias and hypokalemia | - 65-85 kDa glycoprotein  
- Recombinant form is produced by expression in human cells.  
- Commercial preparations: **Eltrombopag & Romiplostim** |
| **Myeloid GFs**             |                                                                      |                |                                                                      |                                                                                               |                                                                                           |
| rHuG-CSF (Filgrastim)       | - Works on JAK/STAT receptors. - Stimulates proliferation and differentiation of progenitors committed to the neutrophil lineage  
- Activates the phagocytic activity of mature neutrophils and prolongs their survival in the circulation  
- Mobilizes hemopoietic stem cells into the peripheral circulation | - In mobilization of **PBSCs**: Patients or donors are given GM-CSF for 4 days, then leukapheresis, CD34 is used as a marker for the stem cells. At least 5x10^6 CD34 cells/kg should be reinfused to ensure effective engraftment          | 1. Cancer Chemotherapy-Induced Neutropenia: G-CSF accelerates neutrophil recovery, leading to reduced episodes of febrile neutropenia, need for antibiotics and days of hospitalization, but do not improve survival.  
(G-CSF is reserved for risky patients)  
(GM-CSF can produce fever on its own) | *Toxicity:*  
- Bone pain  
- Fever, malaise, arthralgia, myalgia.  
- Capillary Leak Syndrome: peripheral edema, pleural or pericardial effusions  
- Allergic reactions.  
- Splenic rupture. | *In Autologous Stem Cell Transplantation: High dose chemotherapy regimens cause extreme myelosuppression → counteracted by reinfusion of the patient’s own hematopoietic stem cells which are collected before the chemotherapy  
- Originally purified from cultured human cells  
- Produced in a bacterial cell expression system – 175 amino acids, 18 kD mol. wt.  
- Has a half-life of 2-7 hours.  
- Pegfilgrastim: Filgrastim covalently conjugated with polyethylene glycol (Injected once per chemotherapy cycle) |
| rHuGM-CSF (Sargramostim)    | Has broader actions. Works on JAK/STAT receptors  
Stimulates proliferation and differentiation of early and late granulocytic progenitor cells as well as erythroid and megakaryocyte progenitors.  
- With interleukin-2, also stimulates T-cell proliferation.  
- Mobilizes peripheral blood stem cells, but less than G-CSF |                |                                                                      |                                                                                               |                                                                                           |

**Done by: Rama Abbady**