5. Filgrastim (G-CSF) 300 mcg, 480 mcg pre-filled syringes (Grastofil®)
   • Hematopoietic agent
   • Grastofil® is a lower cost biosimilar brand of G-CSF (Neupogen®)
   • The two brands are considered “switchable” at any point during therapy for BCCA and HIV/AIDS approved indications, as response to therapy can be readily monitored.
   • The following formulary restrictions will be applied when G-CSF is ordered:

<table>
<thead>
<tr>
<th>Formulary Restriction</th>
<th>Filgrastim Brand Dispensed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications outlined in BCCA Benefit Drug List &amp; patients registered with BCCA</td>
<td>Grastofil®</td>
</tr>
<tr>
<td>Approval of Centre for Excellence in HIV/AIDS</td>
<td>Grastofil®</td>
</tr>
<tr>
<td>Hematology Apheresis Unit donors</td>
<td>Neupogen®</td>
</tr>
<tr>
<td>Pediatrics</td>
<td>Neupogen®</td>
</tr>
</tbody>
</table>

Deletions

1. Droperidol injection (Inapsine®)
2. Ferumoxytol injection (Feraheme®)
3. Vitalux® AREDS multivitamin tabs with lutein
   • Replacement: Vitalux® Advanced caplets (contains lutein 5 mg)
4. Ofloxacin 0.3% eye drops (Ocuflox®)

Table 1. Quinolone Ophthalmic Interchange

<table>
<thead>
<tr>
<th>Eye Drop Ordered</th>
<th>Eye Drop Dispensed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gatifloxacin 0.3% (Zymar®)</td>
<td>Moxifloxacin 0.5% (same number of drops and frequency)</td>
</tr>
<tr>
<td>Ofloxacin 0.3% (Ocuflox®)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Filgrastim (G-CSF) Restrictions
**New Drug/Drug Products**

**Idarucizumab (Praxbind®)**
Adapted with permission from LMPS P&T Newsletter

Idarucizumab is a specific reversal agent for the novel oral anticoagulant dabigatran (Pradaxa®). It has been added to BCHA formulary for use in patients on dabigatran with severe life-threatening bleeding or who require emergent procedures within 8 hours where normal hemostasis is required.

**Mechanism of Action**
Idarucizumab is a monoclonal antibody that binds specifically to dabigatran, preventing dabigatran from binding to thrombin. Idarucizumab is structurally similar to thrombin but has ~350 times greater affinity for dabigatran than does native thrombin, thereby forming a stable complex and reversing the anticoagulant effect of dabigatran.1

**Pharmacokinetics/Pharmacodynamics**
Normalization of abnormal bleeding tests occurs within minutes; hemostasis in patients with bleeding is restored at a median of 11.4 hours.2 Duration of activity is at least 24 hours. Idarucizumab is metabolized to small peptides and a portion is renally cleared (32% within 6 hrs); the terminal half-life is 10.3 hours.1

**Literature Evaluation**
There is one uncontrolled prospective cohort study, RE-VERSE AD, supporting the use of idarucizumab as a reversal agent for dabigatran.2 This was a single arm, prospective study of 2 groups of patients on dabigatran primarily for atrial fibrillation:

- **Group A** (n=51): overt, uncontrollable or life threatening bleeding requiring a reversal agent
- **Group B** (n=39): patients requiring urgent surgery or other invasive procedure that could not be delayed for at least 8 hours.

All patients were given idarucizumab 2.5 g IV bolus x 2 doses no more than 15 minutes apart. The primary endpoint was maximum reversal of anticoagulant effect of dabigatran based on dilute thrombin time (dTT) or ecarin clotting time (ECT), within 4 hours after idarucizumab administration.

This interim analysis showed that the median maximal percentage reversal in both groups was 100% (95%CI 100 to 100). Idarucizumab normalized laboratory values in 88-98% of patients within minutes (dTT normalized in 93-98% patients, ECT normalized in 88-89% patients). Median time to restoration of hemostasis in patients who presented with bleeding (Group A) was 11.4 hours, and median time to surgery (Group B) was 1.5 hours (range 1.2-26.5 hours). Normal intraoperative hemostasis was reported in 92% of patients.

There were 21 serious adverse events reported (some patients experienced more than 1 event): 18 deaths (9 in each group), 5 thrombotic events, 2 GI hemorrhages, 1 wound infection, 1 delirium, 1 right ventricular failure, and 1 pulmonary edema.

**Dosage**
Idarucizumab 5 g (administered as two separate 2.5 g/50 mL bolus doses, given no more than 15 minutes apart.

The elimination half-life of dabigatran is expected to be longer in patients with renal impairment. Thus, renal function should be considered when deciding whether the use of idarucizumab is indicated.

<table>
<thead>
<tr>
<th>Renal Function (eGFR)</th>
<th>Appropriate Window for Idarucizumab Administration after Last Dose of Dabigatran</th>
</tr>
</thead>
<tbody>
<tr>
<td>Above 50 mL/min</td>
<td>Up to 2 days</td>
</tr>
<tr>
<td>30-50 mL/min</td>
<td>Up to 4 days</td>
</tr>
<tr>
<td>Less than 30 mL/min</td>
<td>Up to 6 days</td>
</tr>
</tbody>
</table>

**Adverse Effects**
- Hypersensitivity reactions (fever, rash, pruritus, bronchospasm)
- Others: hypokalemia (7%), constipation (7%), pneumonia (6%), delirium (7%)
- Note, patients are at risk for a thromboembolic event as reversing anticoagulation with idarucizumab will expose patients to the thrombotic risk of the underlying disease.

**Monitoring**
- Signs and symptoms of bleeding
- Baseline CBC, INR/PTT, TT, fibrinogen, eGFR
- Repeat PTT and TT at 4, 12, and 24 hours after idarucizumab administration

**When to Restart Anticoagulation**
Anticoagulation with dabigatran or other therapies may be considered 24 hours after idarucizumab is administered if the patient is stable and there are no signs of bleeding.

**Conclusion**
Idarucizumab reverses the anticoagulant effect of dabigatran within minutes, with cessation of bleeding at a median of 11.4 hours. The regional Pre-Printed Order for idarucizumab (PPO #988) is posted on the VCH intranet.

**References**