Title: ABCIXIMAB (REOPRO®) SHORTAGE CECCV-20

Situation:
On April 12th, Janssen Biotech, Inc. announced an indefinite stock out of abciximab (ReoPro®) in the United States. Product supply will no longer be available by April 16, 2018 and stock outs could potentially come earlier at local sites.

Background:
In September of 2016, Trinity Health implemented a transforming operation (TO) initiative with recommendations for anticoagulation use during primary PCI according based on the type of P2Y12 inhibitor used that incorporated patient risk factors for bleeding and acute stent thrombosis. When indicated for use, eptifibatide (Integrilin®) is the preferred glycoprotein IIb/IIIa inhibitor (GPI) agent for percutaneous coronary intervention (PCI). Abciximab is the current second line agent, which is restricted to patients with end-stage renal disease (ESRD) and those with a previous reaction to eptifibatide.

Assessment:
Due to the indefinite duration of the abciximab shortage, the approach to treat patients with ESRD undergoing PCI needs to be re-evaluated. The current ACC/AHA guidelines recommend all GPsIs(abciximab(ReoPro®), double-bolus eptifibatide(Integrilin®), and high-bolus dose tirofiban (Aggrastat®)equally for the treatment of NSTE-ACS and for PCI2-3. Eptifibatide requires dose reductions for patients with CrCl <50 mL/min and is contraindicated in patients with ESRD. Tirofiban has an FDA approved renal dose recommendation for all patients with aCrCL < 60 mL/min. The K/DOQI Clinical Practice Guidelines for Cardiovascular Disease in Dialysis Patients list tirofiban and abciximab as the preferred GPI agents. There is data to support use of tirofiban in patients with renal insufficiency and ESRD on hemodialysis.

Recommendation:
For patients requiring GPI treatment, based on the type of P2Y12inhibitor used and patient risk factors (as previously recommended by the transforming operation workgroup), eptifibatide will remain the preferred glycoprotein IIb/IIIa inhibitor (GPI) agent for percutaneous coronary intervention (PCI)

- Due to clinical equivalency and indefinite shortage of abciximab, it is recommended to remove abciximab from the Trinity Health formulary and replace it with tirofiban as the second line GPI agent, which will be restricted for use in ESRD patients for PCI

- The recommended dosing strategy for tirofiban for ESRD patients is to utilize a high bolus dose 25 mcg/kg followed by the maintenance infusion of 0.075 mcg/kg/min until the P2Y12agent has clinical effect, up to a 6 hour infusion

Tirofiban may be continued until P2Y12agent has clinical effect: 2 to 4 hours after prasugrel or ticagrelor load is given or 4 to 6 hours after clopidogrel load is given or up to 6 hours
If the clinical situation of the patient dictates, a prolonged infusion may be utilized, up to 18 hours as needed

References/ Citations:

Abciximab (Reopro®) Shortage presentation
Final Decision and Action Planning Phase

**CEC Decision for Implementation:**

1. Drug shortage precluded our final decision and an accelerated decision was made by the Trinity Health System Pharmacy & Therapeutics Committee (P&T)
2. Regional ICLT to communicate to functional teams and areas.
3. Abciximab removed from the Trinity Health Formulary
4. Pharmacy will continue to monitor future accessibility Abciximab.

<table>
<thead>
<tr>
<th>Teams</th>
<th>Actions</th>
<th>When</th>
</tr>
</thead>
<tbody>
<tr>
<td>CMO</td>
<td>Communicate information to Department of Pharmacy &amp; Cardiovascular Services</td>
<td>By November 30, 2018</td>
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<tr>
<td>CNO</td>
<td>Ensure Cardiovascular caregivers and leaders are aware of drug shortage and removal</td>
<td>By November 30, 2018</td>
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<tr>
<td>Pharmacy</td>
<td>Remove from Trinity Health Formulary and cascade to all pharmacy services</td>
<td>By November 30, 2018</td>
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<tr>
<td>Informatics</td>
<td>FYI Only</td>
<td>By November 30, 2018</td>
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<td>MG PS</td>
<td>Cascade to Cardiovascular practices</td>
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<td>CIN/ACO</td>
<td>Cascade to Cardiovascular practices</td>
<td>By November 30, 2018</td>
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Submitted by: Mary Lynn MacKool, Director CV CEC; Stephen Rosenblum, Medical Director CV CEC

CEC/CLG/CSG: CEC

Date: October 1, 2018
ABCIXIMAB (ReoPro®) SHORTAGE

Maria Pusnik B.S. PharmD BCPS
Clinical Pharmacy Manager
Trinity Health
Situation

• On April 12\textsuperscript{th} Janssen Biotech, Inc. announced an \textit{indefinite} stock out of abciximab (ReoPro®)

• Product supply will no longer be available by April 16, 2018
  - Stock outs could potentially come earlier at local sites
Background

In September of 2016, Trinity Health implemented a transforming operation initiative (TO) to reduce variation in practice for antithrombotic therapy during percutaneous coronary intervention (PCI)

- Eptifibatide (Integrilin®) is the preferred glycoprotein IIb/IIIa inhibitor (GPI) agent for (PCI)
- Abciximab remained on Trinity Health formulary as the second line agent, restricted to patients with end-stage renal disease (ESRD) or those with a previous reaction to eptifibatide
The current ACC/AHA guidelines recommend all GPIs (abciximab, eptifibatide, and tirofiban) equally for the treatment of NSTE-ACS and for PCI.

Due to the indefinite duration of the abciximab shortage, the approach to treat patients with ESRD undergoing PCI needs to be re-evaluated.

- Eptifibatide is contraindicated in patients with ESRD according to FDA labelling.
- Tirofiban has an FDA approved renal dose recommendation for all patients with a CrCL < 60 mL/min and is eliminated by hemodialysis.
- K/DOQI Clinical Practice Guidelines for Cardiovascular Disease in Dialysis Patients lists either tirofiban or abciximab as the preferred GPI agents.
- There is data to support use of tirofiban in patients with renal insufficiency and ESRD on hemodialysis.
Proposed Recommendation - Agent

(Proposed) Recommendation – for discussion

• For patients requiring GPI treatment, eptifibatide will remain the preferred GPI agent for PCI

• Recommend to remove abciximab from the Trinity Health formulary and replace it with tirofiban as the second line GPI agent, which will be restricted for use in ESRD patients for PCI
Assessment – Dosing and Duration

• The FDA approved dose for tirofiban in patients with a CrCl less than 60 mL/min is a standard high-dose bolus of 25 mcg/kg followed by a reduced maintenance infusion of 0.075 mcg/kg/min for up to 18 hours.

• Short duration GPI is a recommended bleeding avoidance strategy
  - FABOLUS PRO trial: With DAPT, near-complete platelet inhibition for at least 6 hours, up to 24 hours, with a short 2-hour infusion
Proposed Recommendation: Dosing and Duration

*(Proposed)* Recommendation – for discussion

- Tirofiban dose (for ESRD patients): Standard high-dose bolus of 25 mcg/kg followed by the maintenance infusion of 0.075 mcg/kg/min

- Duration of infusion
  - Until the P2Y$_{12}$ agent has clinical effect, up to 6 hours
    - 2 to 4 hours after prasugrel or ticagrelor load is given
    - 4 to 6 hours after clopidogrel load is given
  - If the clinical situation of the patient dictates the infusion may be prolonged, up to 18 hours
### Pharmacy Summary

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>CEC Action</th>
<th>Measure of Success</th>
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<tbody>
<tr>
<td>1. Recommend to remove abciximab from the Trinity Health formulary and replace it with tirofiban as the second line GPI agent, which will be restricted for use in ESRD patients for PCI</td>
<td>Vote</td>
<td>Removal of abciximab from formulary and replace with tirofiban</td>
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<td>2. Tirofiban dose (for ESRD patients): Standard high-dose bolus of 25 mcg/kg followed by the maintenance infusion of 0.075 mcg/kg/min</td>
<td>Vote</td>
<td>Agree on tirofiban dose for ESRD patients</td>
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