Direct Oral Anticoagulants (DOACs) use in the Setting of Feeding Tubes and Bariatric Surgery

- DOACs are absorbed at various locations throughout the gastrointestinal tract (see table 1).
- Bariatric surgery results in weight loss by reducing stomach volume (which results in a more alkaline pH) and/or reducing effective intestinal surface area which results in malabsorption.
- There is very little evidence regarding safety and efficacy of DOACs in patients with a history of bariatric surgery or requiring DOAC administration via a feeding tube.
- This document was compiled utilizing current literature incorporating case reports, package inserts, and pharmacokinetic studies as no current randomized controlled trials are available. As always, clinical judgment and a shared decision making approach should be utilized.

### Bariatric Surgery

#### Table 1—DOAC Absorption Locations

<table>
<thead>
<tr>
<th>DOAC</th>
<th>Absorption location</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apixaban</td>
<td>55% in distal small bowel and proximal colon; some gastric and proximal small intestine</td>
<td>pH independent absorption</td>
</tr>
<tr>
<td>Dabigatran</td>
<td>Lower stomach and duodenum</td>
<td>Prodrug; requires acidic environment for absorption (formulated with tartaric acid)</td>
</tr>
<tr>
<td>Edoxaban</td>
<td>Proximal small intestine</td>
<td>pH dependent solubility</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>Primarily stomach with reduced absorption in the proximal small intestine</td>
<td>20mg and 15mg tablets must be taken with a sufficient caloric intake; following bariatric surgery, most patients must adhere to a caloric restriction</td>
</tr>
</tbody>
</table>

#### Transporter Considerations

P-gp concentration is lowest in the duodenum and highest in the distal ileum and colon. Bypassing the proximal portions of the GIT (RYGB, BPD-DS) could lead to decreased drug absorption due to increased efflux of DOAC back into the gut lumen.

CYP3A4 is located along the entire small intestine with slightly increased expression from the duodenum to the middle section of the jejunum with gradually reduced expression in the distal jejunum and ileum. Bypassing the proximal segments (RYGB, BPD-DS) of the GIT could result in a significant increase in oral bioavailability of substrates due to decreased metabolism.

ALL DOACs are substrates of P-gp. Apixaban and rivaroxaban are substrates of CYP3A4.

#### Feeding Tubes

- **Apixaban**: bioavailability is also reduced if administered distal to the stomach. It is recommended to avoid in conjunction with food. Can be given in 60ml DSW. Flushing tube is also preferable. Enteral apixaban is more impacted in presence of nutritional supplementation compared to enteral rivaroxaban.
- **Dabigatran**: must be taken orally and should not be administered through an enteral feeding tube. 5
- **Edoxaban**: no studies have been conducted to assess edoxaban use in enteral administration therefore it should be taken as an intact tablet.
- **Rivaroxaban**: bioavailability is reduced if administered distal to the stomach. It is recommended to flush tubing prior to and after administration. Can be given in 50mL sterile water, applesauce, or juice.

#### Take Home Points:

- There is minimal evidence regarding the use of DOACs in patients with a history of bariatric surgery. Thus, **warfarin remains the preferred oral anticoagulant** in this patient population as effectiveness can be measured through INR monitoring. 1,2
- Rivaroxaban should be used with extra caution due to the caloric restrictions associated with gastric bypass, as well as reduction in plasma levels as seen in observational studies.
- If a patient is unable or unwilling to use warfarin, it is important to consider type of bariatric surgery, location of DOAC absorption, pH dependent/ independent solubility, transporter mechanisms and to conduct shared decision making prior to initiating DOAC therapy.
- Dabigatran and edoxaban are not recommended for administration via enteral feeding tubes. Rivaroxaban and apixaban can be administered via enteral feeding tubes if terminated in the stomach (nasogastric or gastric tubes).

### References:


Produced by Candace Bryant, PharmD., BCPS and Nilsam Naik, Pharm.D., BCPS
Tennessee Valley Health System Veterans Affairs
January 2019