**Novel Oral Anticoagulants (NOACS) Peri-Operative Management**

**Background:**

Four NOACs (apixaban, dabigatran, rivaroxaban and edoxaban) are approved for clinical use in Canada based on findings from large randomized trials.

The peri-operative management of NOAC-treated patients aims to interrupt anticoagulant therapy (if necessary) so there is no (or minimal) residual anticoagulant effect at the time of surgery, and to not incur an increased risk for post-operative bleeding.

There are 3 important considerations for peri-operative management of patients taking a NOAC:

1. Reliable laboratory tests to confirm the absence of a residual anticoagulant effect of NOACs are not widely available.
2. Half-lives of NOACs differ and increase with worsening renal function, affecting when a drug should be stopped before surgery.
3. NOACs have rapid onset of action, with a peak anticoagulant effect occurring 1-2 hours after oral intake.

In the absence of laboratory tests to reliably measure their anticoagulant effect, the peri-operative administration of NOACs should be influenced by:

1. Drug elimination half-life (with normal renal function),
2. Effect of renal function on drug elimination half-life, and
3. Bleeding risk associated with the surgery/procedure type (table 3)
4. Whether patient is to receive spinal/epidural anesthesia.

**Peri-Operative Management:**

**Patients Receiving Dabigatran**

***Pre-Operative Management (Table 1):***

* **Minor surgery/procedure**: Stop dabigatran 1 day before surgery/procedure (i.e., skip 2 doses before a surgery/procedure), which corresponds to approximately 2 half-lives elapsed between stopping dabigatran and surgery. There may be a 12-25% anticoagulant effect at the time of surgery, which is acceptable for a minor surgery/procedure.
* **Major surgery/procedure including neuraxial anesthesia**: Stop dabigatran 3 days before surgery (i.e., skip 6 doses), which corresponds to approximately 4-5 half-lives elapsed between stopping dabigatran and surgery. This ensures minimal (3-6%) residual anticoagulant effect at the time of surgery and allows patients to have spinal anesthesia or high bleeding risk surgery (e.g., intracranial or cardiac).
* If renal function is moderately impaired (CrCl 30-49 mL/min), 1-2 additional days of interruption is required to ensure elimination of any residual anticoagulant effect, as 80% of dabigatran is cleared by the kidneys.

***Post-Operative Management (Table 2):***

Resumption of dabigatran 150 mg or 110 mg twice daily should be done cautiously after major surgery or in patients at increased bleeding risk, as this is a therapeutic-dose which is higher than that used for post-operative VTE prevention

**Patients Receiving Rivaroxaban**

***Pre-Operative Management (Table 1):***

* **Minor surgery/procedure**: Stop rivaroxaban 1 day before surgery/procedure (i.e., skip 1 dose), which corresponds to approximately 2 half-lives elapsed between stopping rivaroxaban and surgery.
* **Major surgery/procedure including neuraxial anesthesia**: Stop rivaroxaban 2 days before surgery (i.e., skip 2 doses), which corresponds to approximately 4-5 half-lives elapsed between stopping rivaroxaban and surgery.

***Post-Operative Management (Table 2):***

Resumption of rivaroxaban 20 mg (or 15 mg if usual dose) once daily should be done cautiously after major surgery or in patients at increased bleeding risk, as this is a therapeutic-dose which is higher than that used for post-operative VTE prevention (See Thromboprophylaxis: Orthopedic Surgery guide).

**Patients Receiving Apixaban**

***Pre-Operative Management (Table 1):***

* **Minor surgery/procedure**: Stop apixaban 1 day before surgery/procedure (i.e., skip 2 doses), which corresponds to approximately 2 half-lives elapsed between stopping apixaban and surgery.
* **Major surgery/procedure including neuraxial anesthesia**: Stop apixaban 2 days before surgery (i.e., skip 4 doses), which corresponds to approximately 4-5 half-lives elapsed between stopping apixaban and surgery.

***Post-Operative Management (Table 2):***

Resumption of apixaban 5 mg twice daily should be done cautiously after major surgery or in patients at increased bleeding risk, as this is a therapeutic-dose which is higher than that for post-operative VTE prevention (See Thromboprophylaxis: Orthopedic Surgery guide).

**Patients Receiving Edoxaban**

***Pre-Operative Management (Table 1):***

* **Minor surgery/procedure:** Stop edoxaban 1 day before surgery/procedure (i.e. skip 1 dose), which corresponds to approximately 2-3 half-lives elapsed between stopping apixaban and surgery.
* **Major surgery/procedure including neuraxial anesthesia**: Stop edoxaban 2 days before surgery (i.e. skip 2 doses), which corresponds to approximately 4-5 half-lives elapsed between stopping edoxaban and surgery.

***Post-Operative Management (Table 2):***

Resumption of edoxaban 60 mg or 30 mg daily should be done cautiously after major surgery or in patients at increased bleeding risk, as this is a therapeutic-dose.

**Table 1. Suggested Guide for *Pre-Operative* Management of Patients Receiving a NOAC**

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| --- | --- | --- | --- |
| **Drug (Dose Regimen)** | **Renal Function** | **Minor Surgery/Procedure\***  **(Low Bleeding Risk)**  *12-25% residual anticoagulant effect at time of surgery acceptable* | **Major Surgery/Procedure Including neuraxial procedures \*†**  **(High Bleeding Risk)**  *< 10% residual anticoagulant effect at time of surgery acceptable* |
| **Dabigatran** (twice daily) | Normal renal function or mild impairment (CrCl ≥50 mL/min) | Give last dose 2 days before surgery/procedure (i.e., skip 2 doses) | Give last dose 3 days before surgery/procedure (i.e., skip 4 doses) |
|  | Moderate renal impairment (CrCl 30-49 mL/min) | Give last dose 3 days before surgery/procedure (i.e., skip 4 doses) | Give last dose 5 days before surgery/procedure (i.e., skip 8 doses) |
| **Rivaroxaban** (once daily) | Normal renal function, mild or moderate impairment (CrCl ≥ 30 mL/min) | Give last dose 2 days before surgery/procedure (i.e., skip 1 dose) | Give last dose 3 days before surgery/procedure (i.e., skip 2 doses) |
| **Apixaban** (twice daily) | Normal renal function, mild or moderate impairment  (CrCl ≥ 30 mL/min) | Give last dose 2 days before surgery/procedure (i.e., skip 2 doses) | Give last dose 3 days before surgery/procedure (i.e., skip 4 doses) |
| **Edoxaban** (once daily) | Normal renal function or mild impairment (CrCl ≥50 mL/min) | Give last dose 2 days before surgery/procedure (i.e., skip 1 dose). | Give last dose 3 days before surgery/procedure (i.e., skip 2 doses) |

\*No anticoagulant taken on the day of surgery/procedure.

†Neuraxial procedures include spinal anesthesia, epidural catheter insertion and epidural catheter removal.

**Table 2. Suggested Guide for *Post-Operative* Management of Patients Receiving a NOAC**

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| **Drug** | **Minor Surgery/Procedure (Low Bleeding Risk)** | **Major Surgery/Procedure (High Bleeding Risk)** |
| **Dabigatran** | Resume on day after surgery (~24 hours post-operative) | Resume 2 days after surgery (~48 hours post-operative) |
| **Rivaroxaban** | Resume on day after surgery (~24 hours post-operative) | Resume 2 days after surgery (~48 hours post-operative) |
| **Apixaban** | Resume on day after surgery (~24 hours post-operative) | Resume 2 days after surgery (~48 hours post-operative) |
| **Edoxaban** | Resume on day after surgery (~24 hours post-operative) | Resume 2 days after surgery (~48 hours post-operative) |

**Tablet 3. Patient Stratification for Bleeding Risk**

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| **High:**   * Any surgery or procedure with neuraxial (spinal or epidural) anesthesia * Neurosurgery (intracranial or spinal) * Cardiac surgery (e.g., CABG, heart valve replacement) * Major intra-abdominal surgery * Major vascular surgery (e.g., aortic aneurysm repair, aortofemoral bypass) * Major orthopedic surgery (e.g., hip or knee replacement) * Lung resection surgery * Urological surgery (e.g., prostatectomy, bladder tumor resection) * Extensive cancer surgery (e.g., pancreas, liver) * Intestinal anastomosis surgery * Reconstructive plastic surgery * Selected procedures (e.g., kidney biopsy, prostate biopsy, cervical cone biopsy, pericardiocentesis, colonic polypectomy)   **Moderate:**   * Other intra-abdominal surgery (e.g., laparoscopic cholecystectomy or hernia repair) * Other general surgery (e.g., breast) * Other intrathoracic surgery * Other orthopedic surgery * Other vascular surgery * Non-cataract ophthalmologic surgery * Gastroscopy or colonoscopy with biopsies * Selected procedures (e.g., bone marrow biopsy, lymph node biopsy) * Complex dental procedure (e.g., multiple tooth extractions)   **Low (Non-Dental):**   * Cataract surgery * Dermatologic procedures (e.g., biopsy) * Gastroscopy or colonoscopy without biopsies * Coronary angiography * Permanent pacemaker insertion or internal defibrillator placement (if bridging anticoagulation is not used) * Selected procedures (e.g., thoracentesis, paracentesis, arthrocentesis)   **Low (Dental):**   * Dental extractions (1 or 2 teeth) * Endodontic (root canal) procedure * Subgingival scaling or other cleaning |

**Special Considerations:**

**Patients Having Minor Procedures:**

In NOAC-treated patients who require dental procedures (e.g., extraction, root canal), cataract surgery or minor skin procedures, it is likely safe to not interrupt anticoagulation (as is done in warfarin-treated patients) but data to support such a practice are lacking.

**Need for Bridging in NOAC-treated Patients**:

In general, the rapid offset and onset of action of NOACs obviated the need for “heparin bridging” as is done in selected warfarin-treated patients.

All information can be referenced to original website: [www.thrombosiscanada.ca](http://www.thrombosiscanada.ca)

**Thrombosis Canada. 2016. Thrombosis Canada Clinic Guidelines [online] Available at: <http://thrombosiscanda.ca/>. Accessed 30 March 2017.**