Conversion of Anti-Coagulants to Heparin Before and After Elective Surgery

- Clinical Policy Bulletins
- Medical Clinical Policy Bulletins

Number: 0200

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Policy

Scope of Policy

This Clinical Policy Bulletin addresses conversion of anti-coagulants to heparin before and after elective surgery.

1. **Medical Necessity**

   Aetna considers continuous intravenous heparin infusion medically necessary for members taking apixaban (Eliquis), dabigatran (Pradaxa), edoxaban (Savaysa), rivaroxaban (Xarelto), or oral anti-coagulants (warfarin) who require the maintenance of anti-coagulation prior to and after diagnostic or therapeutic procedures. For most members, pre-procedure weaning of the oral anti-coagulant may be safely accomplished on an outpatient basis. When circumstances arise that might compromise the member's state of anti-coagulation such that thrombotic complications may occur, up to 3 inpatient pre-procedure days may be considered medically necessary.

2. **Related Policies**

   - CPB 0255 - Inpatient Admission Prior to Surgery (Preop Days)
   - CPB 0346 - Low-Molecular-Weight Heparins and Thrombin Inhibitors

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CPT Codes / HCPCS Codes / ICD-10 Codes

HCPCS codes covered if selection criteria are met:

Code	Code Description
J1642	Injection, heparin sodium, (Heparin Lock Flush), per 10 units
J1643	Injection, heparin sodium (pfizer), not therapeutically equivalent to J1644, per 1000 units
J1644	Injection, heparin sodium, per 1,000 units
S9336	Home infusion therapy, continuous anticoagulant infusion therapy (e.g., heparin), administrative services, professional pharmacy services, care coordination, and all necessary supplies and equipment (drugs and nursing visits coded separately), per diem

Other HCPCS codes related to the CPB:

Apixaban (Eliquis), Dabigatran (Pradaxa), Edoxaban (Savaysa), Rivaroxaban (Xarelto) **–no specific code**

ICD-10 codes covered if selection criteria are met:

Z79.01	Long term (current) use of anticoagulants

Background

The most common indications for warfarin therapy are atrial fibrillation, the presence of a mechanical heart valve, prior thromboembolism, a documented left ventricular thrombus or a history of venous thromboembolism with or without a pulmonary embolism.

Patients receiving long-term warfarin therapy may present a problem if they require surgery because the interruption of anti-coagulant therapy increases their risk of thromboembolism. Rational decisions regarding the appropriateness of peri-operative anti-coagulation depends on individual patient factors and can only be made when the risk of peri-operative thromboembolism is balanced against the risk of peri-operative bleeding.

After warfarin therapy is discontinued, it generally takes several days for its anti-thrombotic effect to recede. Most invasive procedures can be performed safely when the international normalized ratio (INR) is less than 1.5.

Finlay et al (2010) stated that many patients undergoing catheter ablation of atrial flutter (AFL) require peri-procedural anti-coagulation. These researchers compared a strategy of conversion to low-molecular-weight heparin (LMWH) peri-procedure to uninterrupted warfarinization in a non-randomized, case-controlled study. A total of 101 consecutive patients requiring peri-procedural anti-coagulation for catheter ablation of typical AFL were studied. The first 51 patients underwent conversion to LMWH (enoxaparin 1 mg/kg body weight) with a warfarin pause (LMWH group), the subsequent 50 continued with uninterrupted oral anti-coagulation (warfarin group). Primary endpoint was a composite of major and minor bleeding complications and groin symptoms. Fewer patients in the warfarin group reached the primary endpoint (36.0 % versus 56.8 %, p = 0.013). Four patients in the LMWH group but no patient in the warfarin group required hospital admission for bleeding-related complications. Cost analysis showed mean cost per patient of anti-coagulation with LMWH to be pounds sterling 100.9 (95 % confidence interval [CI]: 94.46 to 107.30) compared to pounds sterling 10.23 (95 % CI: 4.49 to 15.97) in the warfarin group (p < 0.0001). Trans-esophageal echocardiography (TEE) was performed prior to ablation in 11 patients in the warfarin group and in 3 patients in the LMWH (p = 0.019). When TEE costs were included, costs were pounds sterling 125.00 ($188.25) (95 % CI: 96.80 to 153.60) for the LMWH strategy and pounds sterling 108.5 ($163.40) (95 % CI: 54.92 to 162.1) for the warfarin group (p < 0.0001). The authors concluded that catheter ablation of typical AFL without interruption of warfarin appears safer and more cost-effective than peri-procedural conversion to LMWH. It could be used as a routine anti-coagulation strategy for the ablation of right-sided arrhythmias.

Pre-Procedure Regimen

The treating physician should determine the INR targets required for best protection against thromboembolism while minimizing the risk of bleeding for the planned procedure. For most patients, the literature indicates that warfarin therapy may be discontinued 3 to 4 days prior to the date of the planned elective surgery to allow the INR to fall spontaneously. On the 2nd day after discontinuing warfarin, the INR may be checked as an outpatient and when the anti-thrombotic threshold value is reached, the patient may be admitted to the hospital for continuous intravenous heparin infusion. In most cases, this occurs on the day before or the day of the planned procedure.

Post-Procedure Regimen

When the physician decides to restart oral anti-coagulation after the procedure, an effort should be made to time the discontinuance of intravenous heparin with the establishment of adequate anti-thrombotic protection in the inpatient setting. The literature indicates that conversion back to pre-procedure levels of oral anti-coagulation can also be bridged by using subcutaneous injections of LMWH in the home setting after discharge.

Conversion from Anti-Coagulants to Heparin

Wendte et al (2016) discussed the case of a patient requiring conversion from apixaban to heparin in the setting of acute kidney injury (AKI). A 70-year-old man was initiated on 5-mg apixaban twice-daily for new-onset, non-valvular atrial fibrillation (NVAF) with a CHA2DS2-VASc score of 4, indicating a high risk of stroke. Soon after starting apixaban, he experienced pulmonary edema (PE) with pneumonia requiring hospitalization. During the course of hospitalization, the patient developed AKI requiring hemodialysis, and apixaban was stopped due to concerns about altered pharmacokinetics and impaired drug elimination in this setting. A heparin infusion was started 36 hours after the last dose of apixaban was administered. Anti-factor Xa levels were monitored consistent with the hospital's standard practice protocols. The initial and repeat anti-factor Xa concentrations were elevated (1.8 to 4.4 IU/ml) for up 72 hours after stopping the heparin infusion. Given the suspected interference of apixaban with standard anti-factor Xa level monitoring, the heparin protocol was modified to reflect drip-rate adjustments based on activated partial thromboplastin times (aPTTs). The hospital protocol for heparin infusions was re-instituted on hospital day 7, with dosage adjustments based on anti-factor Xa levels. The patient remained on a continuous heparin infusion for AF for the remainder of his hospitalization without complications or bleeding events. The authors concluded that a 70-year-old man with new-onset NVAF and receiving apixaban discontinued this therapy and was given heparin instead due to AKI. His heparin dosage was successfully adjusted based on anti-factor Xa levels and aPPTs.

Faust et al (2016) stated that assays that measure inhibition of factor Xa activity (i.e., anti-Xa assays) are widely used in U.S. institutions to monitor intravenous (IV) heparin therapy and, in some cases, for monitoring other types of anti-coagulation therapy. Clinicians have raised concerns that the use of anti-Xa assays to monitor heparin levels in hospitalized patients who must be transitioned from oral factor Xa inhibitor therapy to IV unfractionated heparin (UFH) infusions could yield unquantifiable or inaccurate results, resulting in unnecessary UFH dose reductions and potential treatment failures; the manufacturer labeling of oral factor Xa inhibitors (apixaban, edoxaban, and rivaroxaban) does not provide specific guidance on this issue. Results of a literature review indicated that residual effects of oral factor Xa inhibitor use can result in substantial interference with the currently available chromogenic anti-Xa assays but negligible to moderate effects on global coagulation assays, which measure aPTT or prothrombin time. Thus, during the transition from an oral factor Xa inhibitor to IV UFH therapy, it may be prudent to consider an aPTT assay for anti-coagulation monitoring. The authors concluded that the use of oral factor Xa inhibitors appeared to affect the accuracy of anti-Xa assay results, with results of global coagulation assays affected to a lesser degree.

In a case-series study, Zochert et al (2019) presented 3 patients with AKI taking apixaban or rivaroxaban and transitioning to a heparin infusion. Case 1 was a 78-year-old man admitted with respiratory failure, acute decompensated heart failure (HF), and AKI. He was taking apixaban for atrial flutter. He was transitioned to an IV heparin infusion and had 2 consecutive heparin anti-factor-Xa levels greater than 2 units/ml. Heparin was held and resumed about 36 hours later when the apixaban anti-Xa level was less than 50 ng/ml. Case 2 was a 55-year-old man admitted with AKI, taking apixaban for a recent deep vein thrombosis (DVT). Apixaban anti-Xa levels were monitored; and IV heparin was initiated when the level was less than 100 ng/ml, about 56 hours after the last apixaban dose. Case 3 was a 64-year-old woman admitted with sepsis and AKI taking rivaroxaban for PE, which occurred 2 weeks before admission. Rivaroxaban anti-Xa levels were monitored; and IV heparin was initiated about 36 hours after the last dose when the level was less than 100 ng/ml. The management strategy did not lead to any thrombotic outcomes; however, 1 patient experienced bleeding. The authors concluded that specific anti-Xa levels for rivaroxaban and apixaban appeared to be helpful in the transition of 3 patients to unfractionated heparin infusions in the setting of AKI. These levels provided enhanced, individualized care and likely helped avoid over and under anti-coagulation.

In a retrospective chart review, Smith et al (2020) determined a patient's clinical course based on the use of an aPTT or heparin anti-Xa assay when transitioning from rivaroxaban or apixaban to an unfractionated heparin infusion. This study was caried out to examine how unfractionated heparin infusions were managed at a tertiary care hospital in the setting of recent apixaban or rivaroxaban administration. Patients were separated into 2 cohorts based on the chosen heparin infusion monitoring assay: heparin anti-Xa or aPTT. The primary composite outcome was total number of bleeding and thrombotic events; the secondary composite outcome was average incidence of heparin infusion holds and rate changes per patient. Data were collected from 76 patients (heparin anti-Xa = 69, aPTT = 7). Due to the limited number of patients within the aPTT cohort, these data were excluded from the analysis, and heparin anti-Xa descriptive statistics were reported without statistical comparisons. In the heparin anti-Xa group, a total of 10 bleeds and 1 thrombus were discovered. Furthermore, the average number of infusion holds and rate changes was 0.841 and 2.65 times per patient, respectively, for those patients monitored via heparin anti-Xa assay. The authors concluded that in the presence of a recently administered oral anti-Xa anticoagulant, more down-titrations occurred in the initial 6 hours of the heparin infusion when measuring anti-Xa activity, and most up-titrations occurred after 36 hours. Baseline heparin anti-Xa activity may be a useful tool to identify patients with residual plasma concentrations of apixaban and rivaroxaban to help better individualize heparin therapy.

Gloucestershire Hospitals (NHS Foundation Trust) guidance on “Converting between anticoagulants” (Morgan and Gettings, 2021) stated the following: “Stop apixaban and start unfractionated heparin infusion/LMWH at the time the next dose of apixaban would be due”.

UpToDate’s review on “Apixaban: Drug information” (2022) provided the following information regarding “Transitioning from apixaban to unfractionated heparin continuous infusion, low-molecular-weight heparin, or fondaparinux”: “Start the parenteral anticoagulant when the next dose of apixaban was scheduled to be given”.

In a retrospective, cohort analysis, Dingus et al (2022) compared the safety and effectiveness of monitoring UFH infusions using an activated partial thromboplastin time (aPTT) titration scale versus utilizing an UFH-calibrated anti-Xa titration scale aided by a novel institutional guideline in patients transitioning from an factor Xa inhibitors (FXai; apixaban, rivaroxaban) to UFH infusions. This study was carried out on adult patients transitioning from an FXai to an UFH infusion at 2 medical centers from June 1, 2018, to November 1, 2020. One institution employed aPTT while the other institution primarily used UFH-calibrated anti-Xa. The primary endpoint was a composite of death, major bleeding, or new thrombosis during the hospitalization with a planned non-inferiority analysis. Secondary outcomes were also collected including the amount and duration of UFH administered between cohorts. The incidence rate of the primary composite endpoint was 6.3 % in the anti-Xa group and 11 % in the aPTT group ($p < 0.001$ for non-inferiority, $p = 0.138$ for superiority) meeting non-inferiority criteria. No statistical differences were observed in new thrombosis, major bleeding, or any bleeding. The authors concluded that this study represented the 1st report of a comparison between aPTT versus anti-Xa monitoring in relation to clinical outcomes for patients transitioning from an FXai to an UFH infusion. A transition guideline primarily using an UFH-calibrated anti-Xa assay appeared to be a safe alternative to aPTT monitoring and could aid in facilitating the management of patients during these complex transitions.

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Policy History

- Last Review 04/16/2025

  Effective: 02/19/1998

  Next Review: 02/12/2026

- Review History

- Definitions

Additional Information

- Clinical Policy Bulletin Notes