

Clinical Pharmacy Program Guidelines for Pradaxa

Program	Prior Authorization
Medication	Pradaxa (dabigatran etexilate)
Issue Date	3/2011
Pharmacy and Therapeutics Approval Date	3/2017
Effective Date	4/2017

1. Background:

Indications

Stroke prevention in patients with non-valvular atrial fibrillation (AF): Indicated to reduce the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation.

Treatment of Treatment of deep vein thrombosis (DVT) or pulmonary embolism (PE): Indicated for the treatment of DVT and PE in patients who have been treated with a parenteral anticoagulant for 5-10 days.

Reduction in the Risk of Recurrence of DVT or PE: Indicated to reduce the risk of recurrence of DVT and PE in patients who have been previously treated.

Prophylaxis of venous thromboembolism (VTE) after orthopedic surgery: Has been used for the prevention of acute venous thromboembolism (VTE) after total hip replacement.

Off Label Uses

Prophylaxis of venous thromboembolism (VTE) after orthopedic surgery: Has been used for the prevention of acute venous thromboembolism (VTE) after total knee replacement

2. Coverage Criteria:

A. Continuation of Therapy Upon Hospital Discharge

1. Initial Authorization

- a. Pradaxa will be approved as continuation of therapy upon hospital discharge

Authorization will be issued for 35 days.

B. Stroke Prevention in Patients with Non-Valvular Atrial Fibrillation (AF)

1. Initial Authorization

a. Diagnosis of atrial fibrillation (AF)

-AND-

b. Patient does not have an artificial heart valve

-AND-

c. One of the following:

(1) History of failure, contraindication, or intolerance to all of the following:

- Xarelto
- Eliquis
- Savaysa

-OR-

(2) Continuation of prior Pradaxa therapy

Authorization will be issued for 12 months.

C. Prophylaxis of venous thromboembolism (VTE) after orthopedic surgery (hip replacement: labeled; knee replacement: off-label)

1. Initial Authorization

a. One of the following:

- Patient has or is scheduled to have total knee replacement surgery
- Patient has or is scheduled to have total hip replacement surgery

Authorization will be issued for 35 days.

D. Treatment of deep vein thrombosis (DVT) or pulmonary embolism (PE)

1. Initial Authorization

a. Diagnosis of one of the following:

- Deep vein thrombosis (DVT)
- Pulmonary embolism (PE)

-AND-

b. One of the following:

(1) History of failure, contraindication, or intolerance to all of the following:

- Xarelto
- Eliquis
- Savaysa

-OR-

(2) Continuation of prior Pradaxa therapy

Authorization will be issued for 6 months.

E. Reduction in the risk of recurrence of deep vein thrombosis (DVT) and pulmonary embolism (PE)

1. Initial Authorization

a. Previous diagnosis of one of the following:

- Deep vein thrombosis (DVT)
- Pulmonary embolism (PE)

-AND-

b. Patient must have been treated with an anticoagulant [eg, warfarin, Pradaxa (dabigatran), Eliquis (apixiban), Xarelto (rivaroxaban)] for at least 3 months prior to request.

-AND-

c. One of the following:

(1) History of failure, contraindication, or intolerance to all of the following:

- Xarelto
- Eliquis
- Savaysa

-OR-

(2) Continuation of prior Pradaxa therapy

Authorization will be issued for 12 months.

3. Endnotes

- A. Non-valvular atrial fibrillation is defined as occurring in the absence of hemodynamically significant valvular disease, or a prosthetic heart valve [3]
- B. In the RE-LY trial, comparing dabigatran with adjusted-dose warfarin for prevention of stroke in patients with non-valvular atrial fibrillation, dabigatran demonstrated superior efficacy to warfarin. [2]
- C. In the RE-COVER trial, comparing dabigatran with adjusted-dose warfarin for the treatment of acute venous thromboembolism following initial therapy with a parenteral anticoagulant, dabigatran demonstrated non-inferiority to warfarin for prevention of recurrent VTE with a similar rate of major bleeding and less clinically relevant non-major bleeding and less any bleeds. [4]
- D. The duration of therapy in the RE-COVER study was 6 months. Approximately 60% of the study participants had cancer. [4] The ACCP guidelines recommend treatment with a vitamin K antagonist (VKA) for duration of 3 months for patients with DVT or PE due to a transient (reversible) risk factor, and that all patients are then evaluated for the risks and benefits of indefinite therapy. At least 3 months of therapy is recommended for an unprovoked DVT or PE; indefinite anticoagulant therapy is recommended for patients with a first unprovoked proximal DVT or PE and a low risk of bleeding when this is consistent with the patient's preference, and for most patients with a second unprovoked DVT. At least 3 months with a low-molecular-weight heparin (LMWH) is recommended for patients with VTE and cancer followed by treatment with LMWH or a VKA as long as the cancer is active. [9]
- E. Dabigatran demonstrated non-inferiority to enoxaparin 40 mg SC once daily for prophylaxis of VTE after total knee replacement surgery in the RE- MODEL trial and inferiority to enoxaparin 30 mg SC bid in the RE-MOBILIZE trial. Rates of major bleeding were similar between comparators in both trials. [5,6]
- F. Dabigatran demonstrated non-inferiority to enoxaparin 40 mg SC once daily in the RE-NOVATE trial with a similar rate of major bleeding. [7]
- G. The duration of therapy was 6-10 days in the RE- MODEL trial, 12 to 15 days in the RE-MOBILIZE trial, and 28 to 35 days in the RE-NOVATE trial. [5-7] The ACCP guidelines recommend a duration of thromboprophylaxis for a minimum of 10 days and for > 10 days and up to 35 days for total knee replacement or total hip replacement. [8]
- H. On December 19, 2012, the FDA announced that Pradaxa should not be used to prevent stroke or blood clots in patients with mechanical heart valves, also known as mechanical prosthetic heart valves. [13]The RE-ALIGN trial was recently stopped because the Pradaxa users were more likely to experience strokes, heart attacks, and blood clots

forming on the mechanical heart valves than the warfarin users. [13] The FDA is requiring the addition of a contraindication of Pradaxa in patients with mechanical heart valves. The use of Pradaxa in another type of valve replacement made of natural biological tissue, known as a bioprosthetic valve, has not been evaluated and cannot be recommended. [1]

- I. Examples of severe valvular disorder include, but are not limited to, severe mitral stenosis, the presence of a bioprosthetic heart valve, etc.
- J. The duration of therapy of Pradaxa for the extended treatment of acute VTE in the REMEDY study was 18 months. Authorization for 12 months based on Medicare length of auth rules.[14]
- K. If extended therapy is required, ACCP guidelines suggest treatment with the same anticoagulant chosen for the first 3 months. [15]

4. References

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Program	Prior Authorization – Pradaxa (dabigatran etexilate)
Change Control	
Date	Change
March 2011	New drug policy
March 2012	Annual Review. Added specification to diagnosis requirement, non-valvular atrial fibrillation.
March 2013	Added criteria for continuation after hospital discharge, treatment of acute VTE, and prophylaxis of VTE after orthopedic surgery. Updated criteria for atrial fibrillation, now includes conditions that are contraindicated for use with Pradaxa. Added dosing, availability, background, and endotes section. Updated references.
Dec 2015	Added requirement of a trial of the preferred alternative products or as continuation of existing therapy. Pradaxa is non-preferred and the plan has three other preferred products. Removed age requirement for Prophylaxis of venous thromboembolism (VTE) after orthopedic surgery. Renamed “Treatment of acute venous thromboembolism (VTE) (off-label)” to “Treatment of deep vein thrombosis (DVT) or pulmonary embolism (PE)” as this is an FDA approved

	<p>indication. Removed age requirement and requirement to for a trial of warfarin from this section. Added different preferred alternative trial requirement of the preferred alternative products or as continuation of existing therapy.</p> <p>Added new section for Reduction in the risk of recurrence of deep vein thrombosis (DVT) and pulmonary embolism (PE) as this is an FDA approved indication. Includes requirement for a trial of the preferred alternatives Xarelto and Eliquis as these drugs are preferred and are FDA approved for this indication.</p> <p>Added formulary note outlining the preferred and non-preferred products in the anticoagulant class.</p>
June 2016	Updated policy template. Updated prosthetic heart valve definition for Non-Valvular Atrial Fibrillation. Prophylaxis of venous thromboembolism (VTE) after orthopedic surgery- hip replacement: Updated to a labeled indication.
October 2016	Archive policy. High approval rate of prior authorizations.
March 2017	Reinstated policy. Updated policy template.