

## ANTICOAGULATION REVERSAL: PART I—PHARMACOLOGY OF AGENTS USED FOR REVERSAL

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### INTRODUCTION

Uncontrolled bleeding in the setting of therapeutic anticoagulation is a risk associated with all anticoagulation therapy. In addition to holding anticoagulation therapy, pharmacologic antidotes to anticoagulants and fresh frozen plasma (FFP) can be administered to reverse the anticoagulant effect. These reversal agents differ in terms of their target, onset of action, duration of reversal effect, and adverse effect profile. Such agents may directly antagonize the anticoagulants' pharmacological effects or replace normal coagulation factors (*return of hemostasis*).

Patients who are receiving anticoagulation therapy are either at high risk for a thromboembolic event or are being treated for a thromboembolic event and are, therefore, at greater risk for developing a clot. The greatest concern with reversal of anticoagulation is the potential for creating a prothrombotic state in the patient, leading to exacerbated thromboembolic complications. Assessment of the patient's need for reversal based on the urgency of the clinical situation, the associated degree of reversal needed, and the degree to which a patient is anticoagulated at the time of assessment of the need for reversal will dictate the reversal approach(s) used. This chapter will review the pharmacologic agents used for reversal of anticoagulation, including dosing, administration, onset and duration, and adverse effects associated with anticoagulant reversal agents. Chapter 9 will discuss patient-specific assessments of reversal strategies used in anticoagulation therapy.

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### APPROACHES TO REDUCING THE PHARMACOLOGIC EFFECTS OF ANTICOAGULATION

When considering the treatment options to reversing anticoagulation through the use of reversal agents, the approach to selection of the reversal agent(s) needs to account for balancing two things: (1) the urgency of the bleeding event, and the associated emergence of the reversal need with the anticipated timing of response and degree of reversal response (partial versus complete reversal); and (2) the

onset and offset of the reversal agent administered (see **Figure 8-1**), and as the bleeding event is related to the clinical situation and mitigating risks in therapies on exacerbating clots (**Table 8-1**). An elevated coagulation effect beyond the desired target level of anticoagulation without bleeding can be corrected by simply holding the anticoagulation without administration of any reversal agent (**Table 8-2**). However, a patient experiencing a life-threatening bleeding event (i.e., intracranial hemorrhage) or a bleeding event that has the potential for resulting in permanent disabling consequences (i.e., ocular bleeding) may require rapid and complete reversal of the anticoagulant effect.

**TABLE 8-1: Approaches to Reversing Anticoagulation Effects<sup>a</sup>**

<b>Approach</b>	<b>Consideration</b>
Holding the anticoagulant	Goal is hours to days, allowing a natural reduction in pharmacologic effects. It depends on urgency to reverse effect and patient's ability to eliminate the effects of the agent within the desired time period.
Removing drug	If before the drug is absorbed, can administer activated charcoal. Bivalirudin and dabigatran can be removed by dialysis. Drug effects may persist if elimination is impaired (organ failure, drug interactions).
Antidote	Administration of an agent that directly inhibits the pharmacologic effects of an anticoagulant. Goal is minutes to hours to reduce pharmacologic effects, usually when a patient is at high risk of harm or that harm is already occurring.
Establishing hemostasis	Administration of an hemostatic agent (i.e., a procoagulant) that promotes normal coagulation.
Revision of the anticoagulation approach	Goal is to reduce therapy target usually related to changes in risk acceptance. Usually does not involve an antidote.

<sup>a</sup>**Note:** Approach may include complete or partial reduction of anticoagulation.