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**INDICATIONS**

Idarucizumab is indicated for reversing the anticoagulant activity of dabigatran in patients requiring emergency surgery/urgent procedures or experiencing life-threatening or uncontrolled bleeding. Approval was based on the accelerated approval process that used data from healthy volunteers; the continued marketing approval of idarucizumab is contingent upon the completion of a case series clinical study (REVERSE-AD). Idarucizumab is not indicated or useful as a reversal agent for any other anticoagulant or antithrombotic therapy. Idarucizumab has also been used in vitro to facilitate proper diagnosis of coagulation disorders or thrombophilia in patients treated with dabigatran.

**CLINICAL PHARMACOLOGY**

Idarucizumab is a humanized mouse monoclonal antibody fragment of immunoglobulin G1 (IgG1) that specifically binds dabigatran and its acylglucuronide metabolites. Dabigatran is a direct thrombin inhibitor that binds free and clot-bound thrombin, which prevents the conversion of fibrinogen to fibrin and the eventual formation of a clot. By binding dabigatran, idarucizumab reverses the anticoagulant effects of dabigatran. Idarucizumab has a high affinity for dabigatran (350 times greater than for thrombin) and maintains its effects for up to 24 hours.

Idarucizumab is able to immediately decrease the plasma levels of dabigatran below the limit of detection in humans (including older patients 65 to 85 years of age and patients with renal impairment).
Idarucizumab rapidly (within 5 minutes) reverses dabigatran-induced anticoagulation and blood loss in a dose-dependent manner in animals, corresponding to a dose-dependent increase in fibrinopeptide A (FPA) (a marker for fibrin formation).\textsuperscript{4,9,10,13-18} Ex vivo porcine studies showed idarucizumab restored coagulation parameters, including prothrombin time, activated partial thromboplastin time (aPTT), clotting time, clot formation time, and maximum clot firmness, to baseline values, while prothrombin-complex concentration (PCC), activated PCC, and recombinant activated factor VII did not restore all parameters to baseline levels.\textsuperscript{5} Another ex vivo porcine evaluation found that the addition of tranexamic acid and fibrinogen concentrate enhanced idarucizumab’s ability to reverse dabigatran activity.\textsuperscript{12}

In some patients, idarucizumab may cause dabigatran to redistribute from peripheral compartments into the plasma, which may be associated with re-elevation of coagulation parameters (eg, diluted thrombin time [dTT], ecarin clotting time [ECT], activated partial thromboplastin time [aPTT], and thrombin time).\textsuperscript{1}

Idarucizumab does not impact coagulation parameters or thrombin plasma levels unless the patient has been pretreated with dabigatran.\textsuperscript{1,4,6} If continued dabigatran therapy is desired, dabigatran can be reinitiated 24 hours after the last dose of idarucizumab without any changes to the pharmacokinetics/pharmacodynamics of dabigatran.\textsuperscript{1,11}

**PHARMACOKINETICS**

When administered alone, idarucizumab plasma concentrations over time are similar to concentration-time profiles when concomitantly administered with dabigatran.\textsuperscript{1}

Idarucizumab plasma levels increase proportionally with increasing doses (between 20 mg and 8 g). The median time-to-peak plasma concentration after intravenous (IV) administration of idarucizumab 4 g was 1.06 hours when infused over 1 hour and 10.06 minutes when infused over 5 minutes.\textsuperscript{6}

Idarucizumab distribution follows multiphasic disposition kinetics with limited extravascular distribution. Volume of distribution is 8.9 L after a single IV dose of idarucizumab 5 g.\textsuperscript{1}

Because idarucizumab is a protein drug, it is metabolized by peptidases into smaller peptides and amino acids. These may be eliminated from the body or reabsorbed for general protein synthesis.\textsuperscript{1}

Clearance of idarucizumab is 47 mL/min, with an initial half-life of 47 minutes and a terminal half-life of 10.3 hours.\textsuperscript{1} Dabigatran, on the other hand, has a half-life of 12 to 14 hours.\textsuperscript{8} The clearance of idarucizumab is reduced in patients with mild or moderate renal impairment, which leads to increased levels of idarucizumab (43.5% or 83.5% increase in area under the curve [AUC], respectively). However, this increase in idarucizumab levels does not affect its reversal capability.\textsuperscript{1}

Following IV administration of a single dose of idarucizumab 5 g, 32.1% was excreted in the urine within 6 hours and less than 1% within the following 18 hours. The remainder of the dose is assumed to undergo protein catabolism and be excreted via the kidneys.\textsuperscript{1} Trace amounts of idarucizumab were detectable in plasma for up to 15 to 24 hours after administration, depending on the dose administered.\textsuperscript{6}

Population pharmacokinetic analyses indicate that pharmacokinetics of idarucizumab are not influenced by age, gender, race (White vs Asian), or body weight.\textsuperscript{1}

**COMPARATIVE EFFICACY**

**Indication:** Bleeding Related to Dabigatran Therapy

**Guidelines**

**Guideline:** Guidance on the emergent reversal of oral thrombin and factor Xa inhibitors

**Reference:** Kaatz S, et al, 2012\textsuperscript{19}

**Comments:** To emergently reverse dabigatran anticoagulant effects, oral activated charcoal, hemodialysis or hemoperfusion, fresh frozen plasma (FFP), recombinant activated factor VII, or PCC may be used. Additionally, patients requiring urgent reversal of dabigatran-based anticoagulation should be treated with supportive measures (eg, fluid resuscitation, red blood cell transfusions) as needed. Immediate discontinuation of dabigatran will facilitate the reversal of dabigatran-based anticoagulation in patients with normal renal function. Oral activated charcoal may adsorb dabigatran if dabigatran exposure is recent (within 2 hours of symptoms). Hemodialysis or hemoperfusion may be performed, particularly in patients with poor renal function, in addition to using activated charcoal. As studies indicate, 62% of dabigatran is removed after 2 hours of hemodialysis (68% after 4 hours). Animal studies suggest that FFP and recombinant activated factor VII
decrease the anticoagulant effects of dabigatran. It is difficult to extrapolate the effects of FFP and recombinant activated factor VII from animals to humans; thus, the guideline recommends that FFP and recombinant activated factor VII not be used to attempt reversal of dabigatran effects. PCCs did not produce promising results in a small study in humans; coagulation parameters did not change with PCC exposure. Idarucizumab was not mentioned in this guideline.

**Guideline:** Guideline on the management of bleeding in patients on antithrombotic agents


**Comments:** Minor bleeding from dabigatran exposure can be managed by discontinuing dabigatran, applying direct pressure, and replacing fluids. Activated charcoal can be orally administered to patients if dabigatran is administered within 2 hours of bleeding. Hemodialysis or hemofiltration may be used to accelerate the removal of dabigatran, particularly in patients with poor renal function. There are no well-studied treatments available for treating major bleeding from exposure to dabigatran. PCC, activated PCC, and recombinant activated factor VII did not correct coagulation parameters in animal models treated with dabigatran or in small studies with human volunteers. Idarucizumab was not mentioned in this guideline.

**Studies**

**Drug:** Idarucizumab vs Placebo

**Reference:** Praxbind, 2015

**Study Design:** Randomized, placebo-controlled, pharmacokinetic/pharmacodynamic study

**Study Funding:** Boehringer Ingelheim

**Patients:** 283 healthy volunteers were enrolled in 3 distinct safety, dose-ranging studies to assess the effects of idarucizumab on dabigatran levels and coagulation parameters. Of the 283 healthy volunteers, 224 received at least 1 dose of idarucizumab. The majority of subjects were male and younger than 65 years (median age, 36 years); 19 volunteers were female and 30 were 65 years or older.

**Intervention:** Healthy volunteers were given oral dabigatran 220 mg twice daily for 3 days and another single dose of dabigatran 220 mg 2 hours prior to receiving IV idarucizumab (or placebo) on day 4. Idarucizumab 5 g was given as a single IV infusion over 5 minutes.

**Results**

**Primary Endpoint(s)**

- Coagulation parameters (ie, dTT, aPTT, ECT, thrombin time, and activated clotting time) from 28 subjects showed an immediate decrease with idarucizumab, and the decrease was sustained for up to 24 hours after the infusion of the idarucizumab dose. There were no changes in coagulation parameters with placebo; coagulation parameters decreased at a rate corresponding to the normal rate of elimination for dabigatran.

**Comments:** A single dose of idarucizumab 5 g infused over 5 minutes in healthy volunteers exposed to dabigatran results in an immediate reversal of dabigatran's anticoagulant activity.

**Limitations:** Data were extracted only from idarucizumab product labeling.

**Drug:** Idarucizumab

**Reference:** Pollack CV, et al, 2015 (RE-VERSE AD trial)

**Study Design:** Open-label, prospective cohort, single-arm, multicenter, international study

**Study Funding:** Boehringer Ingelheim

**Patients:** Up to 300 patients 18 years or older taking dabigatran are planned to be enrolled in this ongoing study. Interim results were based on the first 90 patients recruited. All patients were separated into 2 groups based on reason for idarucizumab therapy: group A patients had overt, uncontrolled, or life-threatening bleeding that required a reversal agent, and group B patients had a condition that required emergency surgery or an invasive procedure within 8 hours for which normal hemostasis was necessary. At baseline, patients had a median age of 76.5 years (range, 48 to 93 years); 56% were male; 87% were White, 7% were Asian, and 7% were Hawaiian or Pacific Islander; median weight was 71.9 kg; average creatinine clearance was 62 mL/min (17% with 80 mL/min or greater, 30% with between 50 and 80 mL/min, 22% with between 30 and 50 mL/min, and 13% with less than 30 mL/min); 64% were receiving dabigatran 110 mg twice daily, 32% were receiving dabigatran 150 mg twice daily, and 1% were receiving dabigatran 75 mg twice daily; 96% had atrial fibrillation and 1% had venous thromboembolism; median time since last dose of dabigatran was 15.4 hours; and 76% had elevated dTT and
90% had elevated ECT. Patients were excluded from group A if they had minor bleeding (eg, epistaxis, hematuria) or no clinical signs of major bleeding. Patients were excluded from group B if they were undergoing a surgery or procedure that was elective or associated with a low risk of bleeding. Exclusion criteria for both groups included a contraindication or hypersensitivity to study drug (ie, hereditary fructose intolerance to the sorbitol constituent).

**Intervention:** Patients were given an IV bolus infusion of idarucizumab 5 g (2 vials of 2.5 g administered within 15 minutes). No dose adjustment was allowed; no partial doses and no repeat doses were given.

**Results**

**Primary Endpoint(s)**
- Median change in maximum percentage reversal of dabigatran's anticoagulant activity (based on dTT and ECT) at 4 hours after the second infusion from the end of the first infusion was 100% (95% confidence interval [CI], 100% to 100%) for groups A and B. Idarucizumab's reversal of dabigatran-induced anticoagulation occurred shortly after completion of the first IV bolus infusion.

**Secondary Endpoint(s)**
- aPTT and thrombin times were below the upper limit of normal (ULN) as early as following the first infusion, similar to dTT and ECT results.
- Unbound dabigatran levels at 4 hours after the second infusion were near the lower limit of quantification (LLOQ); these low levels were sustained for at least 24 hours in 79% of patients.
- Median time to bleeding cessation in group A patients was 11.4 hours.
- The majority of group B patients (92%) had normal intraoperation hemostasis; only 3 patients were reported to have mild or moderate abnormal hemostasis during their respective operations.
- 18 patients (9 in each study group) died during the study, but no deaths were considered to be related to idarucizumab therapy.

**Comments:** A single dose of idarucizumab 5 g, consisting of 2 infusions of 2.5 g within 15 minutes of each other, completely reversed the anticoagulant activity of dabigatran in patients with uncontrolled bleeding or those in need of emergency surgery or invasive procedures. Reversal of dabigatran activity was observed even before the second infusion of idarucizumab. While the majority maintained low coagulation values (ie, dTT and ECT values below the ULN), some patients experienced a re-elevation of coagulation parameters 12 to 24 hours after the second infusion of idarucizumab. All endpoints were analyzed using the modified intention-to-treat (mITT) population (patients with sufficient data to measure respective endpoints). When measured clotting times (from dTT and ECT tests) exceeded the maximum measurable range, the maximum measurable clotting time (500 seconds) was imputed when concomitant test results (eg, other coagulation tests) were consistent with high clotting times. This study did not include a control group; a placebo control or nonactive treatment group was determined to be unethical and the efficacy of PCC to reverse the effects of dabigatran has not been established with a clinical trial. The efficacy information in the product labeling is based on data from 123 patients with similar results. This study is being conducted in the United States and 36 other countries.

**Limitations:** This phase 3 cohort study is currently ongoing. It is scheduled to continue until 300 patients are enrolled. Study enrollment began June 2014, and the expected completion date is July 2017.
with elevated coagulation parameters who require a second emergency surgery/urgent procedure. However, the safety and efficacy of repeat treatment with idarucizumab has not been established. There are insufficient data regarding the risk of a hypersensitivity reaction, but adverse events reported by patients in clinical trials suggest that idarucizumab may cause hypersensitivity reactions. The risks associated with use in patients with a known hypersensitivity to idarucizumab should be weighed against the benefits of such an emergency treatment. If an anaphylactic reaction or other serious hypersensitivity reaction occurs, immediately discontinue idarucizumab administration and employ supportive standard care until the problem has resolved.

Patients with hereditary fructose intolerance may adversely react to the sorbitol used as an excipient. Possible adverse reactions include hypoglycemia, hypophosphatemia, metabolic acidosis, increase in uric acid, and acute liver failure with deterioration of excretory and synthetic function.

Idarucizumab is not intended for the treatment of minor bleeds (eg, epistaxis, hematuria). Standard supportive care should be used to control minor bleeding episodes.

The efficacy and safety of idarucizumab have not been studied in pregnant women or in pregnant animal models, and the efficacy and safety of idarucizumab during labor and delivery have not been studied. The risk of fetal harm or altered reproduction capacity from idarucizumab exposure is unknown. Administer idarucizumab in pregnant women only if clearly necessary.

The degree to which idarucizumab is excreted in human milk is unknown. It is recommended that caution be used when administering idarucizumab to breast-feeding women, taking into consideration the benefits of breast-feeding and the mother’s clinical need for idarucizumab therapy.

The efficacy and safety of idarucizumab have not been studied in pediatric patients. In clinical trials including 111 participants 65 years or older and 74 participants 75 years or older, there were no differences in efficacy or safety of idarucizumab when compared with younger patients; however, it is possible that some older patients may experience a greater sensitivity to idarucizumab exposure.

No dose adjustments are needed for patients with renal impairment. Idarucizumab has not been studied in patients with hepatic impairment.

**ADVERSE REACTIONS**

Common adverse reactions observed in clinical trials included headache, hypokalemia, delirium, constipation, pyrexia, and pneumonia. Adverse events suggestive of possible hypersensitivity to idarucizumab included pyrexia, bronchospasm, hyperventilation, rash, and pruritus. Thrombotic events were observed in 5 of 123 patients, but these events occurred while not receiving antithrombotic therapy and were attributed to the patients’ respective underlying medical conditions. Although transient elevations in urine proteins were observed, there was no evidence of acute tubular injury or loss of renal function.

Preexisting anti-idarucizumab antibodies occurred infrequently (13%) and the majority (97%) were ineffective at neutralizing idarucizumab’s activity because they targeted the C-terminus instead of the dabigatran-binding sites. Preexisting anti-idarucizumab antibodies did not affect the pharmacokinetics or efficacy of idarucizumab and did not alter the risk of hypersensitivity. Anti-idarucizumab antibodies that may have emerged after idarucizumab therapy were observed in 4% of patients. Of the patients with possible treatment-emergent anti-idarucizumab antibodies, 56% (5 of 9 patients) had specificity for the C-terminus, 22% (2 of 9 patients) had specificity for the variable region, 11% (1 of 9 patients) had mixed specificity, and 11% (1 of 9 patients) had indeterminate specificity.

**DRUG INTERACTIONS**

Idarucizumab specifically targets dabigatran; therefore, idarucizumab does not impact other anticoagulant or antithrombotic pharmacokinetic/pharmacodynamic parameters.

In vitro data indicate that idarucizumab’s ability to reverse dabigatran activity is not affected by coagulation factor concentrations, including 3- or 4-factor PCCs, activated PCC, or recombinant factor VIIa.

Coadministration of volume expanders, including lactated Ringer’s, hydroxyethyl starch (130/0.4) 6%, hydroxyethyl starch (200/0.5) 6%, succinylated gelatin 4%, and washed red blood cells, does not alter idarucizumab’s ability to bind dabigatran or reverse dabigatran-induced anticoagulation.

**RECOMMENDED MONITORING**

Monitor for signs and symptoms of decreased bleeding. Coagulation parameters (eg, dTT, ECT, aPTT, thrombin time) should be closely monitored until normalized to baseline values.
DOsing
The recommended dose is idarucizumab 5 g (2 vials containing 2.5 g each) administered IV; there is limited evidence to support administering another dose of idarucizumab 5 g. Under aseptic conditions, administer idarucizumab either as 2 consecutive infusions or as 2 consecutive bolus injections. Coadministration of supportive standard care may be necessary to manage hypersensitivity reactions.1

Infusions must be prepared in an aseptic environment and administered using aseptic techniques. No other medicinal product should be mixed with idarucizumab and no other infusion should be administered in parallel via the same IV access. If using a preexisting line to administer idarucizumab, first flush the line with sterile sodium chloride 0.9% injection. Prior to administration, parenteral solutions should be visually inspected for particulate matter and discoloration. Once removed from the vial, idarucizumab should be administered immediately or within 1 hour.1

In a dose-ranging study, idarucizumab 1, 2, or 4 g IV was infused over 5 minutes 2 hours after the last dose of dabigatran. Doses of 2 and 4 g reversed dabigatran’s effects on FPA, ECT, and dTT.2,3,4 Another dose-ranging study evaluated idarucizumab 1, 2.5, and 5 g infused IV over 5 minutes 2 hours after the last dose of dabigatran in healthy adults, elderly adults, and renally impaired individuals. Reversal of dabigatran effects were sustained with doses of 2.5 and 5 g, and anticoagulation with dabigatran was reestablished 24 hours after idarucizumab exposure.11

Dabigatran may be reintiated 24 hours after idarucizumab administration without any notable changes to the pharmacokinetic/pharmacodynamic properties of dabigatran.1,11 If possible, anticoagulant therapy should be resumed as soon as possible if the patient has a continued thrombotic risk from their underlying disease.1

Administration of idarucizumab 2 months after initial exposure was found to be equally effective and safe.1,11

Product Availability
Idarucizumab was granted accelerated approval on October 16, 2015.2,25 It is available in packages of 2 single-use vials, each containing a 2.5 g per 50 mL solution that is sterile, preservative-free, colorless to slightly yellow, and clear to slightly opalescent. The buffered (pH 5.3 to 5.7), isotonic (270 to 330 mOsm/kg) solution also contains acetic acid glacial, polysorbate 20, sodium acetate trihydrate, sorbitol, and water for injection.1

Idarucizumab should be stored in the refrigerator at temperatures between 2°C and 8°C (36°F and 46°F). If kept in its original packaging and protected from light, an unopened vial can be stored at room temperature (25°C [77°F]) for up to 48 hours. If exposed to light, an unopened vial can be stored at room temperature for up to 6 hours. The solution should not be frozen or shaken.5

Drug Safety/Risk Evaluation and Mitigation Strategy (REMS)
No REMS is required for idarucizumab.2

Conclusion
Idarucizumab is a novel drug for the treatment of patients who require emergent reversal of dabigatran-induced anticoagulation. Idarucizumab is a humanized mouse monoclonal antibody fragment that specifically targets dabigatran, which binds thrombin (free and clot bound). In the presence of idarucizumab, dabigatran is not available to bind thrombin, which enables thrombin to convert fibrinogen to fibrin and produce clots. Idarucizumab has a short half-life, allowing effective re-anticoagulation with dabigatran 24 hours after the last dose of idarucizumab. A single dose of idarucizumab (2 infusions of 2.5 g within 15 minutes) immediately and completely reversed the anticoagulant effects of dabigatran. The safety and efficacy of repeat administration have not been established but the product labeling recommends an additional dose if the patient’s coagulation parameters remain elevated and the patient is still experiencing clinically relevant bleeding or requires a second surgery. Coagulation parameters should be monitored closely after initiating idarucizumab therapy. Common adverse effects of idarucizumab include headache, hypokalemia, delirium, constipation, pyrexia, and pneumonia.

References
1. Praxbind (idarucizumab) [prescribing information]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals Inc; October 2015.


Continuing Education Case Study Quiz

Goal—The goal of this activity is to educate pharmacists about the use of idarucizumab for the reversal of dabigatran anticoagulant activity.

Objectives—At the completion of this activity, the reader will be able to:
1. Describe the pharmacology and pharmacokinetics of idarucizumab.
2. Discuss the risks associated with the use of idarucizumab.
3. Discuss the potential benefit of idarucizumab for an individual patient.
4. Apply the information on the use of idarucizumab to a case study.

Key Words—idarucizumab, dabigatran, bleeding, new drugs

This CE activity is jointly provided by ProCE, Inc. and Hospital Pharmacy. ProCE, Inc. is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education. ACPE Universal Activity Number 0221-9999-16-024-H01-P has been assigned to this knowledge-based home-study CE activity (initial release date 03-01-2016). This CE activity is approved for 1.5 contact hours (0.15 CEUs) in states that recognize ACPE providers. This CE activity is provided at no cost to participants. Completion of the evaluation and the post-test with a score of 70% or higher are required to receive CE credit. No partial credit will be given.

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1. Idarucizumab has been approved by the US Food and Drug Administration (FDA) for which of the following conditions in patients who are being treated with dabigatran?
   A. Emergency surgery
   B. Urgent procedures
   C. Uncontrolled bleeding
   D. All of the above

2. An older adult currently taking dabigatran presented at the hospital with profuse epistaxis (nosebleed). Which of the following management strategies is least appropriate?
   A. Apply direct pressure to and insert gauze or cotton in the affected nostril(s).
   B. Monitor and wait for this self-limiting event to spontaneously resolve.
   C. Immediately treat with idarucizumab to reverse dabigatran's activity.
   D. Administer volume expanders as needed to replenish blood volume.
3. How quickly does the monoclonal antibody fragment idarucizumab reverse the anticoagu-
lant activity of dabigatran?
A. Within 15 minutes
B. Within 60 minutes
C. Within 5 hours
D. Within 15 hours

4. Administering idarucizumab may cause dabiga-
 tran to redistribute back into the plasma from
the periphery, which would be evidenced by
which of the following observations?
A. Increase in diluted thrombin time (dTT),
  ecarin clotting time (ECT), activated par-
tial thromboplastin time (aPTT), thrombin
time (TT)
B. Decrease in dTT, ECT, aPTT, TT
C. No change in dTT, ECT, aPTT, TT

5. How long after the last dose of idarucizumab
can dabigatran therapy be reinitiated to continue
anticoagulation therapy for a patient’s underly-
ing disease state?
A. 15 minutes
B. 60 minutes
C. 4 hours
D. 24 hours

6. Clearance of idarucizumab is diminished in
patients with mild or moderate renal impair-
ment. How should idarucizumab be dosed in
patients with renal impairment?
A. Administer a single dose of 5 g; 2 doses of
  2.5 g within 15 minutes
B. Administer half a single dose of 5 g; 1 dose
  of 2.5 g
C. Administer twice a single dose of 5 g; 2 doses
  of 5 g within 15 minutes
D. Do not administer idarucizumab in patients
  with renal impairment.

7. Idarucizumab should be administered via which
route of administration?
A. Oral
B. Intravenous
C. Intramuscular
D. Subcutaneous

8. A patient responded to idarucizumab therapy
with hypoglycemia, metabolic acidosis, and
acute liver failure. Which of the following cor-
rectly explains the observed adverse events?
A. Idarucizumab is commonly associated with
  these adverse events.
B. These are some of the serious adverse events
  observed with idarucizumab.
C. The patient has hereditary fructose intolerance
  and reacted to sorbitol.
D. Idarucizumab caused a hypersensitivity reac-
tion in the patient.

9. Once removed from the vial, idarucizumab
should be administered within what timeframe?
A. Within 15 minutes
B. Within 60 minutes
C. Within 12 hours
D. Within 24 hours

10. Which of the following may interact with idaru-
cizumab’s ability to reverse dabigatran activity?
A. Prothrombin complex concentrates and
  recombinant factor VIIa
B. Lactated Ringer’s solution and washed red
  blood cells
C. All of the above decrease the efficacy of
  idarucizumab.
D. None of the above decreases the efficacy of
  idarucizumab.

11. Which of the following is a common adverse
reaction associated with idarucizumab exposure?
A. Headache
B. Bronchospasm
C. Thrombosis
D. Hypovolemia

Case History
Z.B. is a 66-year-old, 82-kg male with nonvalvu-
lar atrial fibrillation and no known medication aller-
gies. In addition to atrial fibrillation, he has diabetes,
high blood pressure, and benign prostatic hyperpla-
sia. Current medications include metformin, glipi-
zide, metoprolol, lisinopril, hydrochlorothiazide, and
dabigatran.
12. This past year, Z.B. had inguinal hernia repair procedure, colonoscopy for a polyp biopsy, cholecystectomy for acute cholecystitis, and transurethral resection of the prostate. For which event would idarucizumab have been necessary?
   A. Inguinal hernia repair procedure
   B. Colonoscopy for biopsy of colon polyp
   C. Cholecystectomy for acute cholecystitis
   D. Transurethral resection of the prostate

13. Z.B. was given a dose of idarucizumab prior to the above event. His coagulation parameters (eg, aPTT and ECT) were observed to be elevated 16 hours after the last dose of idarucizumab. There was no evidence of active bleeding. Which of the following would be the best course of action?
   A. Administer another dose of idarucizumab to reduce potential risk of bleeding.
   B. Begin hemodialysis to remove dabigatran since idarucizumab failed to work.
   C. Administer coagulation concentrates such as prothrombin-complex concentrate (PCC) or recombinant factor VIIa.
   D. Continue to monitor for active bleeding until coagulation parameters normalize.

14. Z.B. responded well to idarucizumab and successfully completed the procedure. Given his medical history, what should have been the next step in Z.B.’s care?
   A. Restart dabigatran 4 hours after the last dose of idarucizumab.
   B. Restart dabigatran 24 hours after the last dose of idarucizumab.
   C. Do not restart dabigatran since idarucizumab was administered.
   D. Initiate warfarin therapy after the last dose of idarucizumab.

15. By the next year, Z.B is no longer taking dabigatran; he was prescribed rivaroxaban. If Z.B. was admitted into the hospital for acute gastrointestinal bleeding today, can he be retreated with idarucizumab?
   A. Yes, idarucizumab can be safely and effectively readministered after 2 months of the last dose.
   B. No, idarucizumab readministration is safe and effective after 4 months from the last dose.
   C. Yes, idarucizumab effectively binds to all factor Xa inhibitors.
   D. No, idarucizumab has not been shown to bind to rivaroxaban.