Idarucizumab (Praxbind) is a new treatment to reverse the effects of the nonvitamin K antagonist oral anticoagulant (NOAC) dabigatran if emergency surgery is needed or to prevent life-threatening or uncontrolled bleeding. This article describes its properties, efficacy and adverse effects.

**KEY POINTS**

- Idarucizumab is a monoclonal antibody fragment against the oral anticoagulant dabigatran
- It is licensed for the rapid reversal of the anticoagulant effects of dabigatran in emergencies or for urgent surgery
- The recommended dose is 5g intravenously
- In an interim analysis of an ongoing trial, idarucizumab rapidly reversed the anticoagulant effects of dabigatran in patients with severe bleeding episodes or who needed surgery
- Treatment was well tolerated
- The absence of comparative studies means its impact on clinical outcomes is unclear
- A 5g dose of idarucizumab (2x2.5g/50ml) costs £2400

By contrast with warfarin, there have previously been no specific drugs to reverse excessive anticoagulation during treatment with a nonvitamin K antagonist oral anticoagulant (NOAC). Management of a bleeding episode involved stopping the NOAC, mechanical compression, surgical haemostasis, fluid replacement and haemodynamic support, and administration of packed red cells, fresh frozen plasma or platelets.¹

Idarucizumab (Praxbind) specifically reverses the effects of the direct thrombin inhibitor NOAC dabigatran. It is a humanised monoclonal antibody antigen-binding fragment (Fab) that binds to dabigatran with very high affinity (approximately 300 times greater than dabigatran’s affinity for thrombin). The Fab-dabigatran complex is formed rapidly but dissociates slowly.

**Indications and dosage**

Idarucizumab is licensed for adults taking dabigatran when rapid reversal of its anticoagulant effects is required for emergency surgery or urgent procedures, or to prevent life-threatening or uncontrolled bleeding.

The recommended dose is 5g, administered as two consecutive 2.5g doses via intravenous infusion or bolus injection. Prolonged clotting time may recur up to 24 hours later and a second 5g dose may be needed if this is associated with clinically relevant bleeding, if potential rebleeding would be life-threatening or the patient needs a second emergency surgery or urgent procedure. The maximum daily dose is not established.

If the patient is clinically stable and adequate haemostasis has been achieved after administration of idarucizumab, other antithrombotic therapy can be started at any time. Treatment with dabigatran can recommence after 24 hours.

No dose adjustment is recommended for age or renal or hepatic impairment. There is no experience of treating children (below the age of 18 years).

Idarucizumab has no known drug interactions, including with warfarin, heparins and NOACs other than dabigatran. There are no contraindications. Reversal of dabigatran’s anticoagulant effects exposes the patient to a risk of thrombosis; anticoagulation should therefore be reinstated when appropriate.

**Efficacy**

In three phase 1 studies (one of which has been published),² idarucizumab reduced plasma concentrations of dabigatran dose dependently, with a 5g dose achieving almost complete suppression in virtually all healthy volunteers (see Figure 1).³,⁴ Complete reversal of the effects of dabigatran as measured by diluted thrombin time (dTT) occurred at

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the conclusion of the infusion, which took about five minutes to administer, and lasted a mean of 59 hours (median 72 hours). Failure to achieve complete reversal was associated with very aberrant measures of coagulation or a body load of dabigatran greater than the binding capacity of administered idarucizumab.

An interim analysis has been published of an ongoing cohort study in 90 patients (of up to 300 patients planned) with serious bleeding or who required an urgent procedure during treatment with dabigatran. Most patients were taking dabigatran for stroke prevention secondary to atrial fibrillation; their median age was 77 years. Bleeding episodes included intracranial haemorrhage, gastrointestinal bleeding and trauma. About half of patients also received fresh frozen plasma or packed red cells. The median time since the last dose of dabigatran was 15.4 hours. The primary endpoint was the maximum percentage reversal of the anticoagulant effect of dabigatran, ie when clotting measures were within normal range, four hours after the administration of idarucizumab.

The median time to cessation of bleeding was 11.4 hours among patients in whom this could be determined. The effect on clotting was evaluated only in patients with abnormal clotting tests at baseline. In 68 patients with elevated dTT, median maximum reversal of dabigatran was 100 per cent. dTT was normalised in 98 per cent of patients with bleeding episodes and undergoing surgery respectively. 

As this was a noncomparative study, the size of the effect of idarucizumab on clinical outcomes is unknown.

Adverse events
There was one death and two thrombotic events among the 22 patients with normal clotting tests at baseline, and 17 deaths and three thrombotic events among the 68 patients with prolonged clotting measures. None of the deaths was attributed to idarucizumab treatment.

The overall frequency of treatment-related adverse events associated with idarucizumab was similar to placebo. In healthy volunteers, idarucizumab was associated with slightly more frequent headache (5.4 vs 1.9 per cent) and skin irritation (2.7 vs 1.9 per cent) than placebo. Idarucizumab appears to have a low potential for immunogenicity.

References

Declaration of interests
None to declare.

Steve Chaplin is a pharmacist who specialises in writing on therapeutics.