

PRAXBIND® – THE SPECIFIC REVERSAL AGENT TO PRADAXA®



To advance anticoagulation care, Boehringer Ingelheim developed Praxbind® (idarucizumab), a specifically targeted reversal agent to Pradaxa® (dabigatran) for use in rare emergency situations when patients require urgent reversal of its anticlotting effect.^{1,2} Boehringer Ingelheim began research on Praxbind® in 2009, before the first marketing authorisation of Pradaxa® for stroke prevention in atrial fibrillation (AF) in 2010.^{3,4}

In 2015, Praxbind® became the first and only specific reversal agent for a non-vitamin K antagonist oral anticoagulant (NOAC) to be approved by regulatory authorities including the US Food and Drug Administration (FDA) and European Medicines Agency (EMA).^{5,6} Praxbind® is indicated for adult patients treated with Pradaxa® who require rapid reversal of its anticoagulant effects prior to urgent procedures / emergency surgery or in life-threatening or uncontrolled bleeding.^{5,6}

About Praxbind®

Praxbind® is a humanized antibody fragment (Fab) designed as a specific reversal agent to Pradaxa®.¹

Praxbind® binds specifically to dabigatran molecules only, neutralising their anticoagulant effect without interfering with the coagulation cascade.^{1,2} This helps physicians focus on other vital aspects of emergency patient management beyond anticoagulant reversal in Pradaxa®-treated patients.

Intended usage

Praxbind® is designed for use in Pradaxa®-treated patients who require urgent anticoagulant reversal:

- Patients requiring urgent procedures / emergency surgery (e.g. surgery for an open fracture after a fall)
- Patients with life-threatening or uncontrolled bleeding complications (e.g. intracranial haemorrhage or severe trauma after a car accident).²

Regulatory milestones

Praxbind® is approved as a specific reversal agent for Pradaxa® in 61 countries and is available in more than 8,200 sites.

- **February and March 2015:** Praxbind® was submitted under an accelerated approval pathway to the US FDA, EMA and Health Canada for use in Pradaxa®-treated patients who require urgent anticoagulant reversal⁷
- **June 2014 and May 2015** respectively: The FDA granted Praxbind® both Breakthrough Therapy and Orphan Drug Designation^{8,9}
- **October 2015 and November 2015** respectively: Praxbind® approved in the US and EU for adult patients treated with Pradaxa® who require rapid reversal of its anticoagulant effects prior to emergency surgery / urgent procedures or in life-threatening or uncontrolled bleeding^{5,6}
- **Future:** Regulatory reviews and submissions in other countries are ongoing. Boehringer Ingelheim plans to make Praxbind® available in all countries where Pradaxa® is licensed.³

Efficacy & safety results from Phase I studies

Phase I studies in healthy volunteers have shown:

- A 5 minute infusion of Praxbind® (>2 g) led to immediate, complete and sustained reversal of Pradaxa® (NCT01688830)¹⁰
- No clinically relevant side effects were identified and Praxbind® did not over activate clot production (a pro-coagulant effect)¹⁰
- Consistent results have also been seen with the dose of 5 g Praxbind® in elderly and renally-impaired individuals (NCT01955720)¹¹
- Praxbind® restored wound-site formation of fibrin, the main component of a blood clot, indicating that Praxbind® both reverses Pradaxa® as well as simultaneously restores coagulation¹²
- Additionally, Pradaxa® treatment could be re-initiated as early as 24 hours after administration of Praxbind® and its anticoagulant effect was restored.¹¹

**Phase III
study:
RE-VERSE
AD™
(NCT02104947)**

The efficacy and safety of Praxbind® has been evaluated in RE-VERSE AD™, a global Phase III patient study in the emergency setting (NCT02104947). This study involved Pradaxa®-treated patients who required an urgent procedure / emergency surgery, or experienced life-threatening or uncontrolled bleeding complications.²



RE-VERSE AD™ was designed to evaluate the types of patients and real-world situations that healthcare professionals may see in the emergency setting. This includes severely ill or injured patients (e.g., patients involved in a car accident with multiple injuries, patients with an aortic aneurysm, patients receiving an organ transplant) who as such require urgent reversal of dabigatran. A total of 503 dabigatran-treated patients aged 18 years or over were enrolled from 173 of 369 initiated centres in 39 countries worldwide.^{2,13,14}

Results from a first interim analysis including 90 patients enrolled in RE-VERSE AD™, simultaneously published in the *New England Journal of Medicine (NEJM)* and presented at the International Society of Thrombosis and Haemostasis 2015 Congress in Toronto, Canada in June 2015, demonstrated that:^{15,16}

- 5 g of Praxbind® immediately reversed the anticoagulant effect of Pradaxa® in patients requiring urgent anticoagulant reversal
- After 4 and 12 hours, laboratory tests showed normal coagulation levels in almost 90% of patients.

In July 2017, final data including 503 patients were presented as a late-breaking abstract at the International Society on Thrombosis and Haemostasis (ISTH) 26th Biennial Congress in Berlin, Germany and simultaneously published in the *NEJM*. The results confirmed the safety and efficacy of Praxbind® in emergency situations by validating that:^{17,18}

- Administration of Praxbind® resulted in immediate and complete reversal of the anticoagulant effect of Pradaxa®
- Reversal was sustained for 24 hours in the majority of patients
- In patients enrolled with acute bleeding for whom cessation of bleeding could be assessed, the median time to cessation of bleeding was 2.5 hours
- In patients enrolled with a need for surgery or intervention, the required procedures could be initiated after a median of 1.6 hours
- In 93.4 percent of patients requiring procedures, haemostasis during the procedure was described as 'normal'
- No safety concerns attributed to Praxbind® were detected
- Mortality rates at 90 days were 18.8 percent in patients admitted with uncontrolled bleeding and 18.9 percent in patients requiring urgent surgery
- Thrombotic events at 90 days occurred in 6.3 percent of patients with uncontrolled bleeding and 7.4 percent of patients requiring urgent surgery, which is consistent with rates reported after major surgical procedures or hospitalisation for uncontrolled bleeding in patients who had taken a vitamin K antagonist.

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