Boehringer Ingelheim

Clinical Study Synopsis for Public Disclosure

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The synopsis - which is part of the clinical study report - had been prepared in accordance with best practice and applicable legal and regulatory requirements at the time of study completion.

The synopsis may include approved and non-approved uses, doses, formulations, treatment regimens and/or age groups; it has not necessarily been submitted to regulatory authorities.

A synopsis is not intended to provide a comprehensive analysis of all data currently available regarding a particular drug. More current information regarding a drug is available in the approved labeling information which may vary from country to country..

Additional information on this study and the drug concerned may be provided upon request based on **Boehringer Ingelheim's Policy on Transparency and Publication of Clinical Study Data**.

1. ABSTRACT

Name of company: Boehringer Ingelheim India Pvt. Ltd.			
Name of finished medicinal product: Praxbind®			
Name of active ingredient: Idarucizumab			
Report date: 06 Oct 2020	**Study number:** 1321-0023	**Version/Revision:** 1.0	**Version/Revision date:**
Title of study:	Post marketing surveillance program of Praxbind® use in India.		
Keywords:	Reversal, Anticoagulant, Urgent procedure, Praxbind®, Pradaxa®		
Rationale and background:	Praxbind® (Idarucizumab) is a humanized monoclonal antibody fragment (Fab) and a specific reversal agent for Pradaxa® (dabigatran etexilate). Praxbind® binds to Dabigatran and its metabolites with very high affinity and neutralises their anticoagulant effect. Thus, Praxbind® is indicated in patients treated with Pradaxa® to neutralise its anticoagulant effect in emergency surgery/urgent procedures or in life-threatening or uncontrolled bleeding. The aim of this Praxbind® drug administration surveillance program is to collect data on Praxbind® prescription patterns in a clinical practice setting in India.		
Research question and objectives:	The main objective of the Praxbind® administration surveillance program is to evaluate the prescription patterns of use of Praxbind® in a clinical practice setting, with special focus on adverse drug reactions (ADRs) and fatal adverse events (AEs).		
Study design:	Multicenter, non-interventional, drug administration surveillance program.		
Setting:	The study was performed in the Clinical Practice Setting. Participating hospitals had readiness for emergency services and access to Praxbind®.		
Subjects and study size, including dropouts:	This program was initiated after the commercial availability of Praxbind® in India. The study was planned to include 25 patients, requiring Praxbind® as prescribed according to the approved Indian label or the patients included in 2 years at selected centers approved by the regulatory authority, whichever is earlier. The patients who had participated in Pradaxa® studies 1160.189 and 1160.248 and received Praxbind® as per requirement were also to be included in this study. Inclusion criteria: 1. Patients treated with Pradaxa® (dabigatran etexilate) capsules with requirement of rapid reversal of the anticoagulant effects of dabigatran: • For emergency surgery/urgent procedures		

	Or • In life-threatening or uncontrolled bleeding 2. Written informed consent in accordance with International Conference on Harmonization Good Clinical Practice (GCP) guidelines and local legislation and/or regulations. Exclusion criteria: • Participation in a Praxbind® clinical trial
Variables and data sources:	Depending on availability of details, data were anonymized from hospital records and medical notes and entered into the Case report forms (CRF). 1. Site characteristics • Multi-specialty hospitals with emergency management facilities and having access to Praxbind®. • Practice type (academic, non-academic, private, Government); • Availability of prescription/medical records at the site. 2. Patient data • Year of birth • Gender: Male or Female • Vital Signs • Physical Examination • Laboratory data • Pregnancy status in case of female patient 3. Medical History • Name, dose and last intake of previous anticoagulant medications (including Pradaxa®); • Pertaining to haemorrhagic risk factors or impact on safety outcomes (e.g. renal impairment, congenital or acquired coagulation disorders, thrombocytopenia or functional platelet defects, recent biopsy, recent surgery, major trauma, bacterial endocarditis, esophagitis, gastritis, gastroesophageal reflux, hepatic disorders, vascular disorders, neoplasms/cancer, inherited vascular disorder [aneurysms, arteriovenous malformation, microangiopathy] and the HAS-BLED score); • Concomitant treatment pertaining to haemorrhagic risk factors or likely to have an impact on safety outcomes (e.g., acetylsalicylic acid, non-steroidal anti-inflammatory drugs, clopidogrel, selective serotonin reuptake inhibitors or serotonin– norepinephrine reuptake inhibitors, strong P-Gp inhibitors [e.g. ketoconazole, clarithromycin, ticagrelor], chemotherapy, radiation therapy). 4. Praxbind® utilization • Department (emergency, operating room, ICU, other patient setting); • Type of surgery / procedure, if applicable; • Information on bleeding event (whether pre and post Praxbind® administration), location (gastrointestinal tract; intracranial; skin, urogenital tract, intramuscular, retroperitoneal, undefined location, other defined location), if applicable, and if the bleeding was life threatening (yes/no); • Indication: life-threatening or uncontrolled bleeding requiring urgent

	medical intervention; emergency surgery or other urgent medical procedure necessitating rapid reversal of the anticoagulant effect of Pradaxa® prior to surgery/procedure, scheduled or planned surgery/procedure; • Dosage and administration (total dose administered and time interval between the administration of the two vials; number of vials taken one after the other, whether immediate administration of the second vial was mandatory); • Whether Praxbind® administration was discontinued prematurely (yes/no); • Whether the patient required an additional 5 g dose for any of the following conditions as per the label: o recurrence of clinically relevant bleeding together with prolonged clotting times, or o if potential re-bleeding would be life-threatening and prolonged clotting times are observed, or o whether the patient required a second emergency surgery/ urgent procedure and had prolonged clotting times. • Information on restart of anticoagulation therapy (anticoagulation treatment including name, dose and start date); • All ADRs (serious and non-serious) associated with Praxbind®; • All AEs with fatal outcome in patients exposed to Praxbind®. Data sources: Data collected from hospital records and medical notes were entered by the site using electronic CRF forms. Descriptive statistics were calculated for safety and other variables. An interim analysis was not performed. **Primary Outcome:** Any suspected ADRs and fatal AEs; with special focus on hypersensitivity and thrombotic events, occurring within 7 days after Praxbind® administration. **Secondary Outcome:** Percentage of patients who either received Praxbind® for emergency surgery/urgent procedures or for life-threatening or uncontrolled bleeding over a period of 2 years.
Results:	Seven sites were initiated for the post-marketing surveillance study in India. A total of 5 patients who had received Praxbind® were enrolled from four sites in this study; 3 were males and 2 were females, aged between 55 and 77 years, with a mean age of 64.8 years (SD 8.44 years). The ethnicity and race of the patients were not collected. All these 5 patients were previously anticoagulated with Pradaxa®. The reasons for Pradaxa® use in these patients were peripheral artery disease and recent acute coronary syndrome (1 patient); atrial fibrillation (2 patients); venous thromboembolism (1 patient); and cerebrovascular accident (1 patient). Four patients were hospitalised with life-threatening or uncontrolled bleeding: gastrointestinal haemorrhage (2 patients), cerebral haemorrhage (1 patient) and anaemia (1 patient). The patient hospitalized for anaemia was diagnosed with iron deficiency anaemia secondary to chronic blood loss, acute on chronic kidney disease, and deranged coagulation profile. One patient who was hospitalized for an urgent procedure experienced

	dysarthria. This patient was found to have a left middle cerebral artery (MCA) occlusion. Four of the 5 patients receiving Praxbind® were administered the full dose (2 vials) of Praxbind®. According to investigator's discretion, one patient received a single vial as the bleeding (per rectum) had stopped. Of the 4 patients receiving Praxbind® for life threatening or uncontrolled bleeding, 3 patients achieved cessation of bleeding and were hemodynamically stabke while the bleeding status in the fourth patient was not known at the point in time of the last reporting. This patient was hemodynamically stable after use of Praxbind®. The fifth patient received Praxbind® for reversal before initiating thrombolysis treatment with tissue plasminogen activator (tPA). After medical treatment, this patient was found to be stable. All the 5 patients completed the study. None of the enrolled patients reported any suspected ADR (serious or non-serious) or fatal AE. None of the patients reported hypersensitivity or thrombotic AEs. No deaths were reported in the study. Two non-serious AEs of abdominal pain and proctalgia were reported in one patient and were considered not related to study drug by the investigator. Data are missing for CHA2DS2-VASc score and HAS-BLED score calculation as respective lab parameters were not reported.
Discussion:	Praxbind® was used according to the approved label and all patients received Pradaxa® prior to initiation of Praxbind®. Due to the small overall size of the study and the low numbers of patients, this may not represent the general usage of Praxbind® in India. In this post-marketing surveillance study, five patients with life-threatening or uncontrolled bleeding or requiring urgent procedure were treated with Praxbind®. Bleeding had ceased in three patients, in one patient, the bleeding status was not known at the time of last reporting but this patient was hemodynamically stable after use of Praxbind®. One patient received study drug for reversal before initiating thrombolysis for acute ischemic stroke (an urgent procedure) treatment and found to be stable after medical treatment. No deaths, suspected ADR (serious or non-serious) or hypersensitivity or thrombotic AEs were reported in the study.
Marketing Authorisation Holder(s):	Boehringer Ingelheim India Pvt. Ltd.
Names and affiliations of principal investigators:	List of name and affiliation of the principal investigator for this study is provided in Appendix 3.