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| Supplementary Table **Supplementary table S1: Definitions of various variables included in the ETNA-AF-Europe registry** |
| **Patients will be classified in the following categories of edoxaban exposure:**   * Current use: Beginning the day of medication start through date of last use * Recent use: Beginning after the last date of current use continuing for 3 days * Past use: Beginning after 3 days of the last date of current use and continuing through end of study follow-up * Extended-recent use: Beginning after the last date of current use continuing for 30 days\* |
| **Endpoint definition for bleeding events**  **Major bleeding**  A clinically overt bleeding event (i.e. bleeding that is visualised by examination or radiologic imaging) that meets at least one of the following:   1. Fatal bleeding 2. Symptomatic bleeding in a critical area or organ such as:  * Retroperitoneal * Intracranial * Intraocular * Intraspinal * Intra-articular * Pericardial * Intramuscular with compartment syndrome  1. A clinically overt bleeding event that causes a fall in haemoglobin level of 2.0 g/dL (> 1.24 mMol/L) or more†; or a fall of haematocrit of 6.0% or more, adjusted for transfusión   **Major bleeding events will also be further subclassified as:**   * **Life-threatening** - a life-threatening major bleed is defined as a bleeding event that is either intracranial or is associated with haemodynamic compromise requiring intervention * **Non-life threatening**   **Clinically relevant non-major bleeding events:**  A clinically overt bleeding event that requires medical attention that does not fulfil the criteria for a major bleeding event i.e. bleeding requiring medical attention include, but are not limited to, bleeding events that result in the following diagnostic or therapeutic measures:  • Requires or prolongs hospitalisation  • Laboratory evaluation  • Imaging studies  • Endoscopy, colonoscopy, cystoscopy, or bronchoscopy  • Nasal packing  • Compression  • Ultrasound guided closure of an aneurysm  • Coil embolisation  • Inotropic support  • Surgery  • Interruption or stopping anticoagulation at the advice of a physician  • Changing concomitant therapies (e.g. reducing the dose of or discontinuing aspirin) at the advice of a physician  **Minor bleeding event**  Other overt bleeding events that do not fulfil the criteria of a major bleeding event or a clinically relevant non-major bleeding event (e.g. epistaxis that does not require medical attention) will be classified as a minor bleeding event |
| **Adverse drug reaction**  A response to a medicinal product which is noxious and unintended and which occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease or for the restoration, correction or modification of physiological function  It also includes adverse clinical consequences associated with use of the product outside the terms of the Summary of Product Characteristics or other conditions including prescribed doses higher than those recommended, overdoses or abuse  **Serious adverse drug reaction**  Serious adverse reaction is an adverse reaction which:   * Results in death * Is life-threatening * Requires inpatient hospitalisation or prolongation of existing hospitalisation * Results in persistent or significant disability or incapacity * Is a congenital anomaly/birth defect |
| **Effectiveness measures**  Effectiveness will be assessed by the following outcomes:  • Strokes (ischaemic and haemorrhagic)  • Systemic embolic events  • Transient ischaemic attack  • MACE (major adverse cardiovascular events, composite endpoint of non-fatal MI, non-fatal stroke, non-fatal SEE and death due to CV cause or bleeding)  • Venous thromboembolism  • Acute coronary syndrome  • Hospitalisations related to CV condition |

\* A sensitivity analysis will be performed based on the fourth exposure category. †No time interval was specified, interval is specified on the discretion of the treating physician.

CV, cardiovascular; MACE, major adverse cardiac events; MI, myocardial infarction; SEE, systemic embolic events.