# Supplementary files

## Figures and tables

Figure S1. Base case modelled clinical event rates per 1,000 patients for over the full time horizon

Note: There are no adequate and well-controlled head-to-head clinical trials comparing the efficacy and safety of DOACs

Abbreviations: bd, twice-daily; CRB, clinically relevant bleeding; ICH, intracranial hemorrhage; MI, myocardial infarction; od, once-daily; SE, systemic embolism; TIA, transient ischemic attack

Figure S2. Base case deterministic OWSA: ICER per evLYG for apixaban versus comparator arms

Abbreviations: ACM, all-cause mortality; bd, twice-daily; evLY, equal value life-year; evLYG, equal value life-year gained; HR, hazard ratio; HYTG: health years in total gained; ICER, incremental cost-effectiveness ratio; od, once-daily; OWSA, one-way sensitivity analysis.

Figure S3. Base case deterministic OWSA: ICER per HYTG for apixaban versus comparator arms

Abbreviations: ACM, all-cause mortality; bd, twice-daily; HR, hazard ratio; HYTG: health years in total gained; ICER, incremental cost-effectiveness ratio; od, once-daily; OWSA, one-way sensitivity analysis

Figure S4. Probabilistic sensitivity analysis scatter plot (ICER per evLYG) for apixaban versus comparator arms

Abbreviations: bd, twice-daily; evLYG, equal value life-year gained; ICER, incremental cost-effectiveness ratio; od, once-daily

Figure S5. Probabilistic sensitivity analysis scatter plot (ICER per HYTG) for apixaban versus comparator arms

Abbreviations: bd, twice-daily; HYTG, health years in total gained; ICER, incremental cost-effectiveness ratio; od, once-daily

Figure S6. Cost-effectiveness acceptability curve (ICER per evLYG): apixaban (5 mg bd) versus comparator arms

Abbreviations: bd, twice-daily; evLYG, equal value life-year gained; ICER, incremental cost-effectiveness ratio; od, once-daily

Figure S7. Clinical event rates per 1,000 patients during first-line treatment (scenario analysis: alternative treatment effects [informed by Ray et al.[4]])

Note: There are no adequate and well-controlled head-to-head clinical trials comparing the efficacy and safety of DOACs

Abbreviations: bd, twice-daily; CRB, clinically relevant bleeding; ICH, intracranial hemorrhage; MI, myocardial infarction; od, once-daily; SE, systemic embolism; TIA, transient ischemic attack.Tables

Table S1. Model inputs

\* MI disutility applied to baseline AF utility

\*\* Weighted average of mild, moderate, and severe stroke

\*\*\* Weighted average of mild, moderate, and severe hemorrhagic stroke

\*\*\*\* Weighted average of major gastrointestinal bleed, major non-gastrointestinal extracranial hemorrhage, clinically relevant nonmajor extracranial hemorrhage

\*\*\*\*\* based on INR testing once monthly

† based on two GP visits annually

Abbreviations: AF, atrial fibrillation; bd, twice-daily; U.S. Bureau of Labour Statistics; CRB, clinically relevant bleeding; ICH, intracranial hemorrhage; MI, myocardial infarction; od, once-daily; SE, standard error; TIA, transient ischemic attack

Table S2. Generic pricing assumptions

\*cycle length of three months

Table S3. Clinical event rate hazard ratios for rivaroxaban with apixaban (scenario analysis: alternative treatment effects [informed by Ray et al. [4]])

\* Ray et al. [4] reported CRB as gastro-intestinal bleeding, MI as ischemic event, ICH as hemorrhagic stroke and TIA as ischemic event

Abbreviations: ACM, all-cause mortality; bd, twice-daily; CRB, clinically relevant bleeding; HR, hazard ratio; ICH, intracranial hemorrhage; MI, myocardial infarction; od, once-daily; SE, standard error; TIA, transient ischemic attack

Table S4. Summary of costs associated with apixaban and rivaroxaban (scenario analysis: alternative treatment effects [informed by Ray et al. [4]])

Abbreviations: ACM, all-cause mortality; bd, twice-daily; CRB, clinically relevant bleeding; HR, hazard ratio; ICH, intracranial hemorrhage; MI, myocardial infarction; od, once-daily; SE, systemic embolism; TIA, transient ischemic attack

## Societal perspective

### Informal care by caregivers

To evaluate the opportunity cost of informal care given by caregivers, the average age of caregivers must be defined to establish the proportion of the population working for that age range (**Table S1**). The average age of stroke caregivers in the US was reported to be 51.6 years [55].

For each event, the calculation used to establish the weekly cost of informal care was:

The mean wage used in the model is $33.32, [36] and the model assumes that the opportunity cost of leisure time for those unemployed is one third of the mean wage. The proportions of patients receiving care is provided in **Table S1**, alongside the number of hours of informal care required. Due to limited data available for the US, the number of hours per week of informal care for MI and TIA were based on UK data. The proportion of MI patients receiving informal care is set to 0% in the base case due to lack of data. The proportion of stroke patients receiving informal care was applied to stroke and TIA events, however due to the transient nature of TIA events, costs associated with TIA were only applied for one cycle.

### Productivity losses

In addition to informal care, potential productivity losses to the economy due to morbidity and/or mortality were modelled. This utilized the proportion of patients leaving work due to illness, along with the median weekly earnings for the relevant age category. The calculation for weekly productivity losses was:

The median weekly earnings and the proportion of patients leaving work due to illness is defined in **Table S1**. Similar to the informal care costs, costs associated with TIA were only applied for one cycle due to their transient nature. Due to limited data available for the proportion of patients leaving work due to illness in the US, the estimates used in the model were based on UK data.

### Social care costs

After a patient had a stroke, an additional cost was applied in each cycle after the stroke event. Two costs were applied in: (1) the incident year and (2) subsequent years. In the first cycle, a larger cost was applied, and for subsequent cycles, a fixed cyclic cost was applied. The cost for the first quarter was calculated by the following formula:

Social care costs for the first year were sourced from a budget impact model for NVAF in the US Medicare population [36]; costs for the subsequent years were assumed based on a cost analysis of stroke care in England [53].