Cost Effectiveness of Rivaroxaban (Xarelto®) for the Primary Prevention of Venous Thromboembolic Events in Adult Patients who have Undergone Total Hip Replacement or Total Knee Replacement.

National Centre for Pharmacoeconomics

September 2008

Cost Effectiveness of Rivaroxaban (Xarelto®) for the Primary Prevention of Venous Thromboembolic Events in Adult Patients who have Undergone Total Hip Replacement or Total Knee Replacement.

1. Rivaroxaban (Xarelto®) is an oral direct factor Xa inhibitor, which is licensed for the prevention of venous thromboembolic events (VTE) in adult patients undergoing elective total hip replacement (THR) or total knee replacement (TKR) surgery. Rivaroxaban 10mg once daily should be initiated 6-10 hours after surgery completion, provided that haemostasis has been established. It should be continued for 5 weeks post THR and for 2 weeks post TKR.

2. In May 2008, Bayer Healthcare submitted an economic evaluation on the cost effectiveness of rivaroxaban for this indication to the National Centre for Pharmacoeconomics to support its application for reimbursement. An amendment to the cost effectiveness report was submitted on the 5th September 2008. The economic evaluation is conducted from the perspective of the Irish Health Services Executive.

3. The cost effectiveness of rivaroxaban was demonstrated using economic modelling. The model was divided into three modules. The first two modules (prophylaxis and post-prophylaxis) constitute the 90 day acute phase and are represented with a decision tree while the third module represents the long term complications phase and is developed as a Markov process. The model assumes that patients enter the model aged 64 years. The model time horizon is 5 years from surgery.

   The evaluation considers the two forms of surgery, THR and TKR, separately.

4. The prophylaxis module of the economic model was supported by two phase-III trials. In RECORD 2, 10mg rivaroxaban once daily for 35 ± 4 days was compared to enoxaparin 40mg once daily for 12 ± 2 days after THR, followed by venography at day 36 ± 4 and follow up for 65 +5 days. In RECORD 3, 10mg rivaroxaban once daily for 12 ± 2 days was compared to 40mg enoxaparin once daily for 12 ± 2 days after TKR, followed by venography on day 13 ± 2 and follow up for 42 + 5 days. Both trials compared rivaroxaban started 6-8 hours post surgery to enoxaparin started 12 hours before surgery and had a double blind, double dummy design. The primary efficacy outcome was the composite of VTE and all cause mortality. The main secondary efficacy outcomes were major VTE (i.e. proximal deep vein thrombosis (DVT), nonfatal PE or death related to VTE) and symptomatic VTE. The primary safety outcome was major bleeding.

   In the prophylaxis module of the model, the probabilities of any VTE, symptomatic VTE, fatal pulmonary embolism (PE), non-fatal PE and major bleeding were derived from the RECORD trials. Probabilities used in the post prophylaxis and chronic phase modules were derived from literature sources.

5. The economic evaluation reported both the mean symptomatic VTE events and the mean expected Quality Adjusted Life Years (QALYs) per patient.

6. Data was presented on the incremental cost effectiveness ratio (ICER).

   Total Hip Replacement:
   The cost utility model predicts that patients on rivaroxaban will accrue higher prophylaxis-related costs but lower costs associated with both VTE events and long-term complications when compared to patients on enoxaparin. The overall costs are lower in the rivaroxaban arm. The model predicts that patients in the rivaroxaban arm will accrue slightly better health outcomes over the five years post surgery. Based on this analysis, rivaroxaban dominates enoxaparin as VTE prophylaxis in a THR population.

   Probabilistic sensitivity analysis indicates that a 35 day course of rivaroxaban is cost effective at a cost effectiveness threshold of €30,000 when compared to a 10 to14 day course of enoxaparin in patients undergoing elective THR.

   Total Knee Replacement:
   The cost utility model predicts that patients on rivaroxaban will accrue higher prophylaxis-related costs but lower costs associated with both VTE events and long term complications. The overall costs are lower in the rivaroxaban arm. The model predicts that patients in the rivaroxaban arm will accrue slightly better health outcomes over the five years post surgery. Based on this analysis, rivaroxaban dominates enoxaparin as VTE prophylaxis in a TKR population.

   Probabilistic sensitivity analysis indicates that a 14 day course of rivaroxaban is cost effective at a cost effectiveness threshold of €30,000 when compared to a 14 day course of enoxaparin in patients undergoing elective TKR.

   These results are based on the assumption that health outcomes derived from a 35 day thromboprophylaxis course in THR patients and a 14 day thromboprophylaxis course in TKR patients will extend for a further 5 years.

7. The results of this economic evaluation indicated that rivaroxaban therapy for the prevention of venous thromboembolic events in adult patients undergoing total hip replacement or total knee replacement was dominant when compared to enoxaparin. We believe that rivaroxaban can be considered cost effective for this particular indication in the Irish healthcare setting.