Proof of added benefit of apixaban in hip replacement

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The clot-inhibiting drug apixaban (trade name: Eliquis) was approved in May 2011 for the prevention of thrombosis (blood clots) after operations to replace a hip or knee joint. In an early benefit assessment pursuant to the "Act on the Reform of the Market for Medicinal Products" (AMNOG), the German Institute for Quality and Efficiency in Health Care (IQWiG) examined the added benefit of apixaban.

IQWiG found proof of minor added benefit for adult patients who had undergone hip replacement: symptomatic clots in the deep veins of the leg occurred less frequently with apixaban treatment than with the comparator therapy.

Symptomatic clots in the deep leg veins also occurred less frequently with apixaban treatment in adults after knee replacement. However participants in the studies suffered clots in the lungs (pulmonary embolisms) more often under treatment with apixaban than the comparator group. From weighing up the benefits and harms (risk of side effects) on the basis of the data presented in the manufacturer's dossier, IQWiG identified no proof of added benefit of apixaban over the appropriate comparator therapy in knee replacement operations.

Enoxaparin as comparator therapy

After the insertion of an artificial hip or knee, there is an increased risk of blood clots (thrombi) that are swept away in the bloodstream and can block a blood vessel in another part of the body. Clots that cause symptoms (symptomatic thromboembolism) may, for instance, occur in the lungs and deep veins of the legs.

Apixaban is approved for the prevention of venous thromboembolism (VTE) in adults following hip or knee replacement surgery. The Federal Joint Committee (G-BA) specified low molecular weight heparins (clot inhibitors), which are approved for the prevention of deep vein thrombosis, as the appropriate comparator therapy. The comparison between apixaban and the drug enoxaparin chosen by the manufacturer in its dossier corresponds to this definition.

Added benefit offset by lesser benefit in knee replacement surgery

Deaths were generally rare in both the relevant studies and mortality with apixaban treatment in hip or knee replacement operations did not differ from that with enoxaparin. With both types of surgery, the incidence of bleeding or other side effects and study withdrawals was also no greater under apixaban than under the comparator therapy. Neither of the relevant studies examined the quality of life.

Both studies showed that apixaban was more effective in preventing symptomatic deep vein thrombosis than the comparator therapy: about one in 1000 patients who took apixaban developed a symptomatic deep vein thrombosis; the figure for patients who injected enoxaparin was about 4 in 1000. A minor added benefit of apixaban is proven in this case.

In hip replacement surgery, there was no difference between the treatment groups in respect of pulmonary embolisms. However after knee replacement, these occurred more frequently under apixaban than under enoxaparin: About 5 in 1000 patients who took apixaban had a pulmonary embolism, compared to about one in 1000 under enoxaparin. This leads to an indication of a lesser benefit of apixaban compared to the comparator therapy. The extent of this lesser benefit was classified as "considerable". From weighing up the benefits and harms on the basis of the data presented in the manufacturer's dossier, IQWiG found no proof of added benefit of apixaban over the appropriate comparator therapy in knee replacement surgery.

G-BA decides on the extent of added benefit

The dossier assessment is part of the overall procedure for early benefit assessment conducted by the G-BA. After publication of the manufacturer's dossier and its assessment by IQWiG, the G-BA initiates a formal commenting procedure which provides further information and can result in a change to the benefit assessment. The G-BA then decides on the extent of the added benefit, thus completing the early benefit assessment.

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