Background

- Chronic kidney disease (CKD) frequently coexists with diabetes, constituting diabetic kidney disease (DKD).
- Gradual loss of renal function, as evidenced by increased albumin excretion rate and decreased glomerular filtration rate (eGFR), is associated with an increase in morbidity and end-stage renal disease (ESRD).
- Background therapies such as angiotensin-converting enzyme inhibitors (ACEs) and angiotensin receptor blockers (ARBs) slow kidney disease progression. Improved treatments for DKD, therefore, should further reduce the rate of disease progression or even halt damage to the kidney and should further reduce the risk for CV mortality and morbidity.

Objectives

- Finerenone (BAY94-8862) is a selective, potent and non-steroidal MRA which blocks the deleterious effect of aldosterone and is being developed for the treatment of patients with DKD.
- An early health outcomes model was developed to investigate the implications of using finerenone in addition to background therapy for DKD, to identify key parameters, risk factors and outcomes drivers, and to support clinical development in designing the trial.

Methods

The model reflects the interdependency of risk factors, risk effects, disease states, and disease progression in DKD. It is based on finerenone’s effect to reduce albuminuria and on underlying diabetic and renal outcomes.

Structure:
- A Markov cohort structure was applied to model disease history, treatment effects, and outcomes for DKD patients. It complies with the National Institute of Clinical Excellence (NICE) modeling guidelines, the perspective is third-party payer with US settings over a 40-year time horizon.
- The model includes a total of 16 health states, focusing on CKD, CV disease, and chronic heart failure (CHF). State transitions in the model are a function of various population characteristics and risk factors. A set of patients with DKD at CKD 1/2 was used from the start of the simulation through the progression of disease states until death.

Population:
- Adults age 50+ with DKD and albuminuria (urinary-albuminuria-cretinione ratio, uAcr,030), including CVD, but without ESRD or CHF. Baseline population characteristics are based on patients in the NHANES dataset 1999-2008. The NHANES data has been weighted in order to reflect the race and small and moderate subpopulations of the US population, which included 31% smokers and 7.6% Afro-Caribbean race. Because the race categories in Manitoba (UKPD, AFN) and Afro-Caribbean in UKPD were taken equivalent to ‘black’ in NHANES.

Progression of disease:
- Risk of transition from micro- to macro-albuminuria and from CKD12 to CKD34 are based on NHANES 1999-2008.
- ESRD and mortality after ESRD are based on the United States Renal Data System (USRDS), 2009.

Disease events:
- Risk of CKD, CHF and CV death are derived from various registries (FH, FHDS) and studies. (ARTC, CARE, CHFS).
- Influence of uAcr and eGFR on the risk of CVD and CHF is based on a published research. Pharmacological costs are drawn from the British National Formulary.

Efficacy:
- Clinical efficacy of finerenone affects the reduction of initial albuminuria which in turn impacts the progression of DKD and morbidity and mortality. 40% uAcr reduction for microalbuminuria, 50% uAcr reduction for macroalbuminuria are based on findings from the phase 2a trial.1 It is assumed finerenone is not applied in patients on dialysis.

Costs and utilities:
- Utilities for hypertension, diabetes, CKD34, CVD, CHF, and ESRD are based on published evidence19
- Chronic health state costs30-31 and acute event costs30-31 are based on published research. Pharmacological costs are drawn from the British National Formulary.

Cost and utilities:
- Chronic health state costs and acute event costs are based on published research. Pharmacological costs are drawn from the British National Formulary.

Efficacy:
- Clinical efficacy of finerenone affects the reduction of initial albuminuria which in turn impacts the progression of DKD and morbidity and mortality. 40% uAcr reduction for microalbuminuria, 50% uAcr reduction for macroalbuminuria are based on findings from the phase 2a trial.1 It is assumed finerenone is not applied in patients on dialysis.

Costs and utilities:
- Chronic health state costs and acute event costs are based on published research. Pharmacological costs are drawn from the British National Formulary.

Efficacy:
- Clinical efficacy of finerenone affects the reduction of initial albuminuria which in turn impacts the progression of DKD and morbidity and mortality. 40% uAcr reduction for microalbuminuria, 50% uAcr reduction for macroalbuminuria are based on findings from the phase 2a trial.1 It is assumed finerenone is not applied in patients on dialysis.

Costs and utilities:
- Chronic health state costs and acute event costs are based on published research. Pharmacological costs are drawn from the British National Formulary.

Efficacy:
- Clinical efficacy of finerenone affects the reduction of initial albuminuria which in turn impacts the progression of DKD and morbidity and mortality. 40% uAcr reduction for microalbuminuria, 50% uAcr reduction for macroalbuminuria are based on findings from the phase 2a trial.1 It is assumed finerenone is not applied in patients on dialysis.

Costs and utilities:
- Chronic health state costs and acute event costs are based on published research. Pharmacological costs are drawn from the British National Formulary.

Efficacy:
- Clinical efficacy of finerenone affects the reduction of initial albuminuria which in turn impacts the progression of DKD and morbidity and mortality. 40% uAcr reduction for microalbuminuria, 50% uAcr reduction for macroalbuminuria are based on findings from the phase 2a trial.1 It is assumed finerenone is not applied in patients on dialysis.

Costs and utilities:
- Chronic health state costs and acute event costs are based on published research. Pharmacological costs are drawn from the British National Formulary.

Efficacy:
- Clinical efficacy of finerenone affects the reduction of initial albuminuria which in turn impacts the progression of DKD and morbidity and mortality. 40% uAcr reduction for microalbuminuria, 50% uAcr reduction for macroalbuminuria are based on findings from the phase 2a trial.1 It is assumed finerenone is not applied in patients on dialysis.

Costs and utilities:
- Chronic health state costs and acute event costs are based on published research. Pharmacological costs are drawn from the British National Formulary.