The evaluation of new medicines for their comparative clinical- and cost-effectiveness encompasses the processes of health technology assessment (HTA) and appraisal. HTA is the scientific process concerned with the generation, synthesis and critique of evidence; whereas appraisal is the function of policymakers in arriving at a decision to inform payers and providers of healthcare. Evidence generation and synthesis is normally performed by the marketing authorisation holder (MAH). In Wales, a country of 3.1m population with a public healthcare provider (the National Health Service), the assessment of evidence submitted by MAHs is conducted by the All Wales Therapeutics and Toxicology Centre, and appraised by the New Medicines Group (NMG) and the All Wales Medicines Strategy Group (AWMSG). Health economists contribute extensively to both processes. Their role in assessing submitted (and other relevant) evidence includes scrutinising the MAH submission for accuracy, assumptions in the economic modelling, plausible parameter estimates and clinical representativeness. Submitted models (usually developed in Excel) are tested to assess the relation between the reported incremental cost-effectiveness ratio (ICER), and changes in model inputs. The plausibility of resource use estimates, especially if based on expert opinion, and unit costs are considered in the context of the decision problem, the pathway of care, and expected patient contact with the health service. Utility values are compared with those of age-matched general public. Unusually high values for a severe disease might signal that the ICER is unreliable. Trial-based and extrapolated estimates of treatment effectiveness are assessed in view of the available data, the use of indirect treatment comparisons and correct application of parametric models. Health economist members of the NMG and AWMSG judge whether new medicines are cost-effective by comparing the most plausible ICER with the threshold range of £20,000 to £30,000 per quality-adjusted life-year (QALY). There is a degree of flexibility around the threshold for certain treatments (for rare diseases and those which extend life at the end of life). Judgements are made of the budget impact, the greater the impact, the more certainty is required in the ICER estimate. Deliberations by all members lead to a vote for final recommendation.