Pharmaceutical removal could be significantly enhanced through cometabolism during nitrification processes. To date, pharmaceutical biotransformation models have not considered the formation of transformation products associated with the metabolic type of microorganisms. Here we report a comprehensive model to describe and evaluate the biodegradation of pharmaceuticals and the formation of their biotransformation products by enriched nitrifying cultures. The biotransformation of parent compounds was linked to the microbial processes via cometabolism induced by ammonium-oxidizing bacteria (AOB) growth, metabolism by AOB, cometabolism by heterotrophs (HET) growth, and metabolism by HET in the model framework. The model was calibrated and validated using experimental data from pharmaceutical biodegradation experiments at realistic levels, taking two pharmaceuticals as examples, i.e., atenolol and acyclovir. Results demonstrated the good predictive performance of the established biotransformation model under different metabolic conditions, as well as the reliability of the established model in predicting different pharmaceutical biotransformations. The linear positive correlation between ammonia oxidation rate and pharmaceutical degradation rate confirmed the major role of cometabolism induced by AOB in the pharmaceutical removal. Dissolved oxygen was also revealed to be capable of regulating the pharmaceutical biotransformation cometabolically, and the substrate competition between ammonium and pharmaceuticals existed especially at high ammonium concentrations.