A general heat transfer correlation to predict the thermal performance of zeotropic mixture flow boiling is essential for an optimal evaporator design in thermodynamic cycles using zeotropic mixtures as working fluids. This work aims at developing a new general correlation to predict the flow boiling heat transfer of zeotropic mixtures in horizontal plain tubes with a significantly better predictive performance than those of the existing correlations. In order to achieve this goal, a database containing 2091 experimental data points of macroscale flow boiling experiments with zeotropic mixtures in horizontal plain tubes from 22 independent research groups was collected. The predictive performances of the existing correlations were evaluated by comparing the predicted values calculated by the existing correlations with the experimental data points. Based on an analysis of the physical phenomena and on the results of the comparison of the existing correlations, two new heat transfer correlations were derived by following two different approaches: (i) modifying existing correlations and introducing a new dimensionless number (the ratio of the temperature glide of the mixture to the saturation temperature), and (ii) using dimensionless analysis coupled with multiple regression. The comparison results for the existing correlations indicate that most of the correlations overestimate the heat transfer coefficient, and only three correlations present a mean absolute percentage deviation below 50%, the lowest being 44.2%. The results suggest that the new correlation developed following the first approach, yields a mean absolute percentage deviation of 29.0%, while the correlation developed by following the second approach yields a mean absolute percentage deviation of 24.6%.