This review article notes that the new generation of antidepressants — selective serotonin reuptake inhibitors and melatonin derivatives — do not have the side effects characteristic of tricyclic antidepressants and can be used in the treatment of patients with cardiovascular pathology in combination with depression. The causes and incidence of QT interval prolongation associated with the use of antidepressants are described. Numerous somatotropic and behavioral effects of tricyclic antidepressants have been demonstrated due to their effects on several receptor groups: α1-adrenoceptors, serotonin, muscarinic, and histamine H1 receptors. We searched PubMed, Embase, Web of Science, eLIBRARY and Google Scholar databases for the use of psychotropic drugs in cardiology practice, giving priority to systematic reviews, randomized clinical trials, supplemented by several cohort studies and the descriptions of some experiments. The data of comparative evaluation of modern antidepressants depending on pharmacological effects and development of adverse events are presented. The above-mentioned drugs, unlike traditional antidepressants, are acceptable for treatment of comorbid depressive disorders in patients with cardiovascular diseases. Proven efficacy among antidepressants are escitalopram, paroxetine, which have a strong cardiotropic effect, and agomelatine, which has proven efficacy in myocardial ischaemia–reperfusion injury.