

The invention concerns substituted 1,4-di-piperidin-4-yl-piperazine derivatives having neurokinin antagonistic activity, in particular NK₁ antagonistic activity, their preparation, compositions comprising them and their use as a medicine, in particular for the treatment of emesis, anxiety, depression, pain, pancreatitis and IBS. The compounds according to the invention can be represented by general Formula (I), and comprises also the pharmaceutically acceptable acid or base addition salts thereof, the stereochemically isomeric forms thereof, the N-oxide form thereof and prodrugs thereof, wherein all substituents are defined as in Claim 1. In view of their capability to antagonize the actions of neurokinins by blocking the neurokinin receptors, and in particular antagonizing the actions of substance P by blocking the NK₁ receptor, the compounds according to the invention are useful as a medicine, in particular in the prophylactic and therapeutic treatment of neurokinin-mediated conditions, such as, for instance CNS disorders, in particular depression, anxiety disorders, stress-related disorders, sleep disorders, cognitive disorders, personality disorders, schizoaffective disorders, eating disorders, neurodegenerative diseases, addiction disorders, mood disorders, sexual dysfunction, pain and other CNS-related conditions; inflammation; allergic disorders; emesis; gastrointestinal disorders, in particular irritable bowel syndrome (IBS); skin disorders; vasospastic diseases; fibrosing and collagen diseases; disorders related to immune enhancement or suppression and rheumatic diseases and body weight control.

