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Vorinostat

National Cancer Institute

Source

National Cancer Institute. Vorinostat. NCI Thesaurus. Code C1796.

A synthetic hydroxamic acid derivative with antineoplastic activity. Vorinostat, a second generation polar-planar compound, binds to the catalytic domain of the histone deacetylases (HDACs). This allows the hydroxamic moiety to chelate zinc ion located in the catalytic pockets of HDAC, thereby inhibiting deacetylation and leading to an accumulation of both hyperacetylated histones and transcription factors. Hyperacetylation of histone proteins results in the upregulation of the cyclin-dependant kinase p21, followed by G1 arrest. Hyperacetylation of non-histone proteins such as tumor suppressor p53, alpha tubulin, and heat-shock protein 90 produces additional antiproliferative effects. This agent also induces apoptosis and sensitizes tumor cells to cell death processes. Vorinostat crosses the blood-brain barrier.