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Karonudib

National Cancer Institute

Source

National Cancer Institute. *Karonudib*. NCI Thesaurus. Code C148140.

An orally available inhibitor of Karolinska nudt1 (MTH1; MutT homologue 1; NUDT1), with potential antineoplastic activity. Upon administration, karonudib targets and binds to the active site of MTH1, thereby preventing the activity of MTH1. This leads to the incorporation of oxidized deoxynucleoside triphosphates (dNTPs) into the DNA of cancer cells, which causes DNA damage, introduces double strand breaks (DSBs), and induces apoptosis in cancer cells. MTH1, a member of the Nudix phosphohydrolase superfamily hydrolyzes oxidized purine nucleoside triphosphates, including 8-oxo-dGTP and 2-OH-dATP, converts them into their corresponding monophosphate forms, and prevents their incorporation into DNA, which allows MTH1-expressing cells to evade cell death. Compared to normal, healthy cells, cancer cells overexpress MTH1, which leads to dysregulation of the cellular redox system and increased reactive oxygen species (ROS) production, which together prevents the incorporation of damaged and oxidized nucleotides into DNA.