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# Dihydroorotate Dehydrogenase Inhibitor AG-636

National Cancer Institute

## Source

National Cancer Institute. *Dihydroorotate Dehydrogenase Inhibitor AG-636*. NCI Thesaurus. Code C158103.

An orally available inhibitor of dihydroorotate dehydrogenase (DHODH), with potential antineoplastic activity. Upon administration, AG-636 specifically targets, binds to and prevents the activation of DHODH, thereby preventing the fourth enzymatic step in de novo pyrimidine synthesis. This prevents uridine monophosphate (UMP) formation, DNA synthesis, cell division and cellular proliferation, causes reactive oxygen species (ROS) formation, enables differentiation and induces apoptosis in susceptible tumor cells. DHODH, a mitochondrial enzyme, catalyzes the conversion of dihydroorotate (DHO) to orotate in the endogenous synthesis of UMP.