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Roflumilast

National Cancer Institute

Source

National Cancer Institute. *Roflumilast*. NCI Thesaurus. Code C76890.

An orally available, long-acting inhibitor of phosphodiesterase (PDE) type 4 (PDE4), with anti-inflammatory and potential antineoplastic activities. Upon administration, roflumilast and its active metabolite roflumilast N-oxide selectively and competitively bind to and inhibit PDE4, which leads to an increase of both intracellular levels of cyclic-3',5'-adenosine monophosphate (cAMP) and cAMP-mediated signaling. cAMP prevents phosphorylation of spleen tyrosine kinase (SYK) and abrogates activation of the PI3K/AKT/mTOR signaling pathway, which may result in the induction of apoptosis. PDE4, a member of the PDE superfamily that hydrolyses cAMP and 3',5'-cyclic guanosine monophosphate (cGMP) to their inactive 5' monophosphates, is upregulated in a variety of cancers and may contribute to chemoresistance; it also plays a key role in inflammation, especially in inflammatory airway diseases.