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Selonsertib

National Cancer Institute

Source

National Cancer Institute. *Selonsertib*. NCI Thesaurus. Code C121943.

An orally bioavailable inhibitor of apoptosis signal-regulating kinase 1 (ASK1), with potential anti-inflammatory, antineoplastic and anti-fibrotic activities. Upon oral administration, selonsertib targets and binds to the catalytic kinase domain of ASK1 in an ATP-competitive manner, thereby preventing its phosphorylation and activation. This prevents the phosphorylation of downstream kinases, such as c-Jun N-terminal kinases (JNKs) and p38 mitogen-activated protein kinase (p38 MAPK). By preventing the activation of ASK1-dependent signal transduction pathways, GS-4997 prevents the production of inflammatory cytokines, down-regulates the expression of genes involved in fibrosis, suppresses excessive apoptosis and inhibits cellular proliferation. ASK1, also called mitogen-activated protein kinase kinase kinase 5 (MAP3K5), is activated in response to oxidative and endoplasmic reticulum (ER) stress, calcium influx and infection. It plays a key role in the development of certain cardiovascular and neurodegenerative diseases, diabetes, as well as certain types of cancer.