## Open Peer Review on Qeios

## **Idronoxil Suppository NOX66**

National Cancer Institute

## Source

National Cancer Institute. Idronoxil Suppository NOX66. NCI Thesaurus. Code C132257.

A proprietary, suppository-based formulation composed of idronoxil, a synthetic flavonoid derivative, surrounded by a proprietary lipid that protects idronoxil from phase 2 degradation, with potential chemo- and radio-sensitizing activities. Upon administration, idronoxil blocks the activity of ecto-NOX disulfide-thiol exchanger 2 (ENOX2; tNOX), a tumor-specific external NADH oxidase that maintains the transmembrane electron potential across the plasma membrane and is overexpressed in certain cancer cell types while absent in normal, healthy cells. Loss of this potential directly inhibits certain pro-survival signal transduction pathways, such as the PARP1/PI3 kinase/Akt signaling pathway. The inhibition of these pathways prevents resistance to standard chemo- and radio-therapy and makes tumor cells more susceptible to the antitumor activity of conventional chemotherapeutic agents and radiotherapy. The formulation prevents detoxification of idronoxil to an inactive form by bypassing phase 2 metabolism; this increases idronoxil's bioavailability as compared to idronoxil alone.