Etirinotecan Pegol

National Cancer Institute

Source

National Cancer Institute. Etirinotecan Pegol. NCI Thesaurus. Code C74069.

An extended-release (ER) formulation composed of irinotecan, which is a semisynthetic derivative of camptothecin and a topoisomerase I-inhibitor prodrug, that is conjugated, via a proprietary biodegradable ester-based linker, to polyethylene glycol (PEG), with antineoplastic activity. Upon administration of etirinotecan pegol (EP), the agent penetrates into the leaky tumor vasculature and accumulates in the tumor. The linker slowly hydrolyzes and releases irinotecan, which leads to sustained exposure of the tumor to irinotecan. In turn, irinotecan is converted to the biologically active metabolite 7-ethyl-10-hydroxy-camptothecin (SN38) by a carboxylesterase. SN38 inhibits topoisomerase I activity by stabilizing the cleavable complex of topoisomerase I and DNA; this results in DNA breaks that inhibit DNA replication and trigger apoptosis. Pegylation provides improved systemic exposure, increases drug penetration into tumors and decreases drug clearance, thereby increasing the duration of therapeutic effects while lowering the toxicity profile.