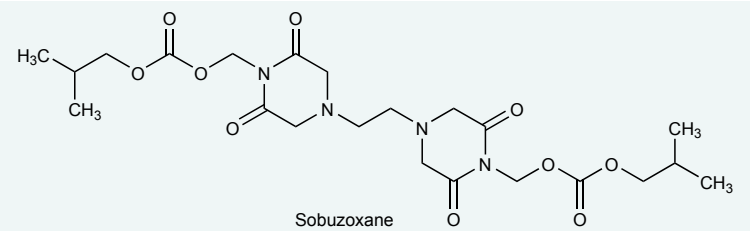
# New Product Highlights

## Sobuzoxane: A novel, selective DNA topoisomerase II inhibitor

DNA topoisomerases are nuclear enzymes that specialize in relaxing the torsional constraints of intertwined DNA strands, thus altering DNA topology. They participate in many essential cellular functions such as DNA replication, recombination, condensation, segregation of replicated chromosomes, transcription and gene expression. Two structurally and functionally distinct classes of topoisomerases have been identified and are referred to as Topo I and Topo II. Topo II is an essential enzyme for cellular survival and therefore, has been a molecular target for the development of anti-cancer drugs.

Sigma-RBI is pleased to introduce the novel topoisomerase II (Topo II) inhibitor, **Sobuzoxane** (MST-16; Prod. No. **S 4692**), an oral bis-(2,6-dioxopiperazine) anticancer agent. Sobuzoxane induces apoptosis through alteration of DNA helicity without inducing cleavable complex formation between DNA and the Topo II enzyme [1]. In contrast to the acridine, anthracycline and epipodophyllotoxin Topo II inhibitors. sobuzoxane, its active metabolite ICRF-154, and other ICRF derivatives (ICRF-159 and ICRF-193) affect the catalytic cycle at a point upstream to cleavable DNA-enzyme complex formation. This action of sobuzoxane and ICRF compounds is similar to that of a newer generation of Topo II inhibitors, merbarone, **aclarubicin** (Prod. No. **A 8959**) and **fostriecin** (Prod. No. **F 4425**). Sobuzoxane has the potential to chelate metal cations and to reverse the metal-anthracycline complexes that facilitate the free radical generation which is responsible for anthracycline-induced cardiomyopathy [2-5]. The absence of stabilized cleavable complex formation and the lack of increase in free radicals are responsible for the higher selectivity and cardiac protective effects associated with sobuzoxane. Sobuzoxane increased the $LD_{50}$ of **doxirubicin** (DOX, Prod. No. **D 1515**) in mice by 1.5 fold [2]. The synergistic anti-tumor effect is accompanied by an increase in the number of cells arrested in the G2M phase of the cell cycle. Sobuzoxane is being evaluated as a chemotherapeutic agent in combination therapy with DOX and **daunorubicin** (Prod. No. **D 8809**) [2].

Sobuzoxane belongs to a new class of Topo II inhibitors with a novel mechanism of action, higher selectivity and fewer toxic side effects. It is a new addition to the current collection of compounds that are used to study Topo II mechanisms in DNA metabolism and in the induction of apoptosis.




Sobuzoxane
Prod. No. S 4692


**References**

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