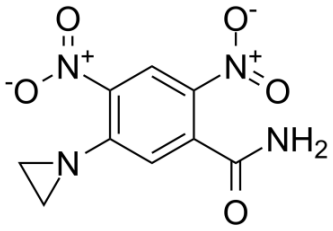
Tretazicar

Cat. No.:	HY-13543
CAS No.:	21919-05-1
Molecular Formula:	$C_9H_8N_4O_5$
Molecular Weight:	252.18
Target:	DNA Alkylator/Crosslinker
Pathway:	Cell Cycle/DNA Damage
Storage:	Powder -20°C 3 years In solvent -80°C 6 months -20°C 1 month



BIOLOGICAL ACTIVITY

Description	Tretazicar (CB 1954), an antitumor prodrug, is highly selective against the Walker 256 rat tumour line. Tretazicar is enzymatically activated to generate a bifunctional agent, which can form DNA-DNA interstrand cross-links. Tretazicar in rat cells involves the reduction of its 4-nitro group to a 4-hydroxylamine by the enzyme NAD(P)H:quinone oxidoreductase 1 (NQO1)[1][2].
In Vitro	Tretazicar (CB 1954) (0.1-1000 μM; 3 days) has sensitivity for retrovirally transduced AB22 (AB22-nr) cells with an IC_{50} of 3 μM[3]. DNA cross-link formation in affected cells is a result of the bioactivation of the drug by the enzyme DT diaphorase (NAD(P)H dehydro-genase (quinone)) in the Walker cells which reduces the 4-nitro group of Tretazicar. The product of this reaction is a difunctional alkylating agent, 5-aziridin-1-yl-4-hydroxylamino-2-nitrobenzamide[4].
In Vivo	Tretazicar (CB 1954) (80 mg/kg; i.p. on days 2 and 9) results in a significant increase in survival[3].

Animal Model:	Female BALB/c mice (AB22-nr, SKOV3 human ovarian tumour xenograft)[3]
Dosage:	80 mg/kg
Administration:	i.p. on days 2 and 9
Result:	The median survival of the AB22-nr was 49 days. Resulted in a significant increase in survival.

REFERENCES

[1]. Knox RJ,et al. Bioactivation of 5-(aziridin-1-yl)-2,4-dinitrobenzamide (CB 1954) by human NAD(P)H quinone oxidoreductase 2: a novel co-substrate-mediated antitumor prodrug therapy. Cancer Res. 2000 Aug 1;60(15):4179-86.

[2]. Knox RJ, et al. CB 1954: from the Walker tumor to NQO2 and VDEPT. Curr Pharm Des. 2003;9(26):2091-104.

[3]. Green NK, et al. Immune enhancement of nitroreductase-induced cytotoxicity: studies using a bicistronicadenovirus vector. Int J Cancer. 2003 Mar 10;104(1):104-12.

[4]. Drabek D, et al. The expression of bacterial nitroreductase in transgenic mice results in specific cell killing by the prodrug CB1954. Gene Ther. 1997 Feb;4(2):93-100.

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