# Product data sheet

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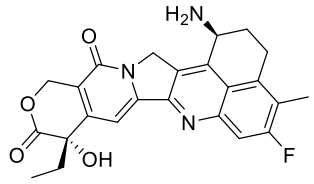
|---|---|
| MedKoo Cat#: 201340<br>Name: Exatecan free base<br>CAS#: 171335-80-1 (free base)<br>Chemical Formula: $C_{24}H_{22}FN_3O_4$<br>Exact Mass: 435.1594<br>Molecular Weight: 435.46 |  |
| Product supplied as: | Powder |
| Purity (by HPLC): | ≥ 98% |
| Shipping conditions | Ambient temperature |
| Storage conditions: | Powder: -20°C 3 years; 4°C 2 years. |
| | In solvent: -80°C 3 months; -20°C 2 weeks. |

**1. Product description:**

Exatecan, also known as DX 8951, is a semisynthetic, water-soluble derivative of camptothecin with antineoplastic activity. Exatecan mesylate inhibits topoisomerase I activity by stabilizing the cleavable complex between topoisomerase I and DNA and inhibiting religation of DNA breaks, thereby inhibiting DNA replication and triggering apoptotic cell death. This agent does not require enzymatic activation and exhibits greater potency than camptothecin and other camptothecin analogues.

**2. CoA, QC data, SDS, and handling instruction**

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

**3. Solubility data**

| Solvent | Max Conc. mg/mL | Max Conc. mM |
|---|---|---|
| | | |

**4. Stock solution preparation table:**

| Concentration / Solvent Volume / Mass | 1 mg | 5 mg | 10 mg |
|---|---|---|---|
| 1 mM | 2.30 mL | 11.48 mL | 22.96 mL |
| 5 mM | 0.46 mL | 2.30 mL | 4.59 mL |
| 10 mM | 0.23 mL | 1.15 mL | 2.30 mL |
| 50 mM | 0.05 mL | 0.23 mL | 0.46 mL |

**5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator**

Please refer the product web page under section of "Calculator"

**6. Recommended literature which reported protocols for in vitro and in vivo study**

In vitro study

Nakada T, Masuda T, Naito H, Yoshida M, Ashida S, Morita K, Miyazaki H, Kasuya Y, Ogitani Y, Yamaguchi J, Abe Y, Honda T. Novel antibody drug conjugates containing exatecan derivative-based cytotoxic payloads. Bioorg Med Chem Lett. 2016 Mar 15;26(6):1542-1545. doi: 10.1016/j.bmcl.2016.02.020. Epub 2016 Feb 8. PMID: 26898815.

In vivo study

Andrikopoulou A, Zografos E, Liontos M, Koutsoukos K, Dimopoulos MA, Zagouri F. Trastuzumab Deruxtecan (DS-8201a): The Latest Research and Advances in Breast Cancer. Clin Breast Cancer. 2021 Jun;21(3):e212-e219. doi: 10.1016/j.clbc.2020.08.006. Epub 2020 Aug 18. PMID: 32917537.

**7. Bioactivity**

Biological target:

Topoisomerase I

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In vitro activity

Trastuzumab conjugates consisting of exatecan derivatives were prepared and their biological activities and physicochemical properties were evaluated. The ADCs showed strong efficacy and a low aggregation rate. The exatecan derivatives were covalently connected via a peptidyl spacer (Gly-Gly-Phe-Gly), which is assumed to be stable in circulation, and were cleaved by lysosomal enzymes following ADC internalization into tumor tissue. These anti-HER2 ADCs exhibited a high potency, specifically against HER2-positive cancer cell lines in vitro. The ADCs, bearing exatecan derivatives which have more than two methylene chains, exhibited superior cytotoxicity. It was speculated that steric hindrance of the cleavable amide moiety could be involved in the drug release. The adequate alkyl lengths of exatecan derivatives (13, 14, 15) were from two to four in terms of aggregation rate. The ADC having a hydrophilic moiety showed good efficacy in a HER2-positive and Trastuzumab-resistant breast carcinoma cell model in mice.

Reference: Nakada T, Masuda T, Naito H, Yoshida M, Ashida S, Morita K, Miyazaki H, Kasuya Y, Ogitani Y, Yamaguchi J, Abe Y, Honda T. Novel antibody drug conjugates containing exatecan derivative-based cytotoxic payloads. Bioorg Med Chem Lett. 2016 Mar 15;26(6):1542-1545. doi: 10.1016/j.bmcl.2016.02.020. Epub 2016 Feb 8. PMID: 26898815.

In vivo activity

DS-8201a resulted in favorable outcomes in HER2-positive heavily pretreated breast cancer patients and also had a promising efficacy in patients with HER2-negative/low-expressing disease, whose options are limited. Interestingly, a recently published phase 2 trial (NCT03248492) reported 60% overall response and 97% disease control in patients with HER2-positive disease previously treated with multiple regimens, including trastuzumab emtansine. On the basis of recent clinical trials, the US Food and Drug Administration granted accelerated approval to DS-8201a in advanced or unresectable HER2-positive breast cancer pretreated with at least two HER2-targeting treatment lines. All preclinical and clinical data of DS-8201a regarding breast cancer was reviewed.

Reference: Andrikopoulou A, Zografos E, Liontos M, Koutsoukos K, Dimopoulos MA, Zagouri F. Trastuzumab Deruxtecan (DS-8201a): The Latest Research and Advances in Breast Cancer. Clin Breast Cancer. 2021 Jun;21(3):e212-e219. doi: 10.1016/j.clbc.2020.08.006. Epub 2020 Aug 18. PMID: 32917537.