

# STATEMENT ON A NONPROPRIETARY NAME ADOPTED BY THE USAN COUNCIL

USAN (NO-145) PRECEMTABART TOCENTECAN

PRONUNCIATION pre sem' tah bart toe" sen tee' kan

THERAPEUTIC CLAIM Antineoplastic, treatment of solid tumors

## CHEMICAL NAMES

Immunoglobulin G1 [235-proline,236-valine,237-alanine,331-serine,332-serine,de-448-lysine], anti-(human carcinoembryonic antigen-related cell adhesion molecule 5) (human monoclonal MBE-748  $\gamma$ 1-chain), complex with human monoclonal MBE-748  $\kappa$ -chain, dimer, 214",214'",222,222',228,228',231,231'-octakis[S-[1-[3-[[2-[[5-[[[[[(1S,9S)-9-ethyl-5-fluoro-2,3,9,10,13,15-hexahydro-9-hydroxy-4-methyl-10,13-dioxo-1*H*,12*H*-benzo[*de*]pyrano[3',4':6,7]indolizino[1,2-*b*]quinolin-1-yl]amino]carbonyl]oxy]methyl]-2-( $\beta$ -D-glucopyranuronosyloxy)phenyl]amino]-2-oxoethyl]amino]-3-oxopropyl]-2,5-dioxo-3-pyrrolidinyl]-L-cysteine]

Immunoglobulin G1-kappa, anti-[*Homo sapiens* CEACAM5 (carcinoembryonic antigen-related cell adhesion molecule 5, CEA, CD66e)], *Homo sapiens* monoclonal antibody; H-gamma1 heavy chain *Homo sapiens* (1-447) [VH (*Homo sapiens* IGHV4-31\*02 (90.9%) -(IGHD) -IGHJ4\*01 (100%), CDR-IMGT [10.7.11] (26-35.53-59.98-108)) (1-119) -*Homo sapiens* IGHG1\*03, G1m3, nG1m1 CH1 R120, CH3 E12, M14,G1v50 delE1.4, P1.3, V1.2, A1.1, G1v60 CH2 S115, S116 (CH1 R120 (216) (120-217), hinge 1-15(218-232), CH2 E1.4>del, L1.3>P (235), L1.2>V (236), G1.1>A (237), A115>S (331), P116>S (332) (233-341), CH3 E12 (357), M14 (359) (342-446), CHS K2>del (447)) (120-447)], (222-214')-disulfide with L-kappa light chain *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV3-15\*01 (94.7%) -IGKJ3\*01 (100%), CDR-IMGT [6.3.9] (27'-32'.50'-52'.89'-97')) (1'-107') -*Homo sapiens* IGKC\*01 (100%), Km3 A45.1 (153'), V101 (191') (108'-214')]; dimer (228-228":231-231")-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, cell line CHO-K1SV, glycoform alfa; substituted at the sulfur atoms of an average of 8 L-cysteinyl residues among 222, 228, 231, 214', 222", 228", 231" and 214'" with radical group 1-{3-[(2-{5-[[[(1S,9S)-9-ethyl-5-fluoro-9-hydroxy-4-methyl-10,13-dioxo-2,3,9,10,13,15-hexahydro-1*H*,12*H*-benzo[*de*]pyrano[3',4':6,7]indolizino[1,2-*b*]quinolin-1-yl]carbonyl]oxy)methyl]-2-( $\beta$ -D-glucopyranuronosyloxy)anilino}-2-oxoethyl]amino]-3-oxopropyl]-2,5-dioxopyrrolidin-3-yl (*tocentecan*)

## STRUCTURAL FORMULA

Heavy chain X, X''

EVQLQESGPG	LVKPSQTLSL	TCTVSDGSVS	RGYYLTWIR	QHPGKGLEWI	50
GYIYYSGSTY	FNPSLRSRVT	MSVDTSKNQF	SLKLSSVTAA	DTAVYYCARG	100
IAVAPFDYWG	QGTLVTVSSA	STKGPSVFPL	APSSKSTSGG	TAALGCLVKD	150
YFPEPVTVSW	NSGALTSQVH	TFPAVLQSSG	LYSLSSVVTV	PSSSLGTQTY	200
ICNVNPKPSN	TKVDKRVPEK	SCDKTHTCPP	CFAPPVAGPS	VFLFPPKPKD	250
TLMISRTEPEV	TCVVVDVSHE	DPEVKFNWYV	DGVEVHNAKT	KPREEQYNST	300

YRVSVLTVL	HQDWLNGKEY	KCKVSNKALP	SSIEKTISKA	KGQPREPQVY	350
TLPPSREEMT	KNQVSLTCLV	KGFYPSDIAV	EWESNGQPEN	NYKTTTPVLD	400
SDGSFFLYSK	LTVDKSRWQQ	GNVFSCSVMH	EALHNHYTQK	SLSLSPG	447

#### Light chain X', X''

EIVLTQSPAT	LSVSPGERAT	LSCRTSQSVR	SNLAWYQQKP	GQAPRLLIYA	50
ASTRATGIPA	RFSGSGSGTE	FTLTISLQSQ	EDFAVYQCQQ	YTNWPFTFGP	100
GTKVDIKRTV	AAPSVFIFPP	SDEQLKSGTA	SVVCLLNNFY	PREAKVQWKV	150
DNALQSGNSQ	ESVTEQDSKD	STYLSLSTLT	LSKADYEKHK	VYACEVTHQG	200
LSSPVTKSFN	RGEC				214

#### Disulfide bridges location

Intra-H 22-97 146-202 262-322 368-426  
 22"-97" 146"-202" 262"-322" 368"-426"

Intra-L 23'-88' 134'-194'  
 23"'-88"" 134""-194""

Inter-H-L 222-214' 222"-214"

Inter-H-H 228-228" 231-231"

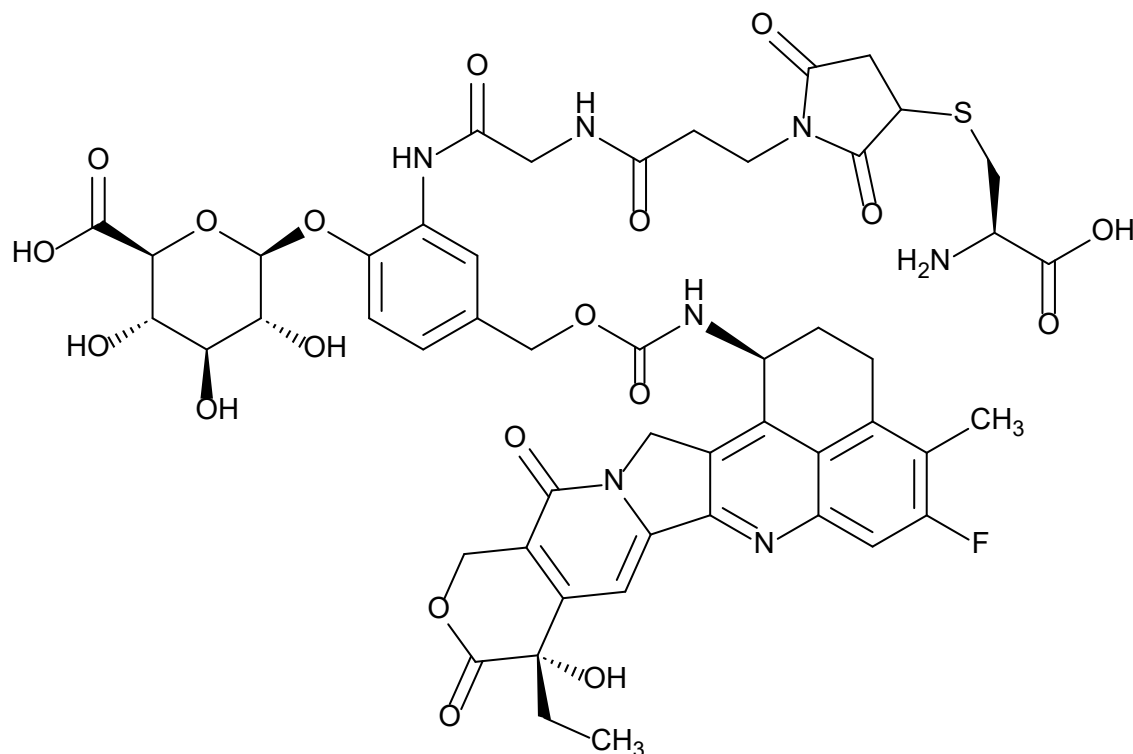
#### N-glycosylation sites

298, 298"

The four inter-chain disulfide bridges are not present, an average of 8 cysteinyl being conjugated each via a thioether bond to a drug linker.

C (222,228,231,214',222",228",231",214")

(tocentecan:mAb ~ 8:1)



MOLECULAR FORMULA

C<sub>6800</sub>H<sub>10306</sub>F<sub>8</sub>N<sub>1758</sub>O<sub>2138</sub>S<sub>40</sub>

MOLECULAR WEIGHT

152.3 kDa (no glycosylation, theoretical)

TRADEMARK	None as yet
SPONSOR	Merck KGaA
CODE DESIGNATIONS	M9140 ADC, MBE-2882, W2882, Anti-CEACAM5- β-gluc-exatecan conjugate
<u>CAS</u> REGISTRY NUMBER	2873366-83-5
UNII	V97BV45YBZ
WHO NUMBER	13008

gbk