

SUMMARY OF PRODUCT

STRUCTURE

Rituximab is a genetically engineered chimeric murine/human monoclonal antibody directed against the CD20 antigen found on the surface of normal and malignant B lymphocytes. The antibody is an IgG₁ K immunoglobulin which is produced by Chinese Hamster Ovary (CHO) cells in suspension. Rituximab binds to the target CD20 antigen via the variable murine regions, while the remainder of the antibody interacts with human immune-effector mechanisms to kill the target cells.

Rituximab is a fusion of the light and heavy chain variable regions of a murine monoclonal anti-CD20 antibody and human kappa light-chain and gamma 1 heavy-chain constant regions. Rituximab consists of two heavy chains (HCs) of 451 amino acids and two light chains (LCs) of 213 amino acids, with an approximate molecular weight of 150 kDa. HCs and LCs are linked by one disulfide bond (S-S) and the HCs by two S-S bridges located in a short hinge domain. Twelve additional cysteine bridges are intramolecular and delimit six different globular domains: one variable (VL) and one constant for the LC (CL); and, one variable (VH) and three constant for the HCs (CH1, CH2 and CH3).

Rituximab is produced by recombinant DNA technology in a mammalian CHO (Chinese hamster ovary) cell culture. These cell lines are genetically modified to specifically express both light chains (LC) and heavy chains (HC) of Rituximab.

Amino Acid Sequence of Rituximab:

Light Chain:

<u>10</u>	<u>20</u>	<u>30</u>	<u>40</u>	<u>50</u>	<u>60</u>
QIVLSQSPAI	LSASPGEKVT	MTCRASSSVS	YIHWFQQKPG	SSPKPWIYAT	SNLASGVPVR
<u>70</u>	<u>80</u>	<u>90</u>	<u>100</u>	<u>110</u>	<u>120</u>
FSGSGSGTSY	SLTISRVEAE	DAATYYCQQW	TSNPPTFGGG	TKLEIKRTVA	APSVFIFPPS
<u>130</u>	<u>140</u>	<u>150</u>	<u>160</u>	<u>170</u>	<u>180</u>
DEQLKSGTAS	VVCLLNNFYF	REAKVQWKVD	NALQSGNSQE	SVTEQDSKDS	TYSLSSTLTL
<u>190</u>	<u>200</u>	<u>210</u>			
SKADYEKHKV	YACEVTHQGL	SSPVTKSFNR	GEC		

Heavy Chain:

<u>10</u>	<u>20</u>	<u>30</u>	<u>40</u>	<u>50</u>	<u>60</u>
QVQLQQPGAE	LVKPGASVKM	SCKASGYTFT	SYNMHWVKQT	PGRGLEWIGA	IYPGNGDTSY
<u>70</u>	<u>80</u>	<u>90</u>	<u>100</u>	<u>110</u>	<u>120</u>
NQKFKGKATL	TADKSSSTAY	MQLSSLTSED	SAVYYCARST	YYGGDWYFNV	WGAGTTVTVS
<u>130</u>	<u>140</u>	<u>150</u>	<u>160</u>	<u>170</u>	<u>180</u>
AASTKGPSVF	PLAPSSKSTS	GGTAALGCLV	KDYFPEPVTV	SWNSGALTSG	VHTFPAVLQS
<u>190</u>	<u>200</u>	<u>210</u>	<u>220</u>	<u>230</u>	<u>240</u>
SGLYSLSSVV	TVPSSSLGTQ	TYICNVNHKP	SNTKVDKKVE	PKSCDKTHTC	PPCPAPELLG
<u>250</u>	<u>260</u>	<u>270</u>	<u>280</u>	<u>290</u>	<u>300</u>
GPSVFLFPPK	PKDTLMISRT	PEVTCVVVDV	SHEDPEVKFN	WYVDGVEVHN	AKTKPREEQY
<u>310</u>	<u>320</u>	<u>330</u>	<u>340</u>	<u>350</u>	<u>360</u>
NSTYRVVSVL	TVLHQDWLNG	KEYKCKVSNK	ALPAPIEKTI	SKAKGQPREP	QVYTLPPSRD
<u>370</u>	<u>380</u>	<u>390</u>	<u>400</u>	<u>410</u>	<u>420</u>
ELTKNQVSLT	CLVKGFYPSD	IAVEWESNGQ	PENNYKTPPP	VLDSDGSFFL	YSKLTVDKSR
<u>430</u>	<u>440</u>	<u>450</u>			<u>460</u>
WQQGNVFSCS	VMHEALHNHY	TQKSLSLSPG	K		

➤ **Theoretical disulfide bonds:**

Intrachain:

- ✓ Cys22(H)-Cys96(H)
- ✓ Cys148(H)-Cys204(H)
- ✓ Cys265(H)-Cys325(H)
- ✓ Cys371(H)-Cys429(H)
- ✓ Cys23(L)-Cys87(L)
- ✓ Cys133(L)-Cys193(L)

Interchain:

- ✓ Cys213(L)-Cys224(H)
- ✓ Cys230(H)-CysH230(H)
- ✓ Cys233(H)-Cys233(H)

Nomenclature information of Rituximab:

Recommended International Nonproprietary Name (INN)	Rituximab
Anatomical Therapeutic Chemical (ATC) code	L01XC02
Chemical Name	Immunoglobulin G 1 (human-mouse monoclonal IDEC-C2B8 gamma1-chain anti-human antigen CD 20), disulfide with human-mouse monoclonal IDEC-C2B8 kappa-chain, dimer.*
Chemical Abstracts Service (CAS) registry number	174722-31-7
Molecular Formula	C ₆₄₁₆ H ₉₈₇₄ N ₁₆₈₈ O ₁₉₈₇ S ₄₄
Molecular weight	~ 150 kDa

Name of the medicinal product

Zytux 100 mg/10 ml Concentrate for solution for infusion

Zytux 500mg/50 ml Concentrate for solution for infusion

Reference Product

Mabthera from Roche

Quantitative and Qualitative composition

Each 10 ml vial contains 100 mg of Rituximab.

Each 50 mL vial contains 500 mg of Rituximab.

Rituximab is a genetically engineered chimeric mouse/human monoclonal antibody expressed in Chinese Hamster Ovary cells.

Each vial of Zytux consist of Polysorbate 80 ,Sodium chloride ,Sodium citrate dihydrate and Water for injections.

Therapeutic indications

Non-Hodgkin's lymphoma (NHL)

Chronic lymphocytic leukaemia (CLL)

Rheumatoid arthritis

Granulomatosis with polyangiitis and microscopic polyangiitis

Pharmacological properties

Pharmacotherapeutic group: antineoplastic agents, monoclonal antibodies, ATC code: L01X C02

Route of Administration

IV