STATEMENT ON A NONPROPRIETARY NAME ADOPTED BY THE USAN COUNCIL

USAN (GH-64)	EFAVALEUKIN ALFA
PRONUNCIATION	ef" a va loo' kin al' fa
THERAPEUTIC CLAIM	Treatment of inflammatory diseases

CHEMICAL NAMES

Immunoglobulin G1 (Fc domain-containing fragment) fusion protein with peptide (synthetic linker) fusion protein with interleukin 2 (synthetic human mutein), dimer

Immunoglobulin G1 γ1-chain C-terminal constant region fragment (Fc) (1-226 without C-terminal Lys, N77G,D136E,L138M variant)-G4S linker (227-231)-human interleukin 2 (232-364, V322K,C356A variant) fusion protein, dimer disulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa interleukin derivative

STRUCTURAL FORMULA

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DKTHTCPPCP APELLGGPSV FLFPPKPKDT LMISRTPEVT CVVVDVSHED 50
PEVKFNWYVD GVEVHNAKTK PREEQYGSTY RVVSVLTVLH QDWLNGKEYK 100
CKVSNKALPA PIEKTISKAK GQPREPQVYT LPPSREEMTK NQVSLTCLVK 150
GFYPSDIAVE WESNGQPENN YKTTPPVLDS DGSFFLYSKL TVDKSRWQQG 200
NVFSCSVMHE ALHNHYTQKS LSLSPGGGGG SAPTSSSTKK TQLQLEHLLL 250
DLQMILNGIN NYKNPKLTRM LTFKFYMPKK ATELKHLQCL EEELKPLEEV 300
LNLAQSKNFH LRPRDLISNI NKIVLELKGS ETTFMCEYAD ETATIVEFLN 350
RWITFAQSII STLT                                       364
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There are 3 mutation sites on AMG 592. The IL-2 mutein domain contains a mutation at V322K with the intent to decrease signaling through the IL-2 receptor and increase regulatory T cells selectivity. The IL-2 domain also carries a C356A mutation with the intent to improve manufacturability. The Fc contains an N77G mutation that reduces interaction of the Fc with immune effector cells through FcγRs

Precursor Nucleotide Sequence

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GACAAAACTC ACACATGCCC ACCGTGCCCA GCACCTGAAC TCCTGGGGGG 50
ACCGTCAGTC TTCCTCTTCC CCCCAAAACC CAAGGACACC CTCATGATCT 100
CCCGGACCCC TGAGGTCACA TGCGTGGTGG TGGACGTGAG CCACGAAGAC 150
CCTGAGGTCA AGTTCAACTG GTACGTGGAC GGCGTGGAGG TGCATAATGC 200
CAAGACAAAG CCGCGGGAGG AGCAGTACGG CAGCACGTAC CGTGTGGTCA 251
GCGTCCTCAC CGTCCTGCAC CAGGACTGGC TGAATGGCAA GGAGTACAAG 300
TGCAAGGTCT CCAACAAAGC CCTCCCAGCC CCCATCGAGA AAACCATCTC 350
CAAAGCCAAA GGGCAGCCCC GAGAACCACA GGTGTACACC CTGCCCCCAT 400
CCCGGGAGGA GATGACCAAG AACCAGGTCA GCCTGACCTG CCTGGTCAAA 450
GGCTTCTATC CCAGCGACAT CGCCGTGGAG TGGGAGAGCA ATGGGCAGCC 500
GGAGAACAAC TACAAGACCA CGCCTCCCGT GCTGGACTCC GACGGCTCCT 550
TCTTCCTCTA TAGCAAGCTC ACCGTGGACA AGAGCAGGTG GCAGCAGGGG 600
AACGTCTTCT CATGCTCCGT GATGCATGAG GCTCTGCACA ACCACTACAC 650
GCAGAAGAGC CTCTCCCTGT CTCCGGGTGG AGGTGGTGGA AGCGCTCCAA 700
CTTCCTCCTC CACTAAGAAG ACTCAATTGC AATTGGAGCA CTTGTTGTTG 750
GACTTGCAAA TGATCTTGAA TGGTATCAAT AATTACAAGA ATCCAAAGTT 800
GACTCGGATG TTGACTTTTA AGTTTTACAT GCCAAAGAAG GCTACTGAGT 850
TGAAGCACTT GCAATGTTTG GAGGAGGAGT TGAAGCCATT GGAGGAGGTT 900
TTGAATTTGG CTCAATCCAA GAATTTTCAC TTGCGGCCAC GGGACTTGAT 950
CTCCAATATC AATAAGATCG TTTTGGAGTT GAAGGGTTCC GAGACTACTT 1000
TTATGTGTGA GTACGCTGAC GAGACTGCTA CTATCGTTGA GTTTTTGAAT 1050
CGGTGGATCA CTTTTGCTCA ATCCATCATC TCCACTTTGA CT 1092
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Additional Modifications

Intrachain Disulfide bridges: C41-C101; C147-C205; C289-C336

Interchain Disulfide bridges: C6-C6; C9-C9

Glycosylation: Each polypeptide chain contains a major O-linked glycosylation site at threonine 234 of the IL-2 mutein domain

MOLECULAR WEIGHT	Theoretical: 83,510 Da Experimental: 83,512 Da
TRADEMARK	None as yet
SPONSOR	Amgen
CODE DESIGNATIONS	AMG 592
CAS REGISTRY NUMBER	2049067-94-7
UNII	YNH9K62UXU
WHO NUMBER	10762

SCS