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New INN nomenclature scheme for monoclonal antibodies

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Suffixes/stems

At the 73rd INN Consultation in October 2021, the INN Expert Group decided to discontinue the use of the stem *-mab* and to divide this group of substances into four different groups, with four brand-new stems, to avoid any confusion between the monoclonal antibodies named according to the old nomenclature and those named according to the new nomenclature. The four new stems cover all the prior uses of stem *-mab* and divide the substances that contain an immunoglobulin variable domain into four INN stems, there being three for monospecific immunoglobulins and one for bi- and multi-specific immunoglobulins, independent of their type, shape and form. The first five INN following this new nomenclature scheme were published in Proposed INN List 126.

As the previous INN nomenclature scheme for monoclonal antibodies, this new INN nomenclature scheme for monoclonal antibodies is used for all substances that contain an immunoglobulin variable domain that binds to a defined target, and that are composed of only immunoglobulin-derived pharmacologically active components. The suffix is preceded by an infix that indicates the target class.

The four new stems are:

***-tug* for "unmodified immunoglobulins"**

The suffix ***-tug*** is used for monospecific full-length immunoglobulins with unmodified[1] constant regions and identical sets of CDRs that recognize the same epitope. This includes monospecific full-length immunoglobulins of any species and of any class (IgG, IgA, IgM, IgD, IgE), for which the amino acid sequence of the constant region of the heavy and light chains is encoded by a single naturally occurring allele. However, they may have engineered glycans and/or deleted C-terminal lysine codon (introduced for homogeneity since this is generally clipped *in vivo* and often during expression). Basically, this group includes all natural immunoglobulin molecules (which might occur as such in humoral responses of the immune system, including the Camelidae heavy-chain-only antibodies), as well as chimeric and humanized antibodies. It also includes immunoglobulins that use identical sets of CDRs to target multiple different epitopes or molecules.

***-bart* for "artificial immunoglobulins"**

The suffix ***-bart*** is used for monospecific full-length immunoglobulins with engineered amino acid changes in the constant regions and identical sets of CDRs that recognize the same epitope. This includes monospecific full-length immunoglobulins of any species and of any class (IgG, IgA, IgM, IgD, IgE) that contain any amino acid change introduced by engineering for any reason anywhere in the constant regions, including hinge (e.g., IGHG4 hinge with Serine>Proline amino acid change), new glycan attachment site, mixed allelic variants that would not occur in nature, altered complement binding, altered neonatal Fc receptor (FcRn) binding, altered fragment crystallizable (Fc)-gamma receptor binding, and

[1] Do not contain any amino acid differences with the native sequence (constant region amino acid changes by comparison with the closest genomic C gene and allele).

stabilized IgA. It also includes immunoglobulins with attachments of further variable domains with identical CDRs and that recognize the same epitope.

-*ment* for "immunoglobulin fragments"

The suffix ***-ment*** is used for monospecific fragments of any kind that do not fall under stem *-tug* or *-bart*, containing at least one immunoglobulin variable domain that contributes to binding, and feature a complete, partial or absent constant region (e.g., monospecific immunoglobulin-derived constructs without an Fc domain, scFv-Fc constructs).

-*mig* for "multi-specific immunoglobulins"

The suffix ***-mig*** is used for bispecific and multispecific immunoglobulins, regardless of the format (conventional or engineered), type (full-lenght or fragments) or shape (extensions or not). This group includes immunoglobulins with a bi- or multi-specificity conferred by different variable domains with different sets of CDRs. It does not include monoclonal antibodies that have multiple specificities through a single set of CDRs (cross-reactivity, e.g., *bimekizumab*).

Note1: Immunoglobulin fusions are only included in the monoclonal antibody nomenclature scheme if both domains have immunoglobulin derived variable domains (e.g., monoclonal antibodies fused with a cytokine is under the *-fusp* nomenclature scheme).

Note2: Antibody-drug conjugates (ADCs) also follow this new monoclonal antibody nomenclature scheme and no special suffix is added, as the second word indicates that the substance is a conjugate.

Infixes

The mechanisms of monoclonal antibodies are complex, that it may be different for different indications, and that this might not be completely understood during development phase. Therefore, the disease/target infix is assigned according to the applicant's proposed known mode of action at the time of the INN request.

The changes for the new scheme are in green.

Prefix	Infix for target class		Suffix
Random	*-ami-*	serum amyloid protein (SAP)/amyloidosis	*-tug*
	-ba-	bacterial	*-bart*
	-ci-	cardiovascular	*-mig*
	-de-	metabolic or endocrine pathways	*-ment*
	-eni-	enzyme inhibition	
	-fung-	fungal	
	-gro-	growth factor and growth factor receptor[2]	
	-ki-	cytokine and cytokine receptor[3]	
	-ler-	allergen	
	-sto-	immunostimulatory	
	-pru-	immunosuppressive	
	-ne-	neural	
	-os-	bone	
	-ta-	tumour	
	-toxa-	toxin	
	-vet-	veterinary use	
	-vi-	viral	

[2] At the 69th INN Consultation, the infix changed from *-gros-* to *-gro-* to avoid a conflict with the infix *-os-*, and at the 74th INN Consultation its definition was enlarged to *growth factors and growth factor receptors*.

[3] At the 70th INN Consultation, it was decided that the antibodies targeting an interleukin receptor would also have the *-ki-* infix. The names discussed at this Consultation are included in Proposed INN List 124.