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Review Article

A Study on BioBetters: Various Aspects and Regulatory Approval Process

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ABSTRACT

A new class of biopharmaceuticals are developed by changing profile in terms of chemistry structure and functionality resulting in enhanced efficacy in terms of reduction in immunogenicity toxicity and improvement in half-life and pharmacodynamic activity. The term "BioBetter" refers to a form of biologic that has been enhanced for safety, and patient compliance while lowering the overall cost of healthcare. Despite the fact that BioBetters generally have advantages, they will still face a number of challenges, including high costs for clinical trials, regulatory approval, patent disputes, and market opportunities. Therefore, the development of BioBetter necessitates striking a careful balance between improving patient medical management without sacrificing innovation for corporate success. Two approaches are followed to develop BioBetters Changes in formulation and engineering the protein molecule. In this article we provided a brief overview of a better development like recombinant fusion, antibody engineering and PEGylation.

Keywords: Biobetters, Biosimilars, Modification, Techniques, Regulatory.

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INTRODUCTION

BioBetters are updated or modified versions of currently marketed and approved biologics that, after alteration, produce drugs with improved selectivity, stability, and toxicity. Because of better research and a wider range of technologies available to make therapeutically enhanced products while taking into account higher safety, increased bioavailability, longer half-life, better efficacy, and immunogenicity, BioBetters are bio superior to licenced biologics. BioBetters have an advantage over biosimilars because, as previously stated, they can obtain patent protection if they can demonstrate a significant improvement over the original and biosimilar competitors' technologies.

However, it may not be possible to patent all BioBetters as the active ingredient is mostly similar to innovator products, unless proven certain significant advantages. Unlike Biosimilars , which are substantially comparable to an approved reference product, a BIOBETTER has the same molecular target and structural elements as the reference products but a better structure or formulation that makes it clinically superior. Biosimilars, as the name implies, will have similar safety and efficacy profiles as reference drugs and are extremely similar to innovator products.

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Biosimilars are only allowed after establishing resemblance to the reference product, as well as having the same active ingredient as the reference product. Biosimilars are not eligible for patent protection or data exclusivity. BioBetters, which are modified versions of biologics, should have higher safety and efficacy than reference products. Biosimilars and BioBetters are both variations on the original biological molecule. While a BioBetter must distinguish itself from the original as depicted in Figure 1.

BioBetters show a number of advantages over biosimilars, they are patentable; because of the validated target, they have a better success rate; these are modified versions of original biologic with much reduced side effects profile; risk of failure is comparatively lower than the newest drug; lower early-stage R&D costs and having data exclusivity of 12 years in the United States.

A BioBetter must demonstrate a considerable improvement in one or more features over the original biologic, such as a different mode of administration, a lower side effect profile, improved action, dosage frequency, and so on as given in Table 1.

KEY INTELLECTUAL PROPERTY DIFFERENCES BETWEEN BIOSIMILARS AND BIOBETTERS

Infringement considerations

BioBetters should be distinct enough to avoid infringement.

Biosimilars should be highly similar to that of biologic in order to be less likely to violate RPS patents.[1-4]

Patent protection

Biosimilar manufactures will have less opportunities to obtain patents covering innovative compositions.

BioBetters will be able to secure strong patent protection because they contain a newer active component, enhanced Drug molecule, or formulation.

Patent litigation scheme

The BPCIA applies to biosimilar manufacturers but not to manufacturers of BioBetters.

BioBetters will follow the typical patent infringement resolution scheme (Table 2).[5,6]

APPROVAL PATHWAY: FDA DATA REQUIREMENTS FOR BIOBETTERS

BioBetters must satisfy FDA stand-alone requirements. "Stand-alone" development program, 351(a). Goal: Following data is necessary to show *de novo* safety and effectiveness of a new product, as shown in Figure 2. BioBetters are more like newer drugs and they should undergo a full BLA and not an abbreviated BLA (aBLA). When compared to originator products, BioBetters are thought to have a different active ingredient.

REGULATORY CHALLENGES OF BIOBETTERS

As FDA requires a full BLA for BioBetter approval it would significantly increase the cost and complexity of obtaining approval.

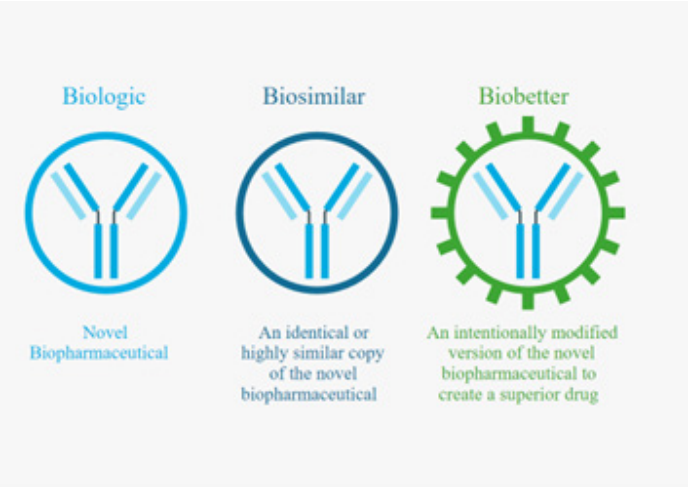

Figure 1: Image of biologic, biosimilar and BioBetter.

There is no specific regulatory pathway for BioBetters till now on which FDA will grant approval on a case-by-case basis. Risk of clinical failure can be high.[7]

MODIFICATIONS THAT MAKE BIOBETTER DIFFERENT FROM BIOSIMILARS

BioBetters are structurally different from the reference product and hence they should be novel for this reason alone to obtain a patent. Some of them includes;

- Have a different amino acid sequence.
- Have a different glycosylation pattern.
- Have a different attachment, such as PEGylation.
- Being a fragment of the reference product or chimeric product.[8,9]

MODIFICATION TECHNIQUES

Glycosylation

To increase circulation times, glycosylation can be modified. Glycosylation is a post-translational modification that affects a number of biologically important processes in eukaryotes including immunogenicity, pharmacokinetics, and pharmacodynamics. As a result, adequate glycosylation control is critical during the production process. Glycosylated proteins include carbohydrates that are sometimes O or N linked to oxygen in the asparagine serine or threonine side chains. During the transit through the endoplasmic reticulum and the Golgi apparatus, N linked glycans are attached in three phases. Synthesis of precursor oligosaccharides is followed by a transfer of the activated polymer block to asparagines, followed by enzymatic trimming. As a result of this step's sensitivity to the culture environment, N glycans need a more in-depth evaluation. The method can distinguish between complex oligosaccharides with a high sialic acid content, high mannose-content glycans, and hybrid varieties. The recognition motif Asparagine-X-Serine-Threonine necessary for N linked glycosylation of Asn, where X can be any amino acid other than proline. O linked glycosylation is more reliant on the secondary structure and accessibility of Ser/Thr than on a consensus sequence. Furthermore, the O linked sugars are progressively joined as solitary monosaccharides in the Golgi. The mature O glycan is produced as a result of further modification by glycosyltransferases. In O linked oligosaccharides, sialic acid is typically the terminal sugar. Sialic acid is available in numerous forms, but only N-acetylneuraminic acid has a positive effect

Figure 2: Approval pathway of BioBetters as per FDA.

on half-life. It is important to note that the ultimate structure of N or O linked glycans is determined by the suitable three 3D structures, as well as the expression of essential enzymes and the availability of sugar substrates in the ER and Golgi, rather than the protein sequence. In the end, this causes the glycan structure to be heterogeneous, which increases the amount of downstream processing and analytical work necessary to create a homogeneous, thoroughly characterised drug substance. Example of BioBetter- Aranesp (Darbepoetin-alfa) manufactured by Amgen is developed using this technique, which resulted in improved half-life and reduced dosing frequency.[10,11]

Bioconjugation

A biomolecule must be present in at least one of the two molecules that are used in the bioconjugation process. Due to the wide range of available amino acids, proteins are particularly diverse biomolecules and serve as significant substrates in bioconjugation reactions. Protein modification relies heavily on bioconjugation reactions. Proteins may now be modified to perform a range of activities, such as cellular monitoring, imaging biomarkers, and specific medicine delivery, due to recent advances in biomolecule research.

Conventional Polymer Conjugation–Pegylation

PEGylation is a biochemical process that changes bioactive molecules with Polyethylene Glycol (PEG), giving proteins, peptides, antibodies, and vesicles several useful properties that are believed to be used in treatment or cell genetic engineering. Examples are Pegasys which is PEGylated interferon, Neulasta which is PEGylated granulocyte colony stimulator and Micera which is methoxypolyethlene glycol-epoetin beta.[12]

Pasylation

In aqueous buffers, biochemical polypeptides consisting of the short l-amino acids Pro, Ala, and/or Ser (PAS) adopt a random coil shape with remarkably comparable biophysical characteristics to PEG. This is the basis for PASylation and PAS sequences, on the other hand, can be coupled with pharmaceutically valuable proteins and peptides via genetically encoded fusion proteins and chemical coupling. Several biologics, including enzymes, growth factors, and peptides, have been successfully PASylated, and the process has been validated in animal models such as mice and monkeys.[13]

Fusion Modification

In this approach, a recombinant protein is fused to a long-lived companion protein, which enhances its pharmacokinetics. Albumin and the Fc fragment of immunoglobulin are two naturally occurring partner proteins used for fusion. Several peptides exhibit half-lives which are not suitable for therapeutic dosage. To tackle this situation, five general techniques for half-life extension have been applied such as: (a) A pharmacologically active peptide or protein is genetically fused with a naturally long-half-life protein or protein domain. (For example, albumin fusion and transferrin fusion). (b) A pharmacologically significant peptide or protein is genetically fused to inactive polypeptide like homo-amino polymer (HAP; HAPylation) and (ELP; ELPylation). (c) Modifying the hydrodynamic radius with techniques such as chemical conjugation to repetitive chemical moieties such as PEG (PEGylation). (d) By significantly increasing the negative charge through polysialylation, the pharmacologically active peptide or protein is fused; The biological drug candidate is fused with a negatively charged highly sialylated peptide known to prolong the half-life of natural proteins like human CG beta sub-unit. (e) Non-covalent attachment of a peptide or protein binding domain to the bioactive protein, resulting in binding to typically long half-life proteins such human IgG or HAS (Table 3).[14] Some of the BioBetters developed using Protein Fusion techniques are.

Table 1: Differences between a Biosimilars and BioBetters.

Biosimilar	BioBetter
Similar active substance as that of reference product.	No structural limitations. It can have different active compounds.
Similar safety and efficacy data.	Improved safety and efficacy profiles.
Approved by demonstrating bio similarity.	By submitting all clinical and non-clinical data, approved either through NDA or hybrid application.
Neither data exclusivity nor patent protection.	Chances of patent or data exclusivity based on innovation.

Table 2: Module submission of BIOBETTER and Biosimilar.

CTD Module	Biobetter	Biosimilar
Quality data	Full	Full+additional comparative data.
Clinical Phase-I	Full	Need full and Abbreviated focus on comparability .
Clinical Phase-II (PK/PD)	Full	Full+large trial-focus on comparability.
Phase II	Full	Not required.
Phase III	Full	One pivotal trial- tendency to extrapolate using a reference product.
Phase IV/Safety	Full	Full

Enbrel

Which is manufactured by Immunex (now Amgen), this BioBetter have following protein format: The protein IgG_1 Fc is fused to p75 exo-domain of TNFR.

Orencia

Which is manufactured by BMS, this BioBetter have following protein format: A fusion protein CTLA4-Fc with modified Fc.

Nplate

Which is manufactured by Amgen, this BioBetter have following protein format: Fc-peptide fusion.

Eylea

Which is manufactured by Bayer-Schering Pharma, this BioBetter have following protein format: VEGFR-Fc fusion.

Humanization

Non-human monoclonal antibodies are prone to causing immune-mediated side effects. As a response, chimeric mAbs were developed by substituting human Fc regions for non-human Fc regions. Humanized mAbs have also been developed by repurposing substantial parts of the Fab regions. Example: Gazyva – Binds to epitope on CD20.[7]

Altering Amino Acid Sequences

During this procedure, peptide sequences are attached to or modified to existing proteins, stabilising them and improving their lifespan without becoming more toxic or losing the required biological activity.

Ekylation

Protein stabilisation is a genetic fusion of repetitive amino acid sequences. The equal ratio of cationic lysine (K) and anionic glutamic acid (E) exists on protein surfaces to enhance stability. On surfaces and nanoparticles, it has been discovered that repeated EK sequences, whether mixed or alternate, produce non-fouling zwitterionic characteristics. This poly (EK), a natural alternative to zwitterionic poly (pCB), is suitable for medical applications due to its biological chemistry, high biocompatibility, and enzyme degradability. According to Liu, *et al*, the C terminus of lactamase can be stabilised by adding poly tails of pre-set lengths by the use of *E. coli* production. This bioinspired "EKylation" approach enables quick creation of target structures and stability when exposed to environmental stressors like high temperature and extremely salty solutions. It also offers the stabilising effects of poly-zwitterions. The widely applicable biocompatible and biodegradable equivalents to synthetic polymer conjugates are provided by this one-step method.[15]

XTEN technology

Schellenberger originally developed the XTEN approach, also called XTENylation. XTENs are genetically fused 864 amino acid unstructured recombinant polypeptides that are very hydrophilic and anionic due to their total composition of alanine, glutamate, glycine, proline, serine, and threonine residues. Protein creation in solution and manufacture are made possible by the XTEN sequence, which has been proven to controllably lengthen the serum half-life of peptides and proteins. It also increases protein water solubility and stability. Both bacterial and mammalian cells can express the sequence, which is frequently linked to the proteins N or C terminus. The XTEN sequence is quickly degraded since it contains only natural amino acids. Few or no immunogenic T cell epitopes are present in XTEN since it doesn't include any hydrophobic amino acid residues. As a result, animal research has shown that immunogenicity is only moderately common, even in the involvement of adjuvants. Furthermore, the XTEN pattern has no known similarity to endogenous human proteins, according to the basic local alignment search tool for proteins analysis, suggesting that cross-reactivity autoimmunity is not found. The recombinant nature of XTEN gives a number of benefits over conventional PEGylation. Genetic fusion of a specified amino acid sequence led to homogeneous end products, in contrast to the more diverse PEGylated proteins. In addition, XTEN products cost less and produce more than PEGylated ones, which need to be chemically coupled and separated from unaltered species, and free PEG.[16]

Approved BIOBETTERS

There is no generally accepted definition of "BioBetter" it is difficult to compile some of the BioBetters that are approved across the world area given in Table 4. Some of the patented BioBetters are given below.

AVONEX and PLEGRIDY

AVONEX and PLEGRIDY are covered by numerous US patents and submissions in addition to a number of foreign analogues. US Patent No. 7,588,755 asserts the utilization of recombinant beta interferon for immunomodulation or the treatment of viral conditions, viral diseases, malignancies, or cancers. The use of AVONEX and PLEGRIDY in the treatment of multiple sclerosis is covered by this patent, which will expire in September 2026.

Tecfidera

Patent number 6,509,376, issued in the United States, claims dimethyl fumarate formulations for use in the treatment of autoimmune illnesses such as multiple sclerosis. This patent expired in 2019; U.S. patent no. 7,320,999, claims treating multiple sclerosis using dimethyl fumarate; Patent no. 8,399,514, claims a dosing regimen of dimethyl fumarate, monomethyl of 480 mg per day.

Tysabri

Tysabri and its use to treat multiple sclerosis are covered by US patents 5,840,299 and 6,602,503, as well as EP 0804237, which expire between 2017 and 2020. (This includes extra protection certificates in various European nations). Additional patents and proposals covering treatment processes involving the material will expire in 2023 in the United States and the European Union.

Fampyra

EP 1732548B1, which claims sustained-release aminopyridine compositions for increasing walking speed in patients with multiple sclerosis, and EP 2377536B1, which claims prolonged aminopyridine mixtures for treating multiple sclerosis, both expire in 2025 but are liable to pending and granted supplemental protection certificates, which, if granted, will extend the term of one of the patents to 2026.

ELOCTATE and ALPROLIX

US patents 7,404,956; 8,329,182; 7,348,004; and 7,862,820 are the key ones. Related European patents EP 1624891 and EP 1625209 are slated to expire in 2024 and may be renewed in at least some countries if accepted. In addition, pending patent applications, if approved, would prolong patent protection until 2034. In the United States, both ELOCTATE and ALPROLIX have regulatory exclusivity until 2026.

Mircera

Hoffmann-La Roche Inc. submitted a patent term restoration application to the Patent and Trademark Office for MIRCERA (U.S. Patent No. 6,583,272).

Remsima SC

Celltrion patented Remsima SC - will be under patent protection until 2037.

Humira

While Humira's US patent was set to expire in December 2016, it was postponed by eight years as global biopharmaceutical companies reached an agreement with AbbVie to produce Humira biosimilars after 2023.[17]

Victoza

Victoza, a proprietary product of Novo Nordisk, Meanwhile, Mylan challenged Victoza patent No. 8,114,833, which covers the drug's production as well as formulation and protects Novo's diabetic drug until early 2026.[18]

FUTURE OF BIOBETTERS

Whether or not BioBetters outperform originators, such new and inventive treatments bring value to patients by improving convenience and providing other treatment alternatives if a disease progresses. For manufacturers, having a target in mind and improving the clinical trial programme will help them enter

Table 3: Half-life extension techniques for BioBetters.

Strategy	Specific approach	Construct	Mechanism for half-life extension
Human protein fusion with a naturally long serum half-life.	Fusion to human IgG Fc domain.	Fusion to the C or N terminus of human IgG Fc. Half-life in human serum is roughly 14 days.	Recycling via FcRn.
	Fusion to HSA.	Genetic fusion to HSA, that roughly has 19 days half-life in human serum.	Recycling via FcRn.
	Fusion to human transferrin.	Fusion to C or N terminus of human transferrin. Which has 12 days half-life in human serum.	Recycling through transferrin.
Non-structured polypeptide fusion.	ELPylation.	Uncharged random coil structures with a large hydrodynamic volume are formed via genetic fusion of polypeptide sequences consisting of PAS.	Size and hydrodynamic radius increase.
	HAPylation.	HAP.	Size and hydrodynamic radius increase.
	GLK fusion.	Fusion with artificial GLK.	Size and hydrodynamic radius increase.
To enhance negative charge, fusion to highly anionic polypeptide is required.	CTP fusion.	Human CG beta sub-unit genetic fusion to CTP peptide to antibody fragment.	CTP sialylation results in an increased negative charge.

CTP: Carboxy-terminal peptide, ELP: elastin-like peptide, Fc: constant fragment, FcRn: neonatal Fc receptor, GLK: Gelatin-like protein, HAP: homo-amino acid polymer, HAS: human serum albumin, Ig: immunoglobulin,

Table 4: List of approved BIOBETTERS.

BIOBETTER	Active ingredient	Manufacturer	FDA approval
Gazyva	Obinutuzumab	Genentech	Nov 1, 2013
Enhertu	Trastuzumab deruxtecan	AstraZeneca and Daiichi Sankyo	Dec 20, 2019 for breast cancer. Jan 15, 2021 for Gastric cancer Aug 12, 2022 for lung cancer.
Zaltrap	Aflibercept	Sanofi and Regeneron Pharmaceuticals, inc.	Aug 3, 2012
Neulasta Onpro	Pegfilgrastim	Amgen	2014
Aranesp	Darbepoetin alfa	Amgen	Sep 17, 2001
Plegridy	Peginterferon beta-1a	Biogen	Aug, 2001
PegIntron	Peginterferon alfa-2b	Schering	Jun, 2001
Pegasys	Peginterferon alfa-2a	Hoffman-La Roche	Sep, 2002
Trulicity	Dulaglutide	Eli Lilly	Sep 18, 2014
Tanzeum	Albiglutide	GlaxoSmithKline	Apr 15, 2015
Alprolix	Coagulation Factor IX, Fc fusion protein	Bioverativ Therapeutics	Mar 28, 2014
Eylea	Aflibercept	Regeneron Pharmaceuticals	2011
Nulojix	Belatacept	Bristol-Myers Squibb company.	Jun, 2011
Arcalyst	Rilonacept	Kiniksa	Feb 27, 2008
Neulasta	Pegfillgrastim	Amgen	Jan 1, 2002
Orencia	Abatacept	Bristol-Myers Squibb company	Dec 15, 2021
Amevive	Alefacept	Astellas Pharma	Discontinued
Ontak	Denileukin Diftitox	Citius Pharmaceuticals	Discontinued
Enbrel	Etanercept	Immunex Corporation	Nov 4, 2016
Victoza	Liraglutide	Novo Nordisk	June 17, 2019
Byetta	Exenatide	AstraZeneca	Oct 20, 2011
Bydureon	Exenatide	AstraZeneca	Oct 23, 2017
Lyxumia	Lixisenatide	Sonofi Winthrop	Jan 31, 2013
Humira	Adalimumab	AbbVie Inc.	Dec 31, 2002
Kadcyla	Trastuzumab emtansine	Genentech	Feb 22, 2013
Lucentis	Ranibizumab	Novartis EuroPharm	Jan 22, 2007
Remsima SC	Infliximab	Celltrion	Sep, 2013
Rybelsus	Semaglutide	Novo Nordisk	Sep, 2019
Granix	Filgrastim	Teva	Aug 29, 2012
Mircera	Methoxy polyethylene glycol-epoetin beta.	Roche and Vifor	Nov 14, 2007

the market sooner. In this regard, BioBetters appear to be one approach to maintain market dominance and guard against biosimilar competition - assuming superiority can be obtained (Table 5). Furthermore, pricing expectations must be reasonable in a world where your competitors are rapidly becoming available with imitation and biosimilar drugs at approximately 30% cheaper prices.

Ensuring market access

Because present treatments are not optimal, BioBetters have a chance for economic success. Understanding the market and designing goods that can provide equality in some clinical domains while improving in others will be beneficial. To accomplish this, manufacturers must keep the following factors in mind to ensure market access:

Table 5: Improved characteristics of BioBetter over biologics.

BioBetter	Reference biologic	Manufacturer	Approval year	Specifications	Characteristics improved over original
Kadcyla	Trastuzumab	Genentech	2013 by FDA	Antibody drug conjugate, combining the HER2 inhibition of trastuzumab and the microtubule inhibition of DM1.	Combination with efficacy greater than that of the current standard of care.
Eloctate	Recombinant antihemophilic factor.	Biogen Idec	2014 by FDA	B-domain-deleted recombinant factor VIII, Fc fusion protein.	Reduced dosage frequency.
Tanzeum	Glucagon-like peptide-2.	GlaxosmithKline	2014 by FDA	GLP-1 receptor agonist-albumin fusion.	Extended half life.
Elonva	FSH (Follicle Stimulating Hormone).	Merk	2010 by EMA	Fusion to FSH and C terminal peptide of Human chorionic gonadotropin.	Single injection instead of seven daily injections.

Table 6: List of various considerations of Biosimilars and BioBetters.

Consideration	Biosimilar	Biobetter
Market acceptance	Some reservation likely-Discount is not as considerable as it is with inexpensive generics. Not identical to reference.	Some reservation likely-More costly than biosimilars.
Pathway	Abbreviated BLA.	BLA
Exclusivity protection	None, unless first interchangeable.	Concurrent 4-yr data exclusivity and 12-yr market exclusivity.
Impact of reference exclusivity protection	Obligated to wait for loss of reference exclusivities.	Not impacted by reference exclusivities.
Cost of Manufacturing including R&D	$100 million to $300 million.	$400 million to $900 million.
Extrapolation	Without particular clinical trials, extrapolation and licensing for reference indications are possible.	Extrapolation not permitted.
R&D	Demonstrating similarity. Opportunity for indication extrapolation.	Target known. Safety issues of references are known. Biomarkers data.
Miscellaneous	Treated as generic to biologic.	Change premium price in association with market exclusivity as a branded medicine.

Satisfy an unmet need

Engage clinicians and payers to identify and solve unmet needs-Understand which characteristics a given product can and cannot satisfy, and be transparent that, while the solution cannot meet every unmet need, some are more significant to payers and physicians than others. The solution should not worsen any unmet needs; Mircera is an example of how the reduction in administration frequency both highlighted and satisfied a previously unmet patient need. As with Kadcyla, payers, patients, and clinicians all gain from the therapeutic options available, despite the absence of superiority.

Market entry and Patent litigations

Securing market access for a BioBetter necessitates a thorough examination of the market landscape for competing products.

To gain a market share advantage against premium biosimilars, BioBetters must enter the market before the patented reference biologic's exclusivity period expires, which is the only time biosimilars can begin production. At the same time, keep in mind that payers are likely following the originator patent expiration and when biosimilars are likely to introduce, so these price tags will be on their sights.[19-21]

BioBetters are improved versions of original biologics that may provide additional value to patients and payers. Premium pricing will be a barrier to patients receiving access to these innovative treatments, therefore producers must gather the necessary proof and develop a market-access plan as given in Table 6.

FINDINGS

BioBetters usually excel than the biologic counterparts in terms of reduced dosage frequency improved efficacy reduction in immunogenetic risks, half-life, greater lower toxic effect, enhanced efficacy and initial starting stage investment.

Higher rate of success as they have target that is validated target.

Development is easy when compared to biosimilar as a simple understanding of mechanism of protein folding along with ensuring effect sufficient instead of creating a replica of biologic as in case of biosimilar.

As BioBetters have a validated target the initial investment for starting stage of R&D is minimum.

The risk of having limited success is less as it is based on a biologic with proven efficacy and safety.

No need to wait till patent expiry of original biologic.

Reduced cost in terms of litigations as they don't claim to be similar with the original biologic.

The basic advantage with BioBetters is the exhibit improvement from biologics and this results in patent filing an acceptance.

Bio better show better clinical efficacy and so they can be priced at premium comparison with biologics.

Being a new molecular entity, they will be having 9-to-10-year data exclusivity in European Union and 12-year data exclusivity in United States.

The chances of successful regulatory approval of BioBetter are high, Meaning lower business risk and higher ROI.

CONCLUSION

The biopharmaceutical industry is rapidly expanding. Biotechnology is a key method for creating biologics with unique mechanisms. With the advancement of time, the need for generic versions of these molecules became noticeable, and biosimilars were founded; however, BioBetters with superiority over the original product despite some similarities- are now available, and as biosimilar competitive pressure emerges, BioBetters may become a suitable strategy for the future. BioBetter development necessitates enormous expenditure as well as a certain level of risk sensitivity, which may be observed in the final cost of the medicine. Because of the therapeutic and economic benefits, they give, they have the potential to change treatment patterns and industrial procedures for a wide range of ailments.[6,20]

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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