PHARMA NEWS

Top developments in biosimilars during 2016

Previous years have been momentous for biosimilars [1] and 2016 is no exception. This paper highlights the various developments that have taken place during 2016 for biosimilars. Important milestones achieved during 2016 were the biosimilar approvals of Inflectra (infliximab-dyyb), Erelzi (etanercept-szzs) and Amjevita (adalimumab-atto) by the US Food and Drug Administration (FDA).

FDA is also reviewing applications for Bioepis/Merck's infliximab biosimilar candidate (SB2), Amgen/Allergan's proposed bevacizumab biosimilar (ABP 215), Mylan/Biocon's proposed trastuzumab biosimilar (Myl-1401O) and for the pegfilgrastim biosimilar candidate (CHS-1701) made by Coherus BioSciences. The agency, however, rejected an application from Sandoz for a pegfilgrastim biosimilar (LA-EP2006) in July 2016. FDA has also accepted an application for follow-on insulin glargine biological MK-1293 via the 505(b)(2) regulatory pathway, which allows FDA to reference previous findings of safety and efficacy for an already-approved product (Lantus), in addition to reviewing findings from studies of MK-1293.

In Europe, the etanercept biosimilar Benepali (SB4) and the infliximab biosimilar Flixabi were approved in January and May 2016, respectively. The European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use also recommended approval of the teriparatide biosimilars Movymia and Terrosa, as well as the insulin glargine biosimilar Lusunda in November 2016. The agency is also currently reviewing biosimilar applications for adalimumab, bevacizumab, etanercept, insulin glargine, insulin lispro, pegfilgrastim, rituximab and trastuzumab.

In October 2016, US biotechnology company Biogen launched its infliximab biosimilar Flixabi in the UK.

In September 2016, Australia's Pharmaceutical Benefits Advisory Committee (PBAC) decided that the etanercept biosimilar Brenzys 'could be marked as equivalent' to the brand-name biological Enbrel (etanercept) on the Australian Pharmaceutical Benefits Scheme. The decision gives pharmacists the authority to substitute Brenzys for its reference product, Amgen/Pfizer's arthritis blockbuster Enbrel (etanercept). The PBAC also endorsed switching between Enbrel and Brenzys, saying that 'the drug, etanercept, is not immunogenic per se, and anti-drug antibodies are rare. Switching between brands of etanercept is unlikely to change this'.

In June 2016, Hospira, now part of Pfizer, announced that its infliximab biosimilar, Inflectra, had received approval from Canada's medicines regulator, Health Canada, in three extra indications: Crohn's disease, fistulising Crohn's disease and ulcerative colitis. In September 2016, Merck Canada announced that it had received approval for its etanercept biosimilar Brenzys (SB4) from Health Canada – the first subcutaneous antitumour necrosis factor (anti-TNF) biosimilar available in Canada.

Elsewhere in South Korea, Samsung Bioepis launched its infliximab biosimilar, Renflexis, which received approval from the Korean Ministry of Food and Drug Safety (MFDS), in May 2016. The MFDS also approved Celltrion's rituximab biosimilar (CT-P10), Truxima, in November 2016.

India-based biologicals specialist Biocon received Japanese regulatory approval for its biosimilar insulin glargine product in March 2016. Another biotech firm Kyowa Hakko Kirin announced in January 2016 that it had made a deal with Sandoz for exclusive marketing rights to Sandoz's biosimilar rituximab in Japan.

Russia's Ministry of Health (*Министерство здравоохранения Российской Федерации; Rosminzdrav*) approved Biocad's non-originator trastuzumab biosimilar, BCD-022, in January 2016.

Meanwhile, India's drug regulator, the Drugs Controller General of India, granted marketing approval for bevacizumab 'similar biologics' from India-based generics makers Reliance Life Sciences and Hetero Group in June 2016. These approvals were followed by the launch of the products in August 2016.

Biologicals naming

The issue of naming for biologicals is a contentious one and this has not changed during 2016. Advocates for distinct names include the Biologics Prescribers Collaborative and the Alliance for Safe Biologic Medicines (ASBM). The Generic Pharmaceutical Association (GPhA), on the other hand, believes that different names could 'erect barriers to patient access to new, more affordable medicines, and jeopardize their safety'. The Academy of Managed Care Pharmacy (AMCP) has also said that distinct names could result in 'lower market adoption and cost-savings' from biosimilars.

The World Health Organization (WHO) introduced the concept of a biological qualifier (BQ) for naming biologicals in 2014. This was followed by a draft proposal on naming biologicals, including biosimilars. In 2016, this has been followed by the proposal to proceed with a provisional implementation of the BQ scheme accompanied by a prospective impact study.

The International Generic and Biosimilar Medicines Association (IGBA) opposes the BQ. Although it says that it welcomes WHO's continuous interest in the development of a global identification system for biologicals, the group stated that the 'IGBA does not support the BQ proposal'. The IGBA added that 'successful product identification and tracking using multiple identification components are already in force'.

FDA has proposed that all biologicals, including biosimilars, have non-proprietary names and that a four-letter meaningless suffix be added to the names to distinguish them from each other [2]. The agency issued final guidance detailing the agency's requirements for the non-proprietary naming of biological products in January 2017. In its guidance FDA outlines how the 'proper name' of a biological will consist of a combination of the 'core name' and a distinguishable suffix, which will be 'devoid of meaning' and be 'composed of four lowercase letters'. For example, the 'proper name' of products containing the fictitious core name biologicamab, could be biologicamab-cznm for the originator biological and biologicamab-hixf for the biosimilar.

Following the approval of the infliximab biosimilar Inflectra (infliximab-dyyb) by FDA, the American College of Rheumatology (ACR) issued a statement supporting the use of distinct

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names for biosimilars. The group stated that 'the ACR supports distinct naming and transparent labelling for all biosimilar products to ensure correct prescribing and dispensing, post-marketing surveillance, prescriber confidence, and enhanced market uptake'. The ACR has also called on FDA to issue guidance on the substitution of biosimilars.

Studies of pharmacists, carried out by the AMCP and the Hematology/Oncology Pharmacy Association (HOPA) and the ASBM found that pharmacists had a preference for distinguishable names. However, the AMCP/HOPA study also found that using the same names for interchangeable biologicals would make pharmacists more likely to dispense biosimilars [3, 4].

State legislation on biosimilar substitution in the US

During 2016, additional state legislation was considered that would allow the substitution of biosimilars. Many of these proposed bills use compromise wording proposed by the GPhA in 2015. The latest states to consider or pass legislation allowing substitution of a biosimilar for an originator biological include Idaho, Kentucky, Michigan and Oregon.

Biosimilars guidance

FDA announced in the beginning of 2016 that it had finalized its guidance for industry on formal meetings between FDA and biosimilars sponsors. The agency also published draft guidance on biosimilars labelling and finalized guidance on clinical pharmacology data to support biosimilarity. Expected draft guidance on interchangeability did not materialize in 2016, but was finally published in January 2017.

In January 2016, EMA released a draft concept paper on the revision of the reflection paper on 'Non-clinical and clinical development of interferon alfa biosimilars'. EMA is proposing to update the guidance based on experience gained with marketing authorization applications of reference products and scientific advice on biosimilar interferon alfa. The agency also introduced a new guideline on the monitoring of biologicals, including biosimilars in August 2016.

The Danish Ministry of Health, in partnership with the country's regulatory agency (*Laegemiddelstyrelsen*), set up an action plan in 2016 to monitor biologicals and improve pharmacovigilance, as well as to improve understanding among healthcare professionals and patients.

Health Canada issued a new draft revised guidance document on the information and submission requirements for subsequent entry biologics (SEBs) in Canada. This update included new information on extrapolation of indications for SEBs [5].

In March 2016, India's Central Drugs Standard Control Organization announced the release of proposed revised guidance for 'similar biologics' in India. These revised guidelines [6] will replace the original guidance issued in September 2012.

Finally, the Biosimilars Working Group (BWG) of the International Pharmaceutical Regulators Forum (IPRF) released a template for Public Assessment Summary Information for Biosimilar (PASIB). PASIB includes key information and summarized details of the biosimilar review and is expected to be of more use to countries that currently do not publish their reviews or do so only in a local language that is not English.

Clinical trials for biosimilars

Clinical trials have been a major feature of 2016, with numerous trials for biosimilars being carried out.

In February 2016, Epirus Biopharmaceuticals reported that it had started a phase III trial of its infliximab biosimilar (BOW015) in patients with active rheumatoid arthritis despite methotrexate therapy. In March 2016, Germany's Merck KGaA reported that it had started a phase III clinical trial of its adalimumab biosimilar (MSB11022) in patients with chronic plaque psoriasis. In April 2016, South Korean electronics giant Samsung and biotechnology company Biogen Idec's joint venture Samsung Bioepis started a phase III clinical trial of a biosimilar version (SB8) of Roche's cancer blockbuster Avastin (bevacizumab).

In March 2016, researchers from Birmingham Children's Hospital presented results from a study of the use of the infliximab biosimilar CT-P13 (Remsima/Inflectra) in children with inflammatory bowel disease. The results, according to the authors, showed that 'the efficacy and safety of biosimilar infliximab (Inflectra) is comparable to the originator infliximab'.

US-based biologicals maker Sorrento Therapeutics (Sorrento) reported in May 2016 that its partner, MabTech, had successfully completed a combined phase II and III clinical trial in China for STI-004, a copy biological for omalizumab (Xolair). STI-004 met its primary endpoint in a multicentre, randomized, double-blind, placebo-controlled, clinical study. Meanwhile, phase III trials in China of cetuximab (STI-001) and infliximab (STI-002) copy biologicals from MabTech reportedly 'met their primary endpoints in confirmatory, randomized, controlled, two-part phase III studies'.

In June 2016, generics giant Mylan and partner Biocon presented data from the companies' phase III HERiTAge study of their biosimilar trastuzumab candidate, Myl-1401O. According to Mylan, the results of the double-blind, randomized, parallel group study confirmed the efficacy, safety and immunogenicity of Myl-1401O compared to Roche's Herceptin (trastuzumab) both given in combination with paclitaxel as first-line therapy every three weeks in patients with *HER2+* metastatic breast cancer. The companies submitted their marketing applications to EMA and FDA in August and November 2016, respectively.

In October 2016, Biocon and Mylan also presented results of a study comparing their biosimilar pegfilgrastim (MYL-1401H) to the originator (Neulasta), which, according to Mylan, 'demonstrated equivalent efficacy'.

Samsung Bioepis also presented the results of studies of three of its biosimilars, Benepali (etanercept), Flixabi (infliximab) and candidate biosimilar SB5 (adalimumab) in June 2016. The data indicated 'comparable outcomes with regards to both the efficacy and safety of treatment' when compared to their respective reference products, according to the company.

PHARMA NEWS

US pharma giant Merck (also known as MSD outside the US) reported positive results in June 2016 from two phase III studies evaluating its insulin glargine biosimilar (MK-1293). In both studies, MK-1293 achieved its primary endpoint by demonstrating non-inferiority in change from baseline haemoglobin A1C (a measure of average blood glucose) and similar safety to Lantus (insulin glargine) after 24 weeks in patients with type 1 and type 2 diabetes.

Results of a study of Amgen and Allergen's trastuzumab biosimilar (ABP 980) compared to Herceptin (trastuzumab), according to Amgen, 'ruled out inferiority compared to trastuzumab but could not rule out superiority based on its primary efficacy endpoint of the difference of the percentage of patients with a pathologic complete response (pCR)', which was defined by the absence of invasive tumour. Overall, adverse events and immunogenicity were also comparable between ABP 980 and Herceptin, according to the company [7].

US-based biosimilars developer Coherus BioSciences (Coherus) reported in July 2016 that follow-on results from a phase I study of its candidate pegfilgrastim biosimilar (CHS 1701) were positive.

Boehringer Ingelheim reported in November 2016 that new data from its phase I INVICTAN-1 study of its bevacizumab biosimilar, BI 695502, had 'met all the pre-defined primary and secondary endpoints'. In addition, the results confirmed that BI 695502 was well tolerated, with no clinically relevant differences in safety or immunogenicity evaluations between the BI 695502 and bevacizumab treatment groups. They also have a phase III study (INVICTAN-2) underway to investigate the safety and efficacy of BI 695502 compared to Avastin in patients with advanced non-squamous non-small cell lung cancer.

Sandoz, which is the generics division of Novartis, reported in November 2016 the publication of the results of its EGALITY study in the *British Journal of Dermatology*. The confirmatory clinical safety and efficacy study shows, according to Sandoz, that its etanercept biosimilar (GP2015) 'is equivalent to the originator biological, Enbrel (etanercept), in more than 500 adult patients over 52 weeks'.

Pharma giant Pfizer reported in November 2016 that its pivotal phase III REFLECTIONS B3271002 study of its trastuzumab biosimilar (PF-05280014) versus Herceptin (trastuzumab) had met its primary endpoint. The trial, according to Pfizer, 'demonstrated equivalence in the primary endpoint of objective response rate (ORR) of PF-05280014 versus Herceptin, taken in combination with paclitaxel, in first-line patients with *HER2+* metastatic breast cancer'. ORR is defined as the proportion of patients with tumour size reduction of a predefined amount and for a minimum period of time.

US-based biotechnology firm Momenta Pharmaceuticals (Momenta) reported on 29 November 2016 that the confirmatory phase III clinical study of its adalimumab biosimilar candidate (M923) developed in collaboration with Baxalta (now part of Shire) had met its primary endpoint. Momenta also said that 'the estimated difference in responders was well within the pre-specified confidence interval, confirming equivalence'.

South Korean biotechnology company Celltrion reported in December 2016 that its pivotal phase III study 'shows equivalence in pharmacokinetic and safety data between CT-P10 and reference rituximab'. Celltrion received approval from the MFDS for its rituximab biosimilar in November 2016. The company submitted its application for approval of CT-P10 to EMA in November 2015. Rival biosimilars maker Sandoz submitted the marketing application for its rituximab biosimilar to EMA for approval in May 2016.

A post-marketing study of the epoetin alfa biosimilar Retacrit claimed that the biosimilar is 'effective and well tolerated in treating chemotherapy-induced anaemia' [8]. And another two-year post-marketing study of the epoetin alfa biosimilar Binocrit claimed the biosimilar to be safe in daily clinical practice. The authors concluded that 'the real-world safety profile of Binocrit, a biosimilar epoetin alfa, is consistent with the profile of originator epoetin alfa' [9].

A study of biological-naïve patients with active rheumatoid arthritis reported that use of biosimilar rituximab resulted in prolonged benefit in the majority of patients and was well tolerated.

A study of originator biological and biosimilar erythropoiesis-stimulating agents (ESAs) in Northern Italy reported no difference in the effects on haemoglobinemia after the first three months of treatment when using a comparable dose. The results, according to the authors, 'suggest that the lowest-cost ESA should be prescribed in chronic kidney disease/cancer patients, irrespective of ESA type' [10].

A study of tumour necrosis factor inhibitors carried out by international authority on health improvement the John Hopkins Bloomberg School of Public Health suggests that biosimilars are just as good as their reference compounds [11].

Authors from the Versilia and Manzoni Hospitals in Italy reported the case of a patient who developed pure red cell aplasia (PRCA) following subcutaneous administration of epoetin zeta, which is one of the two biosimilars of epoetin alfa licensed in Europe. The authors believe this to be the first PRCA case related to epoetin zeta [12].

Separately, researchers from the University of Massachusetts, USA and Newcastle University in the UK argued that clinical trial design should be standardized for future studies of biosimilars. Indeed, they argued that a 'standard clinical trial design be adopted for all biosimilars of a particular [originator biological] in a given disease' [13].

Extrapolation

Extrapolation of indications was once again a topic of interest during 2016 [14, 15]. EMA has stated that 'if clinical similarity can be shown in a key indication, extrapolation of efficacy and safety data to other indication(s) of the reference product may be possible' under certain conditions.

The BWG of IPRF released a draft reflection paper on the extrapolation of indications in the authorization of biosimilars in September 2016. The draft reflection paper suggests that authorization of biosimilars be carried out using a stepwise approach. Where the reference product has more than one therapeutic

indication the group proposes that, once comparability has been demonstrated in one indication, 'extrapolation of clinical data to other indications of the reference product could be acceptable'.

Switching

Switching patients from originator biologicals to biosimilars can be a contentious issue and was also a topic of interest during 2016. The British Society of Gastroenterology released guidance in February 2016 recommending that stable patients be switched to biosimilar infliximab (CT-P13). In March 2016, South Korean biologicals specialist Celltrion presented results of real-world studies supporting the safety and efficacy of switching to biosimilar infliximab.

In February 2016, the Portuguese National Authority of Medicines and Health Products (INFARMED, IP) released a Portuguese position paper on the use of biosimilars in psoriasis. In their recommendation document, although they welcomed biosimilars in the treatment of psoriasis and psoriatic arthritis, they also stated that 'there is no evidence to support switching between a reference biological and a biosimilar and vice-versa, so this should not be recommended'.

In March 2016, researchers from Spain presented results from a study on the use of the infliximab biosimilar Remsima in ulcerative colitis disease patients in clinical practice after six months treatment. The authors concluded that 'Remsima is safe', stating that 'most of the patients with ulcerative colitis who switched from Remicade to Remsima continue in remission after six months of treatment'. They did concede, however, that the follow-up was short and that there was no control group, highlighting the need for further studies.

In October 2016, data presented for the NOR-SWITCH study showed that the group of patients that were switched to biosimilar infliximab, Remsima (CT-P13), had comparable efficacy and safety to those who remained on the originator biological. The study, which was sponsored by the Norwegian Government and included nearly 500 patients at 40 sites across Norway, concluded that 'biosimilar infliximab was not inferior to the originator'.

However, in contrast, a study of antibodies to infliximab, comparing both the originator (Remicade) and biosimilar (Inflectra/Remsima; CT-P13) versions, has shown 'cross-immunogenicity' between the originator and biosimilar in patients with rheumatic diseases. This study therefore suggests that 'switching may not be suitable for patients with immunogenicity' [16].

A study from Italy also found that switching is not limited to reference products and their biosimilars, but also often occurs between originator biologicals and other originator biologicals within the same category [17].

Recently, in January 2017, FDA issued its much anticipated guidance on the interchangeability of biosimilars with their reference biologicals in order to claim 'interchangeability' for the biosimilar, additional information must be submitted that shows that the biological product 'can be expected to produce the same clinical result as the reference product in any given patient' and that 'for a biological product that is administered more than once to an individual, the risk in terms of safety or diminished efficacy of alternating or switching between use of the biological product and the reference product is not greater than the risk of using the reference product without such alternation or switch.' Switching studies, FDA states, 'should evaluate changes in treatment that result in two or more alternating exposures (switch intervals) to the proposed interchangeable product and to the reference product'.

Labelling and reimbursement

In the US, the GPhA has raised concerns over the Centers for Medicare and Medicaid Services (CMS) biosimilars reimbursement policy. The GPhA believes that the proposed rule (CMS-1631-P) 'unfairly disadvantages non-interchangeable biosimilars' and will 'erode the economic incentives that drive the US healthcare system to lower-cost therapeutic alternatives', especially for biosimilars.

The GPhA and the Biosimilars Council have also expressed concern over a requirement in FDA's draft guidance on biosimilar labelling to include a statement on biosimilarity. The groups believe that 'the proposed biosimilarity statement may be confusing' and 'is at best unnecessary'. They go on to say that 'the FDA has never required any similar statement for products found to be therapeutically equivalent, and has not provided sufficient justification for its inclusion in biosimilar labelling'.

Meanwhile, a survey carried out by EuropaBio found that doctors in Europe want more details in biosimilars labelling. Their survey found that the Summary of Product Characteristics was the third most often referenced source of information when prescribing a biological product, including a biosimilar, after peer-reviewed journals (92.4%) and professional guidelines (91.5%). It also found that most physicians preferred modified label samples that included additional information about what data had been generated with which product.

Biosimilars collaborations

Biosimilars deals were also popular during 2016. Mylan agreed an exclusive global collaboration with Momenta to develop, manufacture and commercialize six of Momenta's biosimilar

candidates. Included in the six is a version of Bristol-Myers Squibb's rheumatoid arthritis drug, Orencia (abatacept), however, the other five biosimilars were not specified.

In March 2016, US biotechnology company Oncobiologics and healthcare performance improvement alliance Premier announced that they had entered into a collaboration aimed at increasing the use of biosimilars.

Contract solutions provider SGS announced in March 2016 that it had entered into collaboration with innovative life science company DiscoverX to provide simple and qualified assays for functional comparability, for use in quality control, lot release and stability testing of biosimilars and biobetters.

Indian generics maker Cipla announced a deal to set up South Africa's first biosimilars manufacturing facility. According to Cipla, the state-of-the-art manufacturing site means the creation of Africa's first 'bio-cluster' and will attract world-class research efforts. Construction will begin in early 2017, with full operations expected by the third quarter of 2018.

Japan-based Fuji Pharma and Chong Kun Dang Pharmaceutical (CKD Pharma) made a biosimilars deal for Fuji Pharma to have the exclusive rights in Japan for the development, manufacture, distribution and sale of CKD Pharma's darbepoetin alfa biosimilar (CKD-11101). Separately, US-based biologicals specialist Amgen and Japan-based Daiichi Sankyo announced in July 2016 that they had made an exclusive agreement to commercialize nine biosimilars in Japan. In fact, Japan is proving to be a favourable market for biosimilars. Uptake of biosimilars in Japan is on a par with generics use for some products, making Japan an attractive market for biosimilars makers.

Other biosimilar collaborations made during 2016 included deals between PlantForm and Guelph University for biosimilar trastuzumab, between Lannett and Chinese partner YiChang HEC ChangJiang Pharmaceutica (YiChang) for biosimilar insulin and between Hungary-based Gedeon Richter (Richter) and South Korea-based biologicals specialist DM Bio for biosimilar trastuzumab.

General issues

The increasing number of clinical trials being carried out for biosimilars in 2016, the number of global biosimilar approvals, as well as further FDA approvals and the growing number of biosimilar applications in the US, all suggest that the future for biosimilars is a bright one.

An analysis carried out by the RAND Corporation highlighted the cost-savings to be made and therefore the need for biosimilars. The report concluded that introducing biosimilars of complex biologicals used to treat illnesses, such as cancer and rheumatoid arthritis, could cut spending on biologicals in the US by US$44 billion over the next decade. Furthermore, if countries can negotiate discounts such as those seen in Norway (47–75%) [18] and France (45%), the savings could be even larger.

Biosimilars penetration in Europe still varies widely between different countries. Penetration of biosimilars varies from a low of 0% for HGH in countries such as Belgium and Ireland to an incredible high of 100% for granulocyte-colony stimulating factor in Croatia. In fact, Eastern Europe is leading the way in biosimilars penetration, perhaps driven by economic factors.

One reason for such differences in Europe could be the gap between the regulatory decisions that govern biosimilar approval and the recommendations of medical societies. The fact that the views of medical societies, whose members are the physicians that will prescribe biosimilars, disagree with those of regulators threatens to hold back biosimilar uptake. The problem could be resolved, however, by clinicians and regulators exchanging more information [19].

Another issue is thought to be education regarding biosimilars. A survey of doctors carried out by SERMO, a global social media network, found that half of doctors do not feel that they have enough educational information to prescribe biosimilars to their patients.

To try and address this, in February 2016 the Biosimilars Forum launched a new biosimilars education initiative. The 'Partnership for Biosimilars Education and Access' focuses on raising awareness and encouraging access to biosimilars in the US. FDA has also highlighted trust and education as critical factors in ensuring patient access to biosimilars. As part of its ongoing mission to educate industry, the public and healthcare professionals about biosimilars, FDA released its online educational course for healthcare professionals: 'FDA Overview of Biosimilar Products'. In addition, Merck launched its Biosimilars Clarified (www.merckclarifiesbiosimilars.com), an online resource intended to be used as an educational platform for patients, caregivers and the healthcare community.

In Europe, Medicines for Europe (previously the European Generic and Biosimilar Medicines Association) released its Biosimilars Handbook in February 2016. The handbook describes both the science and technology behind biosimilars, as well as how they are produced and regulated. It is intended to be a reference source for, among others, patients, patient advocacy groups, pharmacists, physicians and prescribers, as well as for payers, politicians and policymakers.

In April 2016, the British Generic Manufacturers Association launched its expert sector group on biosimilars, the British Biosimilars Association. The group is exclusively focused on biosimilars and its main focus will be to try and improve access to biosimilars thus ensuring that patients in the UK can benefit from these life-saving and life-changing medicines to the same extent as those elsewhere in Europe. Currently, the UK lags behind some European countries in the use of biosimilars. A report released in 2016 found that if biosimilar adoption was increased they could halve the cost of treatment in the UK. The UK's healthcare cost watchdog NICE (National Institute for Health and Care Excellence) recommended in January 2016 that rheumatoid arthritis patients indicated for treatment with biologicals should 'start treatment with the least expensive drug'.

Although it is hard to predict where the evolving biosimilars market will lead, given the high cost of biologicals it is clear that biosimilars have the potential to lead to much needed cost savings while still providing patients access to safe and efficacious treatments.

Editor's comment

It should be noted that 'follow-on biologicals' approved in Brazil, 'copy biologicals' approved in China, 'similar biologics' approved in India, 'biocomparables' approved in Mexico, and

'*bioterapéuticos similares*' approved in Venezuela might not have been authorized following as strict a regulatory process as is required for approval of biosimilars in the European Union. The EMA (European Medicines Agency) regulatory requirements ensure the same high standards of quality, safety and efficacy for biosimilars as for originator biologicals, and also include a rigorous comparability exercise with the reference product.

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