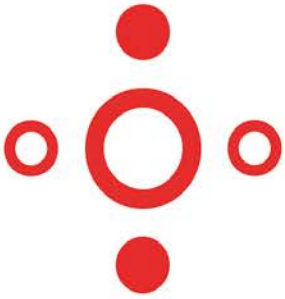
Grŵp Strategaeth Meddyginiaethau Cymru Gyfan
All Wales Medicines Strategy Group



Maximising the opportunity presented by biosimilar medicines

A national strategy for Wales

January 2023

This document has been prepared by the All Wales Therapeutics and Toxicology Centre (AWTTC) and Welsh Government, and has subsequently been endorsed by the All Wales Medicines Strategy Group (AWMSG).

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Summary

Wales' strategy at a glance

A strong market for biosimilar medicines drives commercial competition and offers a greater choice of affordable biological treatments.

Across the NHS, demand for high-cost disease modifying medicines is increasing. The competition in the biological medicines market brought about by the entry of biosimilar medicines stimulates innovation and encourages all manufacturers to increase the value of their offer to the NHS. Early adoption and widespread use of biological medicines offering improved value to the NHS frees up resources so that many more patients benefit from reinvestment in services and improved access to newer innovative therapies.

This strategy sets out the steps the NHS and its partners in Wales will take to support the conditions needed to create a strong, competitive biological and biosimilar medicines' market in the UK benefiting the NHS, patients and the economy of Wales.

To realise the opportunities presented by biosimilar medicines in Wales, we will:

- Be an **international exemplar** for the rapid adoption and widespread uptake of best value biological medicines.
- **Work in partnership** with manufacturers, researchers and the NHS to identify opportunities to maximise the benefits from wider availability of biosimilar medicines for patients and the NHS.
- **Continue to provide 'appraisal-free' market entry** for biosimilar medicines where the brand originator has been positively recommended by NICE or AWMSG; **introduce rapid, streamlined approaches** for facilitating market entry for new biosimilar medicines where the brand originator has not been recommended by NICE or AWMSG.
- **Maximise the number of patients** who can benefit from biological medicines.
- Make **data on biological medicines use and outcomes** openly available to support delivering our aspirations.

Ten actions to deliver the strategy

1. Aligned to Wales' strategy for value-based healthcare we will begin collecting **Patient Reported Outcome Measures** (PROMs) for best value biological medicines.

2. Starting with **the highest value opportunities**, the All Wales Therapeutics and Toxicology Centre (AWTTC) will work with clinicians from across Wales, clinical networks and the Value-based Healthcare team, to compare the number of patients treated in Wales with robust population estimates of those with the potential to benefit.

3. We will utilise AWTTC's expertise to introduce a new, **rapid, streamlined approach for biosimilar medicines** where the reference medicine has not been approved. This will take account of often lower prices available for biosimilar medicines and cover all relevant indications where there is a clinical need.

4. We will continue to develop our approach to **outcomes-based contracting** for medicines including biological medicines.

5. **National Prescribing Indicators** will continue to provide the basis for measuring the uptake of best value biological medicines, including rapid adoption and widespread uptake being a key performance measure within the NHS Wales Delivery Framework.

6. AWTTC will continue to monitor the uptake of biosimilar medicines and use publicly available data from other countries to **compare and improve rates of adoption** and uptake in Wales.

7. Where new biosimilar medicines become available and stimulate improvements in value for NHS Wales, we will work **nationally** with clinical networks, charities and patient advocacy groups and **locally** with clinicians, specialist nurses, pharmacy teams, and patients and their representatives to **support transition to widespread use** of the best value biological medicines.

8. Brand name prescribing will be central to our approach to maximise the value of biosimilar medicines and our contracting approach. **One decision on the best value biological medicines** will be taken nationally and adhered to by all health boards, NHS Trusts, hospitals and clinicians in Wales.

9. Appropriate switching between reference biological medicines and their biosimilar equivalents, and between biosimilar medicines, will be central to our approach to **maximise the value** of biosimilar medicines and our approach to contracting.

10. Keep the success of our actions and our strategy under constant review to ensure we **maximise the benefits of biosimilar medicines for the NHS and people in Wales**.

Purpose

1. This document sets out a clear multifaceted strategy to support the widespread and appropriate adoption of best value biological medicines within NHS Wales, which is enabled by the availability of biosimilars. The strategy supports the safe, effective and consistent use of all biological medicines[1], including biosimilar medicines, ensuring the largest number of citizens can benefit from therapeutic advances and maximising their value to the NHS.

2. How the range of measures described in this strategy will be utilised to support biosimilar entry will depend on factors specific to individual medicines, however the strategy provides a broad framework to foster innovation to the benefit of patients and the NHS.

3. A strong market for biosimilar medicines drives commercial competition, lowers prices and offers a greater choice of affordable biological treatments. In an environment where demand for high-cost disease modifying medicines is increasing, early adoption and widespread use of biosimilar medicines will free up resources so that many more patients benefit from reinvestment in services and improved access to new and innovative therapies.

4. As the predominant purchaser of medicines in the UK, the NHS has a critical role in creating the market conditions necessary to support manufacturers of biological medicines. Our interests are best served by a sustainable, thriving biological medicines market in Wales.

5. Creating the right conditions will mean biosimilar medicines remain available and affordable in the long term and will encourage manufacturers to invest in broadening their portfolios. In turn, this results in more benefit for more patients, the NHS and the economy of Wales. This strategy describes Wales' approach to achieving those results.

Context

The NHS in Wales

6. The NHS in Wales delivers NHS services to the population of 3.1 million people in Wales through seven local health boards, three NHS trusts and two special health authorities.

7. The seven local health boards are responsible for planning and securing the delivery of primary, community and secondary care services alongside specialist services for their areas. These services include dentistry, optometry, pharmacy and mental health services. They are also responsible for delivering services in partnership, improving physical and mental health outcomes, promoting wellbeing and reducing health inequalities across their population.

[1] Any reference to biological medicine or biosimilar medicine includes any medicine made with recombinant active pharmaceutical ingredient (API) or synthetic API, where the Medicines and Healthcare products Regulatory Agency consider the medicines to be interchangeable.

8. All health boards are responsible for delivering or commissioning acute and long term medical care. Velindre NHS Trust is responsible for delivering cancer services to patients in South East Wales on behalf of health boards.

9. In line with A Healthier Wales, Wales' long-term strategy for health and social care, the NHS is increasingly adopting a value-based healthcare approach.

10. Value-based healthcare allows more focus on meeting the goals and preferences of patients, through involving them in decision making, supported by the best evidence to hand. This will help to discard low value practices and reduce unwarranted variation in care, reallocating resource into optimal interventions in support of better outcomes.

11. Health and care organisations in Wales are committed to developing their value-based approaches. For example, through better collection and reporting of outcome data for a range of medical conditions, and looking at unwarranted variation in services and outcomes, to reveal the under and over-use of different aspects of health care.

12. The size and nature of the NHS in Wales – directly accountable to government, with no internal market and minimal commissioner/provider or primary/secondary care split – makes it more agile and less bureaucratic than other healthcare systems, facilitating rapid adoption and spread of practice.

13. The NHS in Wales receives over £8 billion in funding every year and accounts for just under half of all the Welsh Government's day-to-day spending. Of this, annual medicines expenditure (the money paid to purchase medicines for use in hospitals or reimburse pharmacies and dispensing doctors for medicines they purchase and supply in primary care) has risen to around £1 billion.

Biological medicines

14. Biological medicines first emerged in the 1980s, but it was not until the late 1990s that they began to be used extensively across therapy areas in the NHS. After initially finding use in the management of autoimmune conditions like rheumatoid arthritis, psoriasis and Crohn's disease, the use of biological medicines is now widespread across NHS specialities.

15. Biological medicines are derived from living cells or organisms and consist of large, highly complex molecular entities which may be difficult to characterise. Due to the variability of the biological system and the manufacturing process, biologic medicines may show a certain degree of variation, even between batches of the same product.

Biosimilar medicines

16. A biosimilar medicine is a biological medicine that is developed to be highly similar and clinically equivalent to an existing medicine. A biosimilar medicine contains a version of an active substance of an already licensed biological medicine, which is referred to as the 'reference medicine'.

17. Similarity between the biosimilar and its reference medicine must be established based on a comprehensive biosimilar comparability exercise, which confirms that the biosimilar does not have any clinically meaningful differences from the reference medicine in terms of quality, biological activity, safety, efficacy and immunogenicity.

18. Comparability is a well-established concept, used to evaluate manufacturing changes in biological medicines. If a biosimilar is highly similar to the reference medicine and has comparable safety and efficacy in one indication, safety and efficacy data may be extrapolated to other indications already approved for the reference medicine, if scientifically justified. This avoids unnecessary repetition of clinical trials.

19. Biosimilar medicines are not the same as generic medicines, which contain simpler chemical structures and are identical, in terms of molecular structure, to their reference medicines.

The opportunity presented by biosimilar medicines

20. Many of the first wave of brand originator (or 'reference') biological medicines have subsequently lost their patent protection and biosimilar medicines are becoming available across many therapeutic areas.

21. At the time of publishing this strategy there are 17 reference biological medicines where a biosimilar medicine has also been approved for use in the UK (figure one), and many more are in development.

Since the approval of the first biosimilar (Omnitrope®, a somatropin biosimilar to Genotropin®) in 2006, the UK has authorised biosimilar medicines for 17 molecules under 94 brand names:

Somatropin	Rituximab	Follitropin alfa
Filgrastim	Adalimumab	Pegfilgrastim
Epoetin alfa	Bevacizumab,	Insulin glargine
Infliximab	Enoxaparin	Insulin lispro
Etanercept	Teriparatide	Insulin aspart
Ranibizumab	Trastuzumab	

Figure one: Reference biological medicines where a biosimilar medicine is approved for UK use

22. Biosimilar medicines are therapeutically equivalent and, in general, available at greatly reduced cost compared to their reference medicines. The loss of patent protection facilitates market entry for multiple manufacturers, creating competition and driving down NHS costs.

23. As the biosimilar market matures, increased competition between manufacturers has the potential to deliver significant savings to NHS Wales. The NHS Wales Procurement Service estimates a saving of at least £4 million in 2022/23 alone, through extensive adoption of the best value biological medicines in Wales.

24. The benefits of a maturing biosimilar market and extensive adoption of best value biological medicines goes beyond the direct financial saving for the NHS. Driving down prices creates the potential to lower treatment thresholds and make biologic medicines available to more people earlier in the course of their condition, helping to avoid future costs associated with deterioration in people's health.

25. Aligned to Wales' strategy for value-based healthcare we will begin collecting Patient Reported Outcome Measures (PROMs) for best value biological medicines.

Maximising the number of people who benefit from best value biological medicines

26. Routine collection and better use of PROMs will help us to understand the real-world value of biological medicines and potentially widen access so more people are able to benefit from them.

27. Starting with the highest value opportunities, the All Wales Therapeutics and Toxicology Centre (AWTTC) will work with clinicians from across Wales, clinical networks and the Value-based Healthcare team, to compare the number of patients treated in Wales with robust population estimates of those with the potential to benefit.

Bringing biosimilar medicines routinely into NHS use in Wales

Licensing

28. The power regarding licensing of medicines for use in the UK is reserved by UK Government, with the responsibility for licensing activity resting with the Medicines and Healthcare products Regulatory Agency (MHRA).

29. Following its departure from the European Union (EU) on 31 January 2020 and the expiry of the transition period on 31 December 2020, the UK is treated as a 'third country' by the EU and new UK legislation has taken effect, crystallising the regulatory legal frameworks applicable to medicines.

30. To minimise disruption, the regulatory framework for biosimilar medicines that existed before the end of the transition period has effectively been preserved in UK domestic legislation, pursuant to the European Union (Withdrawal) Act 2018 (EUWA), as 'retained EU law'.

31. Biosimilar medicines are regulated under the Human Medicines Regulations 2012 (UK), as amended by the Human Medicines (Amendments, etc.) (EU Exit) Regulations 2019 (UK).

32. Guidance on the licensing of biosimilar products was updated in May 2021 and provides developers of similar biological medicinal products (biosimilar medicines) with a clear outline of the requirements for biosimilar products in

Great Britain and Northern Ireland. The guidance is based on current European Medicines Agency (EMA) biosimilar guidance, but contains additional details about UK reference products, the lack of requirement for *in vivo* studies in animals, and the changes in the requirement for a comparative efficacy trial.

The role of health technology assessment

33. In general, all new medicines and significant license extensions for existing medicines require a health technology assessment (HTA) before they can be routinely adopted for use in the NHS.

34. In Wales, HTA recommendations made by the National Institute for Health and Care Excellence (NICE) and the All Wales Medicines Strategy Group (AMWSG) provide a route into routine use within the NHS in Wales. Health boards and trusts are subject to funding directions requiring them to make recommended treatments available within 2 months of the earliest approval by NICE or AMWSG.

Biosimilar medicines where the reference medicine is approved under HTA

35. In accordance with guidance from AWMSG, existing HTA advice for the 'reference' medicine, published by the AWMSG or NICE, will automatically apply for biosimilar medicines licensed for the same indication and in the same population as the 'reference' medicine.

36. There may be some occasions where a review of the evidence for the biosimilar medicine is deemed necessary, and in that case, NICE will consider producing a quality-assured summary of the evidence via an Evidence Summary. Evidence Summaries do not constitute formal NICE guidance and there is no obligation on health boards to provide funding for recommendations they contain.

Biosimilar medicines where the reference medicine has not been assessed via HTA

37. Currently, in the absence of NICE or AWMSG advice for the 'reference' product, neither the reference product nor any biosimilar medicine is endorsed for use within NHS Wales. Biosimilar medicines are in general available at significantly lower prices than the price offered for a 'reference' medicine at HTA by NICE or AWMSG. We recognise this position is not sustainable and AWTTC will work with stakeholders to overcome this anomaly.

38. In 2023, we will utilise AWTTC's expertise to introduce a new, rapid, streamlined approach for biosimilar medicines where the reference medicine has not been approved. This will take account of the changes to the acquisition costs of the medicines in question following biosimilar entry and cover all relevant indications where there is a clinical need.

Rapid adoption and widespread uptake

The imperative for biosimilar use

39. The NHS use of medicines has increased significantly in recent years due to changing demographics and the increasing availability of new treatments. Medicine expenditure in Wales is now around £1 billion a year. Whilst costs in primary care have remained largely stable, costs in secondary care have increased per annum and by £100 million in the last 6 years, fuelled by wider use of particularly high cost medicines including biological medicines.

40. In 2020/21, 18 of the top 25 medicines by spend in secondary care in Wales were biological medicines with a combined cost of more than £90 million.

41. Over the next 10 years, more than 20 new biosimilar medicines will be launched in the UK. Most recently, a biosimilar version of ranibizumab is now available; a treatment for age-related macular degeneration, a leading cause of blindness affecting 600,000 people in the UK. Rapid adoption and high levels of uptake of the biosimilar ranibizumab will save the NHS in Wales tens of millions of pounds and enable us to treat more patients within finite resources.

42. Reference and biosimilar medicines are more challenging and expensive to develop than generic medicines. Whilst they may not offer the same percentage of price reductions as traditional generic medicines, there are significant savings associated with increased competition between biological medicines, including biosimilar medicines.

43. Competition between different biological medicines, including biosimilar medicines, creates increased choice for patients and clinicians, and enhanced value propositions for individual medicines (such as improved devices, patient services or formulations). When biosimilar medicines have entered the market, the increasing competition enables significant savings to be realised.

44. The NHS in Wales has already made excellent progress in realising the financial benefits of adopting biosimilar medicines. When compared to previous financial years, savings of over £9million (across 5 biological medicines) and £2million (across 6 biological medicines) were realised in 2019/20 and 2020/2021 respectively.[2]

NHS Wales' approach

Procuring for best value

45. Biosimilar medicines are approved as therapeutically equivalent to the reference medicine, as they have to establish that they are just as safe and effective as the reference medicine.

[2] Calculated as the difference in actual spend at NHS contract prices including any discounts offered for reference products.

46. In Wales, a single Wales-wide national procurement process is undertaken for biological medicines every two years to ensure that the competitiveness of the market is regularly assessed and compliance with the Public Contracts Regulations is maintained. The process steers suppliers to submit their best bids for their medicine and any associated services separately to ensure transparency of costs for the NHS.

47. The NHS will be able to choose the best point of access for their patients, with the primary objective of the pricing of biological medicines being to support patient experience and provider preference regarding the care setting (e.g. hospital, home delivery or community pharmacy provision).

48. We will continue to develop our approach to outcomes-based contracting for medicines including biological medicines.

Measuring adoption and uptake

49. Maximising the value of biological medicines doesn't stop at procurement. The barriers to biosimilar adoption are well documented[3] but the NHS in Wales has a proven record of overcoming barriers resulting in widespread uptake (figures two and three).

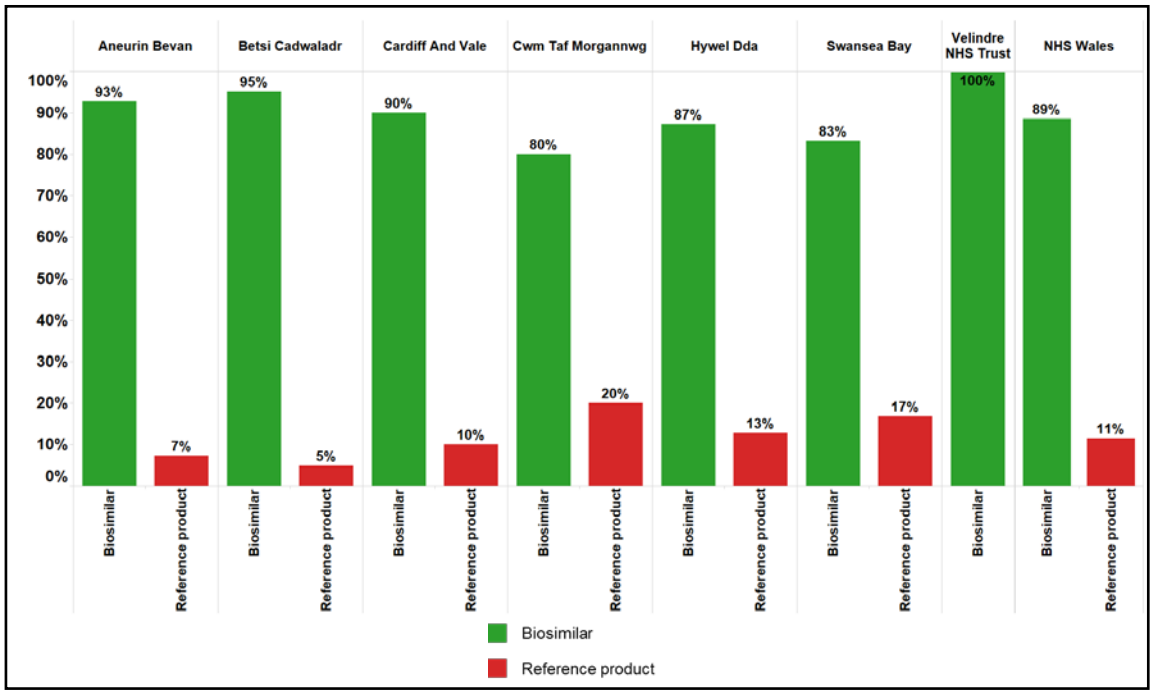

Figure two: Proportion of biosimilar and reference medicines prescribed by health board for the quarter ending March 2022

[3] https://pharmaceutical-journal.com/article/news/low-clinician-engagement-and-patient-resistance-main-barriers-to-biosimilars-uptake-say-ccgs

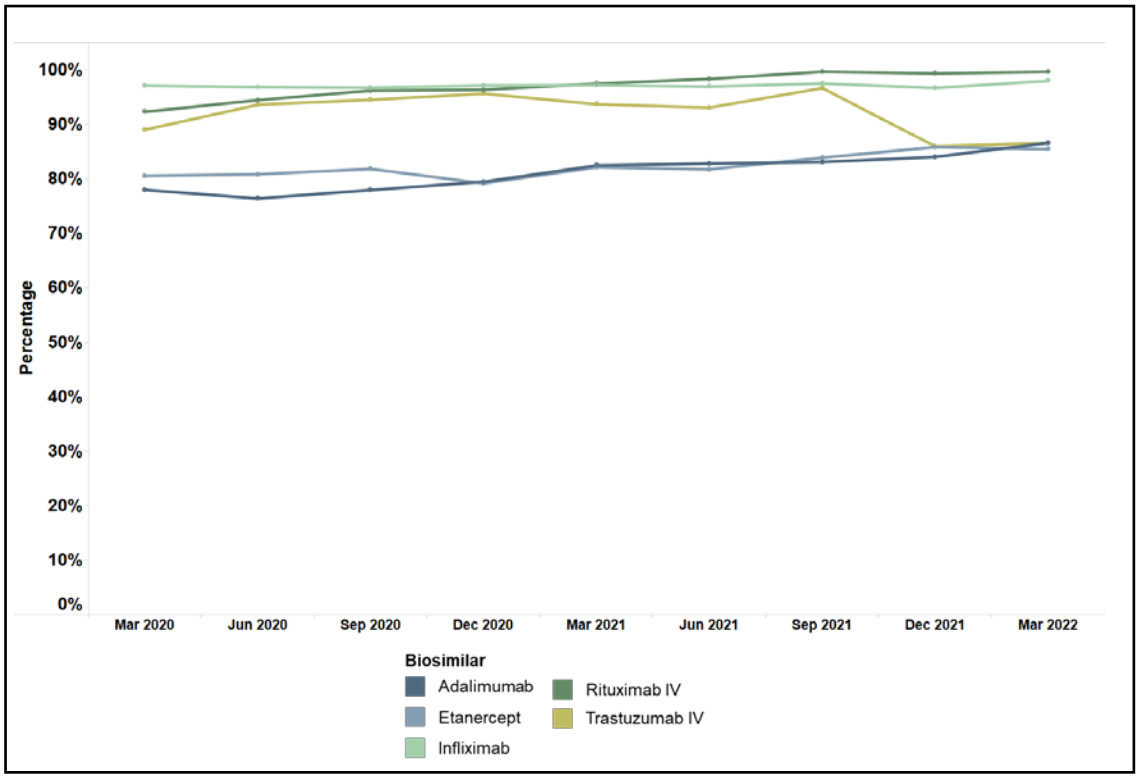

Figure three: Trend (all-Wales) in biosimilar uptake for the quarter ending March 2020 to the quarter ending March 2022

50. National Prescribing Indicators will continue to provide the basis for measuring the uptake of biosimilar medicines (figure four), including rapid adoption and widespread uptake being a key performance measure within the NHS Wales Delivery Framework.

51. AWTTC will continue to monitor the uptake of biosimilar medicines and use publicly available data from other countries to compare and improve rates of adoption and uptake in Wales.

Purpose	To ensure prescribing of best value biological medicines supports cost-efficient prescribing in primary and secondary care in Wales.
Unit of measure	Quantity of best value biological medicines prescribed as a percentage of total 'biosimilar' plus 'reference' product.
Aim	Increase the appropriate use of cost-efficient biological medicines, including biosimilar medicines.

Figure four: Best value biological medicines national prescribing indicator description

Supporting adoption and uptake

52. Monitoring and improving the performance of NHS organisations is integral to delivering the strategy. However, rapid adoption and widespread uptake relies on ensuring our approach is clinically-led and patient-focussed.

53. The decision regarding the choice of biosimilar or reference biological medicine for an individual patient rests with the responsible prescriber in consultation with the patient following the principles of shared decision making. NICE technology appraisal guidance often recommends treatment with the least expensive medicine where there are a number of choices available, considering associated (for example) administration costs, dosages, mode of administration and treatment schedules.

54. Prescribing should be in accordance with the approved indications in the product's summary of product characteristics and ideally be part of a biological medicines review. Prescribers should use all available relevant evidence to guide decisions about the care of an individual patient with the initial selection of the most appropriate biological medicine based on clinical considerations.

55. Prescribers should consider the value propositions offered by different products, including cost and licensed indications, as well as other factors relevant to the use of the product and likely clinical outcomes for each patient.

56. Ensuring prescribers and patients are fully engaged and have access to high quality information to understand and answer their questions about the use of biosimilar medicines is critical to successful adoption and uptake.

57. Where a new biosimilar becomes available and offers the best value for NHS Wales, we will work **nationally** with clinical networks, charities, patient advocacy groups, pharmacy contractors and the pharmaceutical industry and **locally** with clinicians, specialist nurses, pharmacy teams, and patients and their representatives to support transition to widespread use of the best value biological medicine (figure five).

Nationally we will:

- Support the national collaborative network for medicines procurement and logistics support to share best practice and experience in adoption of biosimilar medicines;
- Consult with national clinical networks before and following changes to the selection of best value biological medicines;
- Consult with relevant charities and patient advocacy groups to ensure they are fully informed and engaged in changes to the selection of best value biological medicines and can support messaging with patients;
- Produce supporting tools, resources and patient information to facilitate adoption of biosimilar medicines on a 'once for Wales' basis;
- Work with academics in health psychology to understand and overcome barriers to adoption and use of biosimilar medicines following the COM-B model.

Locally, individual health boards and NHS trusts will:

- Engage and maximise capacity for switching with key clinicians, nurses, pharmacy staff and patient groups;
- Consult and inform patients about planned changes to their treatment and provide opportunities for them to have any concerns addressed by their clinical team;
- Ensure adequate resources are allocated within the local hospital to support the introduction of the biosimilar medicine.

Figure five: Framework of national and local actions to support adoption and uptake

Substitution and switching

58. Substitution – defined here as the practice of dispensing one medicine instead of another equivalent medicine at the pharmacy level without consulting the prescriber – is not permitted for biological medicines, including between biosimilar medicines.

    Switching – defined here as a decision by the responsible prescriber to exchange one medicine for another medicine with the same therapeutic intent in patients who are undergoing treatment.

59. In line with MHRA guidance all biological medicines (including biosimilar medicines) should be prescribed by brand name. As biosimilar medicines often use the same international non-proprietary name (INN) as their reference product, an important way to ensure substitution does not take place is through brand name prescribing. Brand name prescribing should be adhered to by all prescribers of biological medicines, including biosimilars, and is in line with recommendations and advice from the MHRA and NICE.

60. Brand name prescribing will be central to our approach to maximise the value of biosimilar medicines and our contracting approach. **One decision on the best value biological medicines will be taken nationally** and adhered to by all health boards, NHS Trusts, hospitals and clinicians in Wales.

61. Patients who are established on a reference biological medicine can be switched to a biosimilar medicine under the supervision of the specialist prescriber in consultation with the patient. There is extensive practical experience that demonstrates the safety and efficacy of biosimilar medicines in clinical practice in the NHS in Wales.

62. Biosimilar products are considered to be interchangeable with their reference product; which means a prescriber can choose the biosimilar medicine over the reference product (or vice versa) and expect to achieve the same clinical effect (therapeutic equivalence).

63. Appropriate switching between reference biological medicines and their biosimilar equivalents, and between biosimilar medicines, will be central to our approach to maximise the value of biosimilar medicines and our approach to contracting.

Conclusion

64. Biosimilar medicines drive competition and offer a greater choice of best value biological treatments.

65. In an environment where demand for high-cost biological medicines will increase in the coming years, rapid adoption and widespread use of biosimilar medicines can release resources so patients benefit from reinvestment in services and improved access to new and innovative therapies. In turn, pharmaceutical and biopharmaceutical manufacturers will be motivated to develop new and pioneering treatments for future generations.