Biosimilars in Supportive Care

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Biosimilars in supportive care

- Epoetin
  - Available in Europe since 2007, US since 2018
- **Filgrastim**
  - Available in Europe since 2008, US since 2015
- **Infliximab**
  - Available in Europe since 2014, US since 2016

Filgrastim – UK implementation

- First supportive care biosimilar
- Very careful and cautious – reviewed all the literature before implementation
- Encouraged by national commissioning bodies
- Regional tendering process
- Drug & Therapeutics Committee, local chemotherapy group
- Training and education for staff and patients

Impact of biosimilar filgrastim

- The introduction of biosimilar medicines has been shown to increase access to treatment[1]
- Following the introduction of biosimilar filgrastim in the UK, usage in London increased by 40%[2]
- At the same time, it delivered budget savings (despite increased use) for reinvestment - £1million/yr in London alone[1]
- This effect was replicated across Europe - all countries saw a jump in the use of filgrastim following EMA approval (a 5-fold increase in Sweden) with estimated cost savings of 85 million Euros/yr[1]

Filgrastim in the UK – present day practice

- Switch freely between brands depending on **regional procurement contract** (based on best value for money)
- Cost savings £££
- Prescribed generically, pharmacy supply current preferred brand
- Pockets of practice where innovator is still used
  - Paediatrics
  - Stem cell mobilisation for transplant

Filgrastim – safety & efficacy

- Real world data from NEXT (n=2,012) and MONITOR-GCSF (n=1,447) demonstrate that rates of neutropenia, febrile neutropenia, dose delay or reduction as well as incidence of adverse effects were consistent with those reported for the originator products[3,4]
- Stem cell mobilisation: A pooled analysis of 12 autologous and five allogeneic healthy donor biosimilar cell mobilisation studies showed no significant differences between biosimilar vs originator G-CSF in the median number of CD34+ cells mobilised or in the number of G-CSF injections and leukaphoresis procedures required to harvest the target CD34+ cell dose[5]
- Larger 10 year follow up study in progress of 242 healthy volunteer donors - to date no concerns with efficacy or safety[6]
- No sign of induced immunity in any of these studies

Filgrastim – switching brands

- In the Pioneer trial, a group of breast cancer patients receiving TAC chemotherapy switched back and forth between biosimilar and originator filgrastim with each of six chemotherapy cycles and were compared to group treated only with the originator. Repeated switching did not impact efficacy, safety or immunogenicity[7]

Infliximab – UK experience

- Initial evidence from PLANETRA and PLANETAS demonstrated efficacy in rheumatoid arthritis and ankylosing spondylitis[8,9]. Fears over extrapolation of indications allayed by NOR-SWITCH trial[10]
- NHSE/NICE issues guidelines for implementation
- BGS guidelines – advocate use in IBD but brand prescribing and no automatic substitution[11]
- Off label use for treatment of checkpoint inhibitor related colitis followed
- NHS saved £99 million in the year 2017/18 through use of biosimilar infliximab (all use – rheumatology and IBD)[12]

Infliximab – safety, efficacy and switching

NOR-SWITCH:

- 482 patients previously stable on Remicade for at least 6 months were randomised to continue on originator or switch to biosimilar (double-blind)
- After 52 weeks follow up the biosimilar demonstrated non-inferiority in terms of worsening of disease and frequency of adverse events

ISOPP biosimilar implementation survey

Survey responses: 90

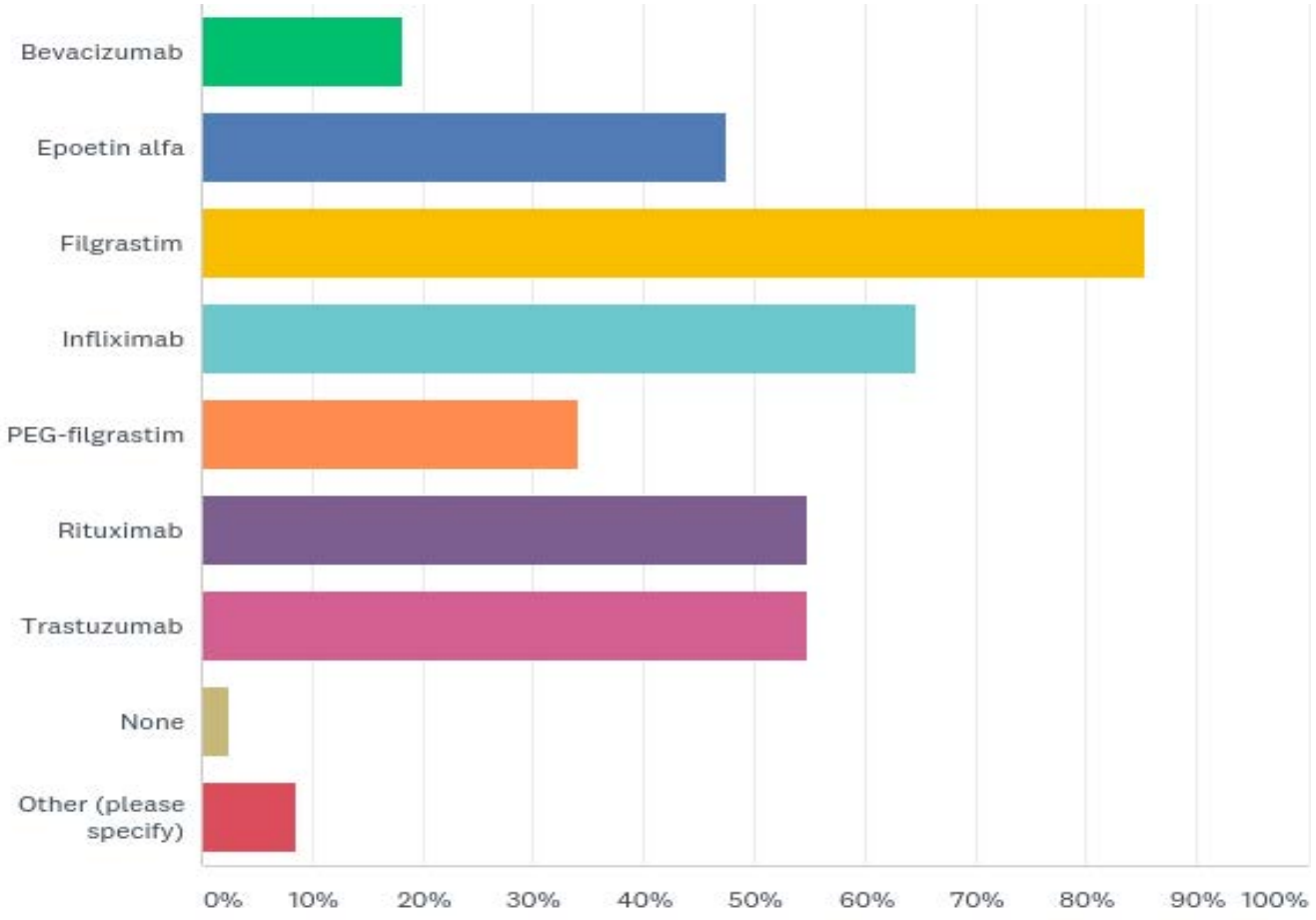
(50 ISOPP members + 40 non-ISOPP members)

This gives us a 19% response rate from the ISOPP membership (265 members)

Respondents represented 27 different countries across 6 continents with the greatest number of responses coming from Japan (18%), Brazil (12%), Australia (10%) and Canada (7%).

The majority of participants work in hospitals of various types, with 19% working in outpatient settings.

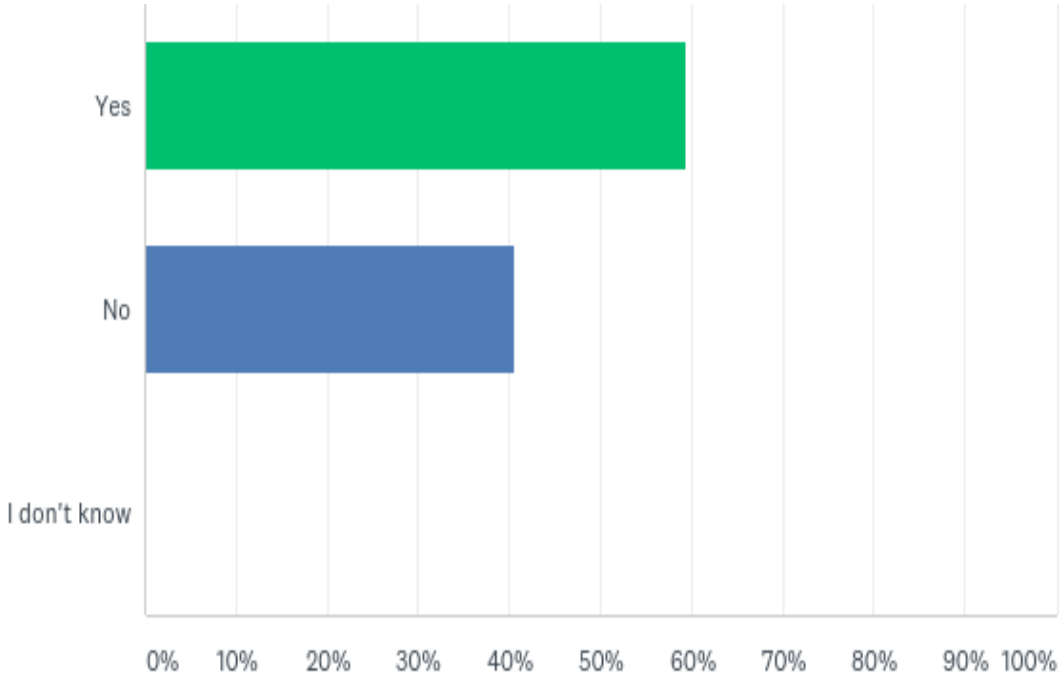
Which biosimilar products are currently available in the country where you practice?



66% of respondents had regulatory pathways for the introduction of biosimilars to their national pharmaceutical market, identifying 20 different licensing agencies responsible for regulating use. Only 5% had no licensing agency.

In the majority of cases (64%) the final decision on whether to use a biosimilar in a particular institution is made by an institutional Pharmacy and Therapeutics Committee with the main influences on that decision being **cost (92%)**, clinical data (73%) and availability (63%)

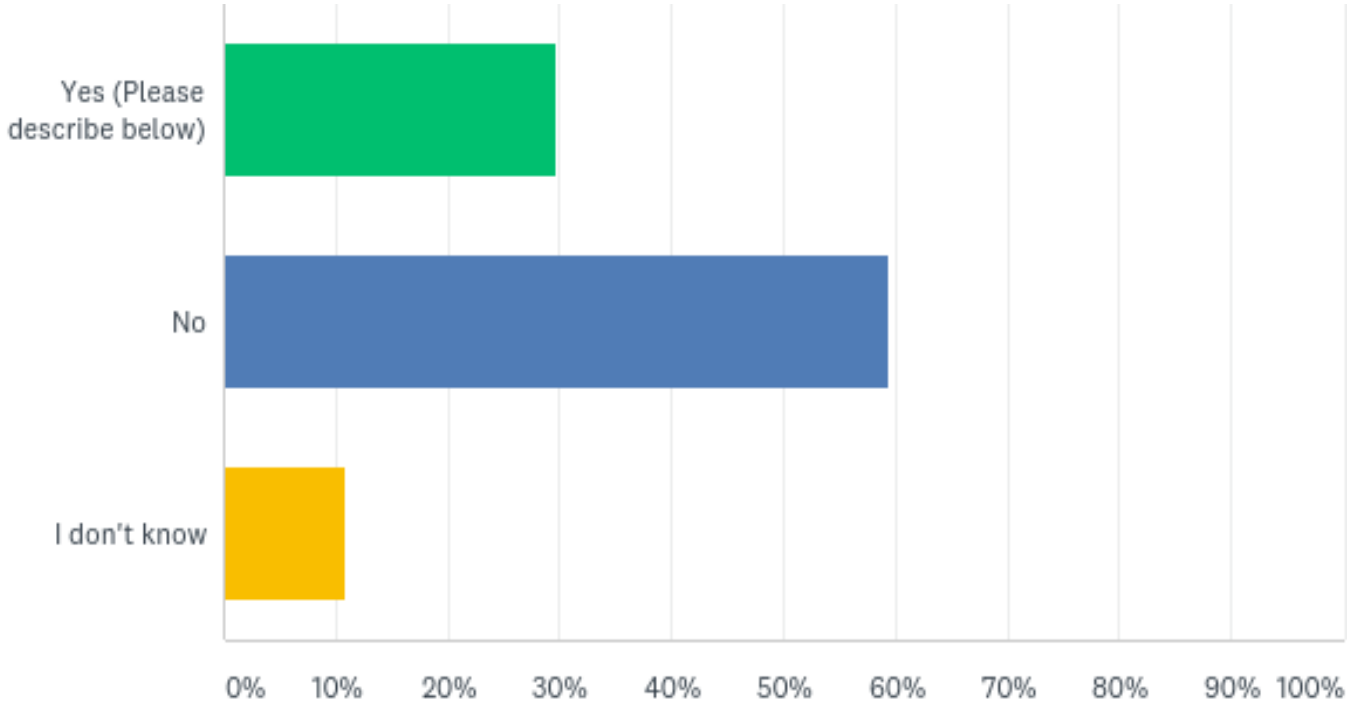
Does partial implementation of a biosimilar occur at your institution (e.g. is a biosimilar ever implemented for use only in certain treatment settings or patient populations)?



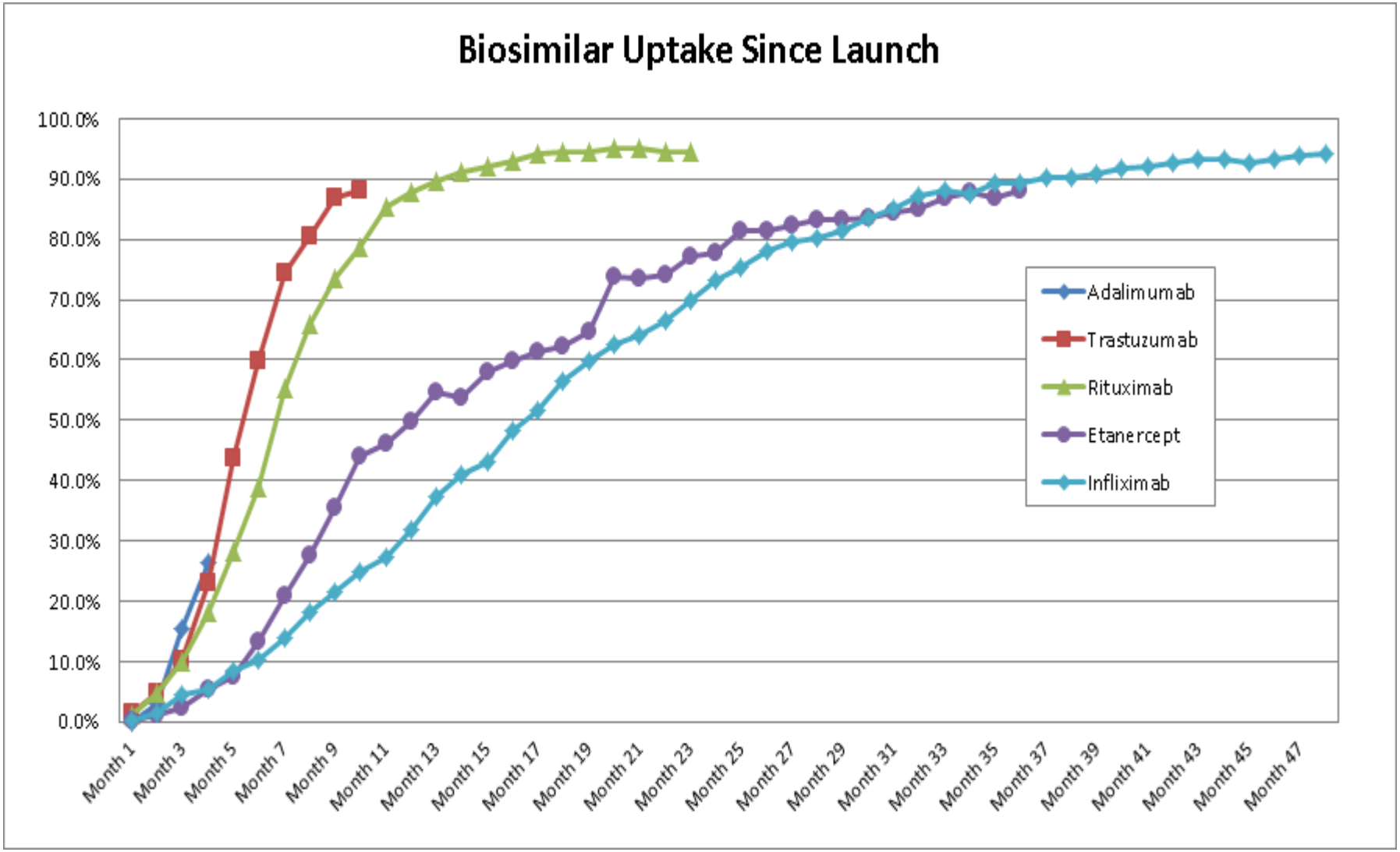
Barriers to implementation of biosimilars

- A reluctance to swap established patients to biosimilars
- Reluctance of prescribers to use biosimilars
- Insurance adaption/ payer preferences
- Lack of regulatory pathways (Kenya)
- Sourcing and Quality (Ghana)

Do any quality assurance or pharmacovigilance mechanisms exist at your institution to monitor the safety of biosimilar products after implementation?



National uptake of Biosimilars in NHS in England



Full year national savings at 98% = £100m

NHS England National Commissioning Framework 2017

- Vanguard Project
  - Stakeholder engagement
  - Toolkit
- National guidelines
- Financial incentives

NHSE commissioning framework for biological medicines, 2017…

Many biological medicines are coming off patent and "biosimilars" are becoming available. These medicines are highly similar to other biological medicines already licensed for use but are typically much cheaper than the originator products. This competition provides the NHS with an opportunity to save hundreds of millions of pounds, whilst also increasing access to these important medicines. There is the potential to realise savings of at least £200-300m per year by 2020/21 if the NHS embraces the use of best value biological medicines in a proactive, systematic, and safe way. Our aim is that at least 90% of new patients will be prescribed the best value biological medicine within 3 months of launch of a biosimilar medicine, and at least 80% of existing patients within 12 months, or sooner if possible. This guidance is designed to support the NHS to achieve this.

And 2019…

As original biological medicines lose their patent protection, biosimilar medicines are becoming available across different therapeutic areas. There are currently 15 'reference' (or 'originator') biological medicines that have biosimilars approved for use in the UK, as well as many in development. As the biosimilar market develops, increased competition between biological medicines has the potential to deliver significant savings to the NHS of at least **£400m to £500m per year by 2020/21** through increased uptake of the best value biologic medicines, including biosimilars.[1]

A big THANKYOU!!!

to the ISOPP Biosimilars Taskforce:

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References

1. Gascon P, Tesch H, Verpoort K, et al. Clinical experience with Zarzio(R) in Europe: what have we learned? *Support Care Cancer*. 2013;21:2925–32

2. Thakrar K. Biosimilar G-CSF: Implementation & lessons learnt. Centre for Medicines Optimisation UK. Available at: http://ccg.centreformedicinesoptimisation.co.uk/files/Kash%20Thakrar%20Biosimiar%20-%20GCSF.pdf (accessed 16 June 2019).

3. Lepretre S, Maloisel F, Kamioner D, et al. Safety of biosimilar filgrastim in patients undergoing neutropenia-inducing chemotherapy: the Next study. *Blood*. 2014;124:4976.

4. Gascon P, Aapro M, Ludwig H, et al. Treatment patterns and outcomes in the prophylaxis of chemotherapy-induced (febrile) neutropenia with biosimilar filgrastim (the MONITOR-GCSF study). *Support Care Cancer*. 2016;24:911–25.

5. Bonig H, Becker PS, Schwebig A, Turner M. Biosimilar granulocyte-colony-stimulating factor for healthy donor stem cell mobilization: need we be afraid? *Transfusion*. 2015;55:430–9.

6. Becker P, et al. Healthy donor hematopoietic stem cell mobilization with biosimilar granulocyte-colony-stimulating factor: safety,efficacy, and graft performance. *Transfusion* 2016;56;3055–3064

7. Blackwell k, et al . A Comparison of Proposed Biosimilar and Originator Filgrastim for the Prevention of Neutropenia in Patients with Breast Cancer Receiving Myelosuppressive Adjuvant or Neoadjuvant Chemotherapy: Phase III, Randomized, Double-Blind Trial (The PIONEER study) Blood 2014 124:5133; http://www.bloodjournal.org/content/124/21/5133

8. Park W, Hrycaj P, Jeka S, et al. A randomised, double-blind, multicentre, parallel-group, prospective study comparing the pharmacokinetics, safety, and efficacy ofCT-P13 and innovator infliximab in patients with ankylosing spondylitis: the PLANETAS study. Ann Rheum Dis 2013;72:1605-12

9. Yoo DH, Hrycaj P, Miranda P, et al. A randomised, double-blind, parallel-group study to demonstrate equivalence in efficacy and safety of CT-P13 compared with innovator infliximab when coadministered with methotrexate in patients with active rheumatoid arthritis: the PLANETRA study. Ann Rheum Dis 2013;72:1613-20

10. Jorgensen, K et al. Switching from originator infliximab to biosimilar CT-P13 compared with maintained treatment with originator infliximab (NOR-SWITCH): a 52-week, randomised, double-blind, non-inferiority trial The Lancet VOLUME 389, ISSUE 10086, P2304-2316, JUNE 10, 2017

11. British Society of Gastroenterology. BSG Guidance on the Use of Biosimilar Infliximab CT-P13 in Inflammatory Bowel Disease Feb 2016 file:///C:/Users/ForemanEm/Downloads/BSG%20Guidance%20on%20the%20Use%20of%20Biosimilar%20Infliximab%20CT-P13%20in%20IBD.pdf (accessed 18/6/19)

12. https://improvement.nhs.uk/news-alerts/nhs-saves-324-million-year-switching-better-value-medicines (accessed 18/6/19)