

Title: How could a new US-UK trade agreement affect NHS drug prices?

Standfirst: Ways in which a trade agreement could affect NHS pharmaceutical expenditure

Author: Dzintars Gotham¹, Melissa J Barber², Andrew M Hill³

1. Independent, London, UK.

2. Harvard T.H. Chan School of Public Health, Harvard University, Boston, MA, USA

3. Department of Translational Medicine, University of Liverpool, UK

Corresponding author:

**Dr Andrew M Hill
microhaart@aol.com**

Word count: currently 2000, limit 2000.

Introduction

The governments of the UK and US are working on the outlines of a US-UK trade agreement.¹ Health has emerged as an early focus of public debate on the putative trade agreement, with many concerned that this may facilitate the privatisation of the National Health Service (NHS). While the UK government has maintained that ‘the NHS is off the table’,² nothing is certain until drafts of the trade agreement can be scrutinised. Importantly, it is unclear whether this would extend to pharmaceuticals also being ‘off the table’. Numerous previous analyses have described the significant effects trade agreements can have on pharmaceutical expenditures.^{3,4,5}

At the same time, the Trump Administration has directed the US Trade Representative to leverage trade agreements to target alleged ‘foreign free-riding’ – in effect, requiring trading partners to pay more for US originator medicines.⁶ In one recent speech, Trump contended that foreign price controls on medicines were “very unfair to this country” and said: “I have directed US trade representative Bob Lighthizer to make fixing this injustice a top priority with every trading partner. And we have great power over trading partners. You’re seeing that already. America will not be cheated any longer and especially will not be cheated by foreign countries.”⁷

We do not know when and whether any draft text will be released to the public: for example, in the Transatlantic Trade and Investment Partnership (TTIP) negotiations between the US and EU, which eventually fell apart, both parties went to extraordinary lengths to keep the negotiated text secret. Nevertheless, we highlight key areas that could affect the NHS drug costs and should be scrutinized when and if a draft becomes available, based on existing trade agreements the US holds with other countries and priorities given by the US pharmaceutical industry lobby at a recent hearing on negotiating objectives held by the US Trade Representative.⁸

Limiting the role of NICE

The National Institute for Health and Care Excellence (NICE) plays a crucial role in negotiating medicine prices and ensuring that prices paid for originator medicines are cost-effective, based on economic evaluations termed health technology assessments (HTAs) and a threshold for what is acceptable cost-per-benefit.

In the US Trade Representative's recent hearing on negotiating priorities for a US-UK trade agreement, the largest US pharmaceutical industry group expressed strong criticisms of the UK's pharmaceutical price negotiation system, claiming that 'the U.K. operates a health technology assessment system that significantly undervalues innovative medicines', and arguing that US-UK trade agreement negotiations 'provide an important opportunity' to ensure that government reimbursement systems provide 'full market access for U.S. products, which includes the setting of reimbursement amount on competitive market-derived pricing, or an equivalent process'.⁹

The US-South Korea trade agreement (KORUS), which the lobby groups recommend as the basis for a US-UK agreement, includes an entire section setting out restrictions on national price control systems, which is unusual among trade agreements. In KORUS, the preferred mechanism is given as 'competitive market-derived prices', and companies are given various avenues of appealing reimbursement decisions. This term is nebulous, but it is likely that 'market-derived' must be something other than 'HTA-derived'.¹⁰ Indeed, in KORUS, US federal procurement programs were eventually exempted from this requirement due to concerns from the public. South Korean government procurement was not exempted, which does not augur well for the UK as the less powerful trading partner in these negotiations.¹¹

Although this is the least clear aspect of a potential trade deal, it is potentially the most costly: If there is no mechanism (or a weak mechanism) for enforcing a given cost-effectiveness threshold, the added costs could be substantial, as illustrated in our simple comparison of US and UK prices for the 20 most costly medicines (Table 1).

NICE evaluates new medicines for cost-effectiveness using a threshold of £20,000-30,000 per quality-adjusted life year gained.¹² Paying more than the accepted cost-effectiveness threshold implies that other services would be displaced without justification, given a finite budget. For example, the NHS have refused to procure lumafactor/ivacaftor, an originator cystic fibrosis medicine with a list price of £105,000 per year.¹³ At this price, 40 years of treatment would cost over £4 million per person, to gain an estimated 6 years of life.¹⁴

Investor-state dispute settlement

Modern US trade agreements often include an 'investor-state dispute settlement' (ISDS) mechanism. ISDS allows foreign companies to bring a case against a government for adopting policies that allegedly violate the terms of a trade agreement. These cases are decided not by a court, but by a tribunal of (normally) three arbitrators, often corporate

lawyers. The cases are often confidential and can result in the government being forced to pay substantial settlements and/or reverse policies. In some cases, this can affect policies aimed at protecting public health – for example, a tobacco company took Australia and Uruguay to ISDS tribunals over plain packaging legislation.¹⁵ If policymakers fear ISDS lawsuits, this may have a chilling effect on public health legislation. One could envision that ISDS may be used to challenge NHS cost control mechanisms –for example, NICE evaluations, the budget impact test, or procurement mechanisms such as parallel importation.

Monopoly rights

Originator pharmaceutical companies are granted temporary monopolies through intellectual property rights – where a patent gives the owner the right to exclude competitors from marketing a generic until the patent expires – and through regulatory ‘exclusivity’ systems – where the medicines regulatory agency is barred from approving a generic for a certain period of time.

Generic competitors are thus barred from entering the market for a certain period of time, during which the originator can command a high price from health systems. Legislators have historically justified this system by describing it as a balance between incentivising innovation and enabling affordable access.

The number of years that the monopoly lasts has a great bearing on costs to the health system and on access to the treatment. For this reason, provisions that would extend the term of patent protection or regulatory exclusivities would have substantial impacts on the NHS drug bill. At present, the period of patent protection granted in the US and UK is fairly similar: standard patent terms are 20 years in both countries, with extensions of up to 5 years available in both countries. However, a different type of monopoly protection, ‘regulatory exclusivities’, may have a greater role.

In terms of regulatory exclusivities, the UK follows the EU system, wherein a regulator may not approve a generic competitor for the first 10-11 years after approval of the originator medicine, irrespective of the type of medicine. The US grants 12 years’ exclusivity for biologic medicines, but less for other types of medicine. The US has often pushed for trading partners to adopt longer regulatory exclusivities and industry highlighted this as a priority.

If the UK agrees to align to US standards in this regard, this could mean 1-2 years' longer monopoly for biologics in the UK. As biologics make up the majority of high-cost medicines, this change could have substantial impact on the NHS drugs budget. For example, adalimumab costs £4,238 per month in the US where only the originator version was available until July this year versus £616 per month in the UK for a biosimilar version. If the NHS paid US prices just for adalimumab, the additional cost in 2018 would have been £2.9 billion (Table 1).

In a general sense, it is argued that trade agreements 'lock in' and 'ratchet up' monopoly protections. Protections are 'locked in', even where they are equivalent to what is already provided in UK law, because once a trade agreement is signed, national legislation can no longer roll back the protections. As a hypothetical example, if UK Parliament later decided that the 10-11 years of market exclusivity that is currently provided for should be reduced to 5 years, this would not be possible if it is already enshrined in the trade agreement. Protections are 'ratcheted up' because, in each consecutive trade agreement, there is a tendency to agree to the higher standards between the Parties. Standards thus become higher and higher (ratcheted up), and it becomes harder and harder for national governments to 'change their minds' about the extent of the monopoly rights granted to Big Pharma (locked in).

Potential effects on NHS pharmaceutical expenditures

We have not attempted to estimate the effect of a trade agreement on NHS drugs expenditure, which will be a highly complex task even when (and if) details on the pharmaceutical-related provisions in the agreement become clear. In lieu of this, we undertook a simple comparison of per capita drug expenditures in the US and UK: If prices of medicines were the same in the UK as they are in the US, how much more would this cost?

According to the Organisation for Economic Co-operation and Development (OECD), in 2016, pharmaceutical expenditure per capita was 2.5 higher in the US than in the UK.¹⁶ The NHS reports that the overall cost of medicines in England was £18 billion in 2017/18 (this figure is based on cost at list price and does not include discounts).¹⁷ We can thus crudely estimate that if prices of medicines in the UK were equal to prices in the US, NHS England pharmaceutical expenditures in 2017/18 would have been an additional £27 billion annually or about £519 million per week.

Another way of illustrating the potential scale of increased expenditures is to look at the drugs medicines with the highest costs to the NHS and calculate what their cost would have been if purchased at US prices (Table 1). This comparison suggests that, for just these 20 medicines, US prices would result in an additional cost to NHS England of £12 billion annually or £226 million per week.

Conclusion

We do not know when a draft text of a US-UK trade agreement will be available for public scrutiny. However, we have highlighted elements that should be carefully scrutinised when and if a draft agreement text becomes available.

Table 1. Estimated additional cost to NHS England if the top 20 most costly medicines were bought at US prices instead of UK prices.

Drug	Total cost for NHS England in 2017/18 ¹⁸	Lowest price in the US	Lowest price in the UK	US-UK price ratio	Estimated additional cost for NHS England if buying at US prices*
Adalimumab	£494,496,000	£4,238	£616	6.88	£2,906,164,989
Aflibercept	£365,579,000	£1,409	£816	1.73	£265,649,289
Etanercept	£219,850,000	£3,844	£644	5.97	£1,093,323,377
Infliximab	£200,697,000	£478	£377	1.27	£53,771,649
Rivaroxaban	£183,209,000	£336	£54	6.23	£957,633,443
Apixaban	£182,294,000	£364	£57	6.39	£982,336,313
Trastuzumab	£163,762,000	£4,723	£1,222	3.87	£469,180,431
Ranibizumab	£153,837,000	£6,048	£551	10.98	£1,534,701,844
Rituximab	£153,521,000	£9,784	£1,345	7.28	£963,536,334
Lenalidomide	£146,805,000	£12,380	£3,780	3.28	£334,018,125
Pembrolizumab	£142,413,000	£14,595	£2,630	5.55	£647,872,792
sofosbuvir-velpatasvir	£129,607,000	£21,868	£13,921	1.57	£73,978,890
Enzalutamide	£121,532,000	No data	£2,930	–	–
elbasvir-grazoprevir	£115,080,000	£7,301	£13,036	0.56	-£50,626,926
dimethyl fumarate	£106,471,000	£6,395	£1,471	4.35	£356,354,246
Imatinib	£103,576,000	£305	£113	2.71	£176,757,212
Ibrutinib	£97,912,000	£10,595	£4,599	2.30	£127,653,527
insulin glargine	£83,764,000	£212	£20	10.60	£804,447,223
glecaprevir-pibrentasvir	£81,562,000	£11,583	£13,922	0.83	-£13,699,661
Pertuzumab	£80,655,000	£3,786	£2,395	1.58	£46,841,979
Total cost of substituting UK prices with US prices					£11,729,895,076

*calculated as multiplying reported cost to NHS England in 2017/18 by a factor of the US-UK price ratio minus 1.

Three sources for prices were used in the US, and two in the UK. The lowest price identified across sources is used. Sources for US were the National Average Drug Acquisition Cost (NADAC) and the Average Sales Price (ASP) as published by the Centers for Medicare & Medicaid Services, and the 'PlanFinder' insurance cost estimator tool. Sources for the UK were prices collected from the British National Formulary (NHS Indicative Prices) and from the electronic Market Information Tool (eMIT). Prices are reported for a representative quantity – in most cases, a typical monthly dose. Price data were collected in June 2019.

Key messages box

- While a US-UK trade agreement is being discussed by the respective governments, draft text is not available at present.
- President Trump has named as a priority the use of trade relations to combat 'foreign free-riding' in the form of price controls on medicines
- US spending on drugs is 2.5 times higher than in the UK. The prices of the top 20 medicines in the UK are 4.8 times higher in the US.
- Trade agreements can influence the prices of medicines in a number of ways
- We outline three key areas of a potential US-UK trade agreement that could cause increased costs: extension of monopoly rights, obligations that weaken the role of the National Institute for Health and Care Excellence, and investor-state dispute settlement

Conflicts of Interest

All authors declare no conflicts of interest.

Licence

“The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, an exclusive licence (or non-exclusive for government employees) on a worldwide basis to the BMJ Publishing Group Ltd ("BMJ"), and its Licensees to permit this article (if accepted) to be published in The BMJ's editions and any other BMJ products and to exploit all subsidiary rights, as set out in our licence.”

Contributors and sources

Dr Dzintars Gotham is a health policy researcher who has served as a consultant for the World Health Organization and numerous civil society organisations working on improving global access to medicines. Melissa J Barber is at the Harvard School of Public Health, USA. Dr Andrew M Hill is a Senior Research Fellow in the Department of Translational Medicine at Liverpool University and a member of the World Health Organisation Fair Pricing Committee. DG prepared the first draft of the analysis based on discussions with co-authors. MJB and AMH provided comments and additions. Dr Dzintars Gotham serves as guarantor for this article.

¹ Office of the United States Trade Representative. Sixth Meeting of the U.S.-UK Trade and Investment Working Group. Available from: <https://ustr.gov/about-us/policy-offices/press-office/press-releases/2019/july/sixth-meeting-us-uk-trade-and>

² *Independent*. Boris Johnson to tell Trump NHS is ‘off the table’ in post-Brexit trade deal. <https://www.independent.co.uk/news/uk/politics/boris-johnson-trump-brexit-trade-deal-nhs-chlorinated-chicken-un-a9117576.html>

³ Lexchin J, Gagnon M-A. CETA and pharmaceuticals: impact of the trade agreement between Europe and Canada on the costs of prescription drugs. *Globalization and health* 2014; 10: 30.

⁴ Kapczynski, Amy and Sampat, Bhaven N. and Shadlen, Kenneth C., Trade Agreements, Patents, and Drug Prices: Continuing the Debate (March 15, 2017). Yale Law & Economics Research Paper No. 572. Available at SSRN: <https://ssrn.com/abstract=2933574> or <http://dx.doi.org/10.2139/ssrn.2933574>

⁵ Shaffer ER, Brenner JE. A Trade Agreement’s Impact On Access To Generic Drugs: The Central America Free Trade Agreement has kept some generic drugs from Guatemala even though they’re available in the United States. *Health Affairs* 2009; 28: w957–68. **AND LOPERT/GLEESON AND FAUNCE**

⁶ President Donald J. Trump’s Blueprint To Lower Drug Prices. 11 May 2018. Available from: <https://www.whitehouse.gov/briefings-statements/president-donald-j-trumps-blueprint-lower-drug-prices/>

⁷ Jopson B, Crow D. Trump blames ‘freeloading’ foreign countries for high drug prices. *Financial Times*. 11 May 2018. Available from: <https://www.ft.com/content/5ec2c642-54b0-11e8-b3ee-41e0209208ec>

⁸ Office of the United States Trade Representative. Trade Policy Staff Committee. Public Hearing On Negotiating Objectives For A U.S.-U.K. Trade Agreement. January 29, 2019. Available from: <https://ustr.gov/sites/default/files/0129USTR.pdf>

⁹ Office of the United States Trade Representative. Trade Policy Staff Committee. Public Hearing On Negotiating Objectives For A U.S.-U.K. Trade Agreement. January 29, 2019. Available from: <https://ustr.gov/sites/default/files/0129USTR.pdf>

¹⁰ Lopert R, Gleeson D. The High Price of “Free” Trade: U.S. Trade Agreements and Access to Medicines. *The Journal of Law, Medicine & Ethics* 2013; 41: 199–223. **AND FAUNCE**

¹¹ Department of Foreign Affairs and Trade Review of Export Policies and Programs. Submission by Assoc. Prof. Thomas Faunce, College of Law and College of Medicine and Health Sciences, Australian National University. Available from <https://dfat.gov.au/trade/topics/review-of-export-policies-programs/Documents/TheAustralianNationalUniversityDrThomasFaunce.doc>

¹² National Institute of Health and Care Excellence. 6.3 Decision-making. Guide to the methods of technology appraisal 2013. Available from: <https://www.nice.org.uk/process/pmg9/chapter/the-appraisal-of-the-evidence-and-structured-decision-making>

¹³ *British Medical Journal* 2019. NHS and Vertex remain deadlocked over price of cystic fibrosis drug. 8th March 2019

<https://www.bmj.com/content/364/bmj.l1094>

¹⁴ Rubin JL, O'Callaghan L, Pelligra C, et al. Modeling long-term health outcomes of patients with cystic fibrosis homozygous for F508del-CFTR treated with lumacaftor/ivacaftor. *Thorax* 2019;13:1753466618820186. doi:10.1177/1753466618820186

¹⁵ Matthew Rimmer. The Chilling Effect: Investor-State Dispute Settlement, Graphic Health Warnings, the Plain Packaging of Tobacco Products, and the Trans-Pacific Partnership. *Victoria University Law and Justice Journal* 2017.

¹⁶ OECD. Pharmaceutical spending. <https://data.oecd.org/healthres/pharmaceutical-spending.htm>

¹⁷ NHS Digital. Prescribing Costs in Hospitals and the Community, England 2017/18. <https://digital.nhs.uk/data-and-information/publications/statistical/prescribing-costs-in-hospitals-and-the-community/2017-18>

¹⁸ See: Prescribing Costs in Hospitals and the Community England 2017/18.

https://files.digital.nhs.uk/47/F07F3B/hosp-pres-eng-201718-report_v3.pdf