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Contributing Editor: **Grant Castle**

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CONTENTS

Preface	Grant Castle, *Covington & Burling LLP*	
Expert analysis chapter	*Continued global pressure on drug pricing and reimbursement for effective market access: A hard pill to swallow?* Lincoln Tsang, Margaux Hall & Hannah Kerr-Peterson, *Ropes & Gray LLP*	1

Jurisdiction chapters

Australia	Greg Williams, Colin Loveday & Sheena McKie, *Clayton Utz*	11
Belgium	Pieter Wyckmans, Michiel D'herde & Pauline Meskens, *Quinz*	27
Brazil	Benny Spiewak & Daniela Guarita Jambor, *SPLAW Advogados*	44
China	Nicolas Zhu, *CMS China*	53
Germany	Dr. Ulrich Reese & Carolin Kemmner, *Clifford Chance Partnerschaft mbB*	62
India	Archana Sahadeva, *Sahadeva Law Chambers*	78
Ireland	Marie Doyle-Rossi & Maree Gallagher, *Covington & Burling LLP*	91
Italy	Sonia Selletti, Mauro Putignano & Francesco Tiboni, *Astolfi e Associati, Studio Legale*	102
Japan	Kazuhiro Kobayashi, *Oh-Ebashi LPC & Partners*	118
Korea	Kyungsun Kyle Choi, Yunjoh Lee & Young Hei Jo, *Kim & Chang*	129
Netherlands	Koosje van Lessen Kloeke, *Leijnse Artz*	136
Norway	Line Voldstad & Thea Åkermoen, *Advokatfirmaet DLA Piper Norway DA*	157
Poland	Agata Zalewska-Gawrych & Zofia Kozłowska, *Food & Pharma Legal Wawrzyniak Zalewska Radcy Prawni sp.j.*	164
Portugal	Francisca Paulouro & Pedro Fontes, *Vieira de Almeida*	173
Spain	Jordi Faus, Lluís Alcover & Joan Carles Bailach, *Faus Moliner*	185
Sweden	Odd Swarting, Per Hedman & Hanna Tilus, *Cirio Law Firm*	207
Switzerland	Dr. Oliver Künzler, Dr. Carlo Conti & Dr. Martina Braun, *Wenger Plattner*	218
United Kingdom	Grant Castle, Brian Kelly & Raj Gathani, *Covington & Burling LLP*	228
USA	Rujul Desai, Anna Kraus & Kristie Gurley, *Covington & Burling LLP*	242

United Kingdom

Grant Castle, Brian Kelly & Raj Gathani
Covington & Burling LLP

Abstract

The UK has a large and complex healthcare system, under which the National Health Service ("NHS") funds the vast majority of medicines prescribed to patients.

The complexities of the system mean there is neither a single pathway to NHS reimbursement for a medicinal product, nor a universal reimbursement list. If and how the NHS funds a product often depends on the setting in which the NHS uses it. However, guidance from the National Institute for Health and Care Excellence ("NICE") plays an important role in determining whether the NHS will support the use of a product. The UK has price control schemes and systems for branded medicines but, in general, leaves the price of generic products open to market forces.

NHS drug expenditure continues to increase, although growth rates vary depending on product type and settings. Reasons for this include: an ageing population with specific needs; the commercialisation of costlier high-tech and rare disease medicines; and the effects of the COVID-19 pandemic. The Government continues to increase funding for the NHS, particularly in response to the pandemic. However, this comes with significant downward pressure on drug budgets and pricing. Commercialising a branded medicine in the UK increasingly entails providing sizeable rebates and discounts to the NHS. This also reflects a clear trend for the NHS and other state organisations to involve themselves directly and indirectly in drug pricing and policy. Commercial negotiations with the NHS and procurement initiatives often have a significant effect on the actual selling price of a product.

The landscape for pricing and reimbursement is increasingly multi-layered. The structure of the NHS and the pricing and reimbursement landscape was subject to major changes in 2021, and these are likely to continue into 2022 and beyond. This has included significant changes to NICE's processes, with changes designed to foster rapid market access for high-potential medicines also under way. 2022 is likely to bring significant structural changes to the NHS, which will very likely affect commissioning and procurement.

Market overview

The UK comprises four constituent nations: England; Wales; Scotland; and Northern Ireland.

The UK has a population of approximately 67 million people, with the vast majority (approximately 56.6 million) resident in England. There is a well-developed healthcare market in the UK dominated by a large and sophisticated public healthcare system, the NHS. The NHS is almost entirely state-funded and mostly free to patients at the point of delivery.

When considering pricing and reimbursement in the NHS, it is important to keep two points in mind. Firstly, the structure and organisation of the NHS vary across the four nations of the

UK, although many key concepts are similar. For the sake of simplicity, this chapter focuses primarily on the NHS in England, which is by far the largest market. Secondly, the way the NHS pays for medicines differs considerably between those supplied in "primary care" (*i.e.*, prescribed by General Practitioners ("GPs") or other community prescribers and dispensed in a community pharmacy or by a dispensing doctor) and "secondary care" (*i.e.*, in hospitals, clinics and similar settings). This distinction is relevant throughout this chapter.

In England, the NHS spent an estimated £17.1 billion on medicines in 2020/21, without taking discounts into account. That represents a 4.56% increase on the prior year. The rate of growth is consistent with longer term trends, albeit the growth rate has slowed significantly relative to 2019/20. This may be attributable to an effort to curb spending following the pandemic, during which costs sharply increased.

In 2020/2021, spending on hospital medicines accounted for 44.3% of the NHS's total expenditure on medicines, which increased by 5.9% on the previous year. Meanwhile, spending on medicines in primary care increased by a more modest 3.8% in 2020/2021. This reflects spending priorities geared towards acute, specialist, hospital-based therapies.

Historically, the NHS in England has spent approximately three-quarters of its drugs budget on branded products.

Pharmaceutical pricing and reimbursement

Regulatory classification

Classification of medicinal products

The Human Medicines Regulations 2012 created three broad regulatory classes of medicines:[1]

1. "Prescription-only Medicines" ("POMs");
2. "General Sale Medicines", which consumers may purchase without a prescription from a wide variety of retail outlets; and
3. "Pharmacy Medicines", which consumers may purchase without a prescription but only from a pharmacy.[2]

The regulatory classification of a new medicine will depend on a number of factors, including whether: (i) the marketing authorisation designates it as a POM, a General Sale Medicine or a Pharmacy Medicine; (ii) by statute, the product must fall into a particular category; or (iii) a competent regulatory authority, such as the Medicines and Healthcare products Regulatory Agency ("MHRA"), has allocated the product to a particular category.

In principle, NHS reimbursement is available to all three classes of medicines. However, the NHS increasingly focuses its expenditure on POMs and therefore aims to dissuade clinicians from prescribing medicines available over the counter.[3]

Eligibility for reimbursement

In primary care, any medicinal product commercially available in the UK is, in principle, eligible for reimbursement (*i.e.*, the NHS agrees to refund the cost of the medicine to the dispensing pharmacist/doctor). The main exceptions to this are where the NHS has "black-listed"[4] a product in the Drug Tariff or placed conditions on reimbursement (*e.g.*, through the so-called "Selected List" in the Drug Tariff).[5] NHS Prescription Services produces the Drug Tariff on a monthly basis on behalf of the Department of Health and Social Care. This provides information on reimbursement of drug costs and remuneration for professional services under NHS pharmacy contracts.

In secondary care, eligibility for reimbursement is more localised and there is greater scope for variation. Prescription, treatment and supply often take place within a single

NHS organisation (*e.g.*, a hospital), which gives that organisation a degree of autonomy over the medicines it chooses to fund (although this autonomy is diminishing as the NHS takes a more centralised approach to achieving cost-efficiency). Local and regional bodies responsible for secondary care, or those that support procurement, will have their own policies and formularies setting out which products are and are not available to a clinician to prescribe. Prescribers in secondary care settings usually only deviate from set policies for clinically justified reasons, such as an individual patient's exceptional circumstances or requirements. In both primary and secondary care settings, guidelines issued by NICE play an important role in determining whether the NHS funds a product and, in practice, whether clinicians prescribe the product to NHS patients (see section "How is the reimbursement amount set?" below, which discusses NICE guidelines).

Who is/are the payer(s)?

The NHS ultimately funds the vast majority of POMs supplied to patients in the UK. In England only, it recovers a small fraction of its costs through flat-rate prescription charges, payable by a small minority of patients (usually, adults aged under 60 in full-time employment and earning over a certain threshold). The UK has a smaller – but ever growing – private healthcare market, funded by patients themselves or through private insurance.

Which NHS organisation is responsible for funding ("commissioning") a medicine and how it arranges that funding are complex questions that often hinge on the type of treatment provided and the treatment setting (primary or secondary care). The main payers and payment structures in England are as follows:

- At least initially, the NHS centrally provides funds for medicines prescribed in primary care. For administrative reasons, actual spending is allocated to local and regional budgets. As such, the reimbursement mechanism in primary care is centralised under the Community Pharmacy Contractual Framework. Community pharmacies, which largely dispense products in primary care, will receive a fixed reimbursement price for a particular product.
- In secondary care, funding and commissioning are more localised. Currently, this falls to approximately 100 local Clinical Commissioning Groups ("CCGs"), who receive funding from the NHS for local health services. Under current plans, 42 local Integrated Care Systems ("ICSs") will replace CCGs as local commissioners. However, as a common principle, it is/will be for each CCG/ICS to obtain value for money in terms of the products and services it commissions and makes available locally. That said, the NHS has become an increasingly centralised force in the directions and guidance it gives to local bodies.
- The NHS commissions Specialised Services (which include treatments for rare cancers, genetic disorders and complex medical or surgical conditions) and Highly Specialised Services for rare diseases (typically to treat no more than 500 patients per year). These mechanisms allow the NHS to provide centralised funding for high-cost products that local bodies (such as CCGs) may find difficult to fund.
- The NHS is responsible overall for commissioning certain "public health" services (such as vaccination programmes).

What is the process for securing reimbursement for a new pharmaceutical product?

As noted above, the NHS funds treatments in a number of different ways. This means there is no single pathway to securing NHS reimbursement for a new product.

Nonetheless, NICE is often considered the gatekeeper to reimbursement, because a positive recommendation for a product or treatment from NICE obliges the NHS to make

funding available for it, usually within three months of the recommendation.[6] A negative recommendation from NICE does not necessarily mean a product is ineligible for supply within the NHS. However, unless other funding arrangements are in place, it provides commissioners with a basis to resist or delay funding. As a matter of practice, NHS clinicians usually prescribe products according to NICE guidelines.

In January 2022, NICE significantly updated its methods and procedures for appraising products and treatments. The new methods manual also covers non-pharmaceutical health technologies, such as devices and diagnostics.

NICE topic selection

NICE aims to conduct a health technology appraisal for all medicines that are new to the UK market or have a significant new therapeutic indication. The process can begin up to 24 months before regulatory approval. NICE's 2022 methods review now includes specific guidance on how it selects topics for appraisal and what methodology to apply. There is an appeals route for companies who object to the decisions taken at this stage.

NICE assessment

NICE evaluates whether the NHS should fund products or treatments (which NICE refers to as "technologies") based on an assessment of clinical and cost-effectiveness. Following the 2022 update, there is a standard review methodology common to most NICE appraisals. Modified criteria and added flexibilities are built-in in specific circumstances, such as for Highly Specialised Technologies ("HSTs"), cancer drugs or technologies that treat severe conditions. NICE's assessment methodology focuses on a technology's incremental cost-effectiveness ratio ("ICER") against an existing reference based on the quality-adjusted life year ("QALY"). These are established health economic concepts that seek to quantify the relative utilities of a technology.

NICE charges companies up to £142,800 to conduct technology appraisals.

Standard criteria for a positive NICE recommendation

Under its standard methodology, NICE issues a positive recommendation if it assesses a product to have an ICER, usually against an existing reference, of less than £20,000. NICE may apply discretion to recommend technologies with ICERs between £20,000 and £30,000, taking into account broader factors such as the degree of uncertainty around the ICER and uncaptured or non-health-related benefits. Historically, it was rare for NICE to give a positive recommendation to a technology whose ICER exceeds £30,000. In its 2022 review, NICE confirmed that there would be significant challenges to recommending products above that threshold.

NICE's cost-per-QALY thresholds have remained fixed since NICE began conducting technology appraisals in the late 1990s. Despite calls to do so, NICE's 2022 review did not adjust them upwards. This makes it increasingly difficult to bring new products below the thresholds.

However, the 2022 methodology revisions did introduce various "decision modifiers" that NICE can include in certain circumstances. A decision modifier – if applied – effectively increases a product's QALY (*e.g.*, x1.2 or x1.7). In turn, this supports a higher product cost, helping to bring the ICER below a recommendation threshold. Decision modifiers enable NICE to recommend technologies that would otherwise achieve an ICER of up to £50,000 (or more in specialised cases). Modifiers must be "ethically" and "evidentially" supportable. NICE suggests it may be prepared to apply a modifier due to the severity of the condition being treated and/or where there is an unmet health need. It remains to be seen how this will work in practice.

NICE's Budget Impact Test

Introduced in April 2017, the "Budget Impact Test" is an additional step for NICE assessments. Any product that is likely to cost the NHS more than £20 million in any of the first three years of its use must be subject to further negotiations between the supplier and the NHS to bring the overall cost down, before it receives a positive NICE recommendation. If these negotiations are unsuccessful, the NHS may apply to NICE to delay funding the product by up to three years, or longer in exceptional cases. The Budget Impact Test was a controversial measure, as many felt it undermined NICE's independent role and brought it closer to helping to manage the NHS's budget. In the second half of 2017, the innovative pharmaceutical industry body, the Association of the British Pharmaceutical Industry ("ABPI"), launched unsuccessful court proceedings to challenge the legality of the test.

Patient Access Schemes and Commercial Access Agreements

If a product does not meet NICE's cost-effectiveness criteria, NICE may still give it a positive recommendation if the drug's supplier and the NHS agree a Patient Access Scheme or enter into a Commercial Access Agreement. Although there are technical differences between the two, they are agreements between a supplier and the NHS that in effect make a product more affordable (*e.g.*, by way of a price discount, rebate or outcome-based pricing). The commercial details are usually kept confidential. NICE will make a recommendation subject to the scheme/agreement.

Managed Access Agreements

Where NICE assesses that the data supporting a product are subject to significant but resolvable uncertainty, NICE may make a positive recommendation subject to a Managed Access Agreement. These agreements enable NHS patients to access treatment, while allowing the company time to resolve evidential uncertainties, usually through additional research or the assessment of evidence for real world clinical usage, before undergoing a NICE re-appraisal. Managed Access can be subject to further conditions, such as a limited patient population, treatment through particular centres, or an overall budget-impact cap. The commercial terms of these agreements (set out in a Commercial Access Agreement) are usually confidential.

Highly Specialised Technologies

NICE provides additional flexibility from standard methodology for HSTs, which are medicines that, according to NICE, satisfy all of the following conditions:

- The disease being treated is "very rare" (typically a prevalence lower than 1 in 50,000).
- Ordinarily, the treatment population in the licensed indication is no higher than 300 patients (and no more than 500 across all indications).
- The disease significantly shortens life or severely impairs quality of life, there are no other satisfactory treatment options, or the technology is likely to offer significant additional benefit over existing treatment options.

For these products, NICE builds in certain allowances to accommodate the likely higher cost and often more limited clinical data. Amongst others:

- NICE will usually recommend HSTs that have an ICER of less than £100,000.
- NICE may also apply a decision modifier to increase the QALY gained depending on the "size of benefit" gained. This can mean the QALY is multiplied by x1 to x3, which helps to reduce the corresponding ICER, improving the changes of meeting the £100,000 cost-effectiveness threshold.
- In its cost-effectiveness assessment, NICE may take additional factors into account, including:

- The overall size of health benefits to patients.
- The robustness of the current evidence and the contribution that the guidance might make to strengthen it.
- The extent of disease morbidity and patient clinical disability with current standard care.

The 2022 methods review introduced a number of changes to the HST programme; the older version had been in place for approximately eight years. NICE's revisions aim to provide a clearer definition of a HST and more structured criteria for routing medicines into the HST programme. Potentially, more products than before will qualify as HSTs and benefit from the added flexibility available.

Cancer Drugs and Innovative Medicines Funds

The NHS ring-fences funding for certain classes of medicine that receive a particular type of recommendation from NICE.

- The Cancer Drugs Fund ("CDF") is in place to enable faster access to promising new cancer treatments. Following its relaunch in 2016, the CDF aims for all new systemic cancer drugs to receive a fast-tracked NICE appraisal. So far, 91 new oncology drugs treating 204 different indications have benefitted from CDF review. NICE will recommend a product to receive funding from the CDF, at a negotiated price, if it has the potential to satisfy the criteria for routine commissioning but there is clinical uncertainty that needs further investigation (*i.e.*, through data collection in the NHS or clinical studies). The drug will remain available within the CDF while more evidence becomes available, at which point NICE will subject it to one of its standard technology appraisal processes. The CDF has provided a route to NHS funding for a number of highly innovative, high-cost oncology technologies, including CAR-T and certain immuno-oncology therapies. The NHS has guaranteed £340 million per year for the CDF.
- Plans for the Innovative Medicines Fund ("IMF") were announced by the NHS in July 2021 to fast-track patient access to clinically promising non-cancer medicines, for which further data is needed to support NICE in making final recommendations around their routine use in the NHS. The IMF would operate in a similar way to the CDF. NICE may recommend a medicine to the IMF if the medicine: addresses a high unmet need; provides significant clinical benefits; represents a step-change in treatment for patients and clinicians; and any evidential uncertainties can be resolved in a reasonable time. The NHS concluded its consultation for the IMF in February 2022, and at the time of writing the finalised fund has yet to be announced.

NICE appeals

Generally, the manufacturer of the product under review, patient groups or clinician organisations who have participated in a NICE assessment may appeal the outcome of the assessment to the NICE Appeal Panel. There are three possible grounds for appeal, which mirror the grounds for judicial review in the English courts:

1. NICE has failed to act fairly;
2. the recommendation is unreasonable in light of the evidence submitted; and/or
3. NICE has acted unlawfully or exceeded its legal powers.

Most appeals are under the first two grounds but, in recent years, some successful appeals against NICE determinations have invoked novel human rights' considerations of the affected patient groups (*e.g.*, children), which are essentially claims that NICE has acted unlawfully.

If an appeal to NICE's Appeal Panel is unsuccessful, a party may challenge the decision by way of judicial review in the High Court.

How is the reimbursement amount set?

In primary care, the NHS usually reimburses products: (i) for the amount set out in the Drug Tariff (if the product is listed there); (ii) at the "NHS list price"; or (iii) in other cases, at the net price at which the dispensing pharmacy/doctor purchased the product. The Drug Tariff lists the reimbursement amount for commonly used, mostly generic products. The NHS reviews Drug Tariff prices each month based on a survey of the market. The NHS list price applies mainly to branded products and is set in accordance with the Voluntary or Statutory Schemes (see section "How are drug prices set? What is the relationship between pricing and reimbursement?" below).

The concept of a "reimbursement amount" is less relevant in secondary care because the NHS usually operates a *payment by results* model. Under this model, providers receive an amount per patient treated, based on the treatment provided, the length of a patient's stay, the complexity of their needs, *etc.* In most cases, this does not take the price of individual products directly into account. However, that is not always the case and the NHS will take a price-focused approach to secondary care products.

How are drug prices set? What is the relationship between pricing and reimbursement?

The Secretary of State for Health has statutory power to limit the price of medicines supplied to the NHS (section 262, NHS Act 2006). However, significant price control mechanisms only really exist for branded products and not for generics (whose prices are broadly controlled by market forces). Branded medicines supplied to the NHS are subject to one of two price control schemes: the Voluntary Scheme for Branded Medicines Pricing and Access ("VPAS"); or the so-called "Statutory Scheme". The UK Government aims for "broad commercial equivalence" between the two schemes, though there are some differences. In terms of membership, the VPAS is by far the more popular scheme, although some companies prefer the alternative for practical reasons.

VPAS

As its name suggests, the VPAS is a voluntary arrangement agreed between the ABPI and the Department of Health. In one form or another, the VPAS has been running in the UK since 1957. The current scheme came into effect on 1 January 2019 and runs for five years.

The VPAS contains complex arrangements for price and profit control. Below are some key features:

- The VPAS aims to cap increases in the amount the NHS spends on branded medicines to 2% *per annum*. To stay within this cap, the scheme's members ("Members") must pay the Department of Health a fixed percentage of their net sales of branded medicines supplied to the NHS ("Scheme Payments"), subject to certain exceptions. Scheme Payments are designed to offset anticipated growth above the agreed 2% limit. Scheme Payment percentages are fixed for one calendar year and apply scheme-wide. The percentage payable depends on the difference between the agreed growth rate and projected growth in sales.
- Scheme Payments are set at 15% of net sales for 2022. This is a significant increase on historical levels (the figure was 5.1% in 2021 and 5.9% in 2020). The sharp increase is largely attributable to higher expenditure on medicines during the pandemic, which meant spending exceeded the 2% agreed annual limit by some distance. Increased Scheme Payments for 2022 and likely 2023 seek to claw back some of this pandemic-fuelled expenditure.
- Members who are small companies (*i.e.*, essentially, those whose sales of branded products to the NHS totalled less than £5 million in the previous year) are exempt from

making Scheme Payments. For medium-sized companies (*i.e.*, essentially, those whose sales of branded products to the NHS totalled between £5 million and £25 million in the previous year), the first £5 million of sales may be exempt from Scheme Payments.

- Not all branded medicines supplied by Members are subject to Scheme Payments. Medicines containing new active substances sold to the NHS within 36 months of their marketing authorisation are outside the net of Scheme Payments. However, sales of those products will still contribute to calculating expenditure grown across the scheme.
- The VPAS also contains pricing controls. A Member may not increase the list price of a product without the prior approval of the Department of Health, which (amongst other things) requires a justification for the increase and an assessment of the Member's profits. In order to avoid stifling innovation, Members have the freedom to set the list price of medicines containing new active substances launched in the UK within 36 months of the grant of a marketing authorisation. However, this still requires Members to confirm that their intended selling arrangements to the NHS will take cost-effectiveness into account. In other words, very high prices would go hand in hand with significant NHS discounts.

The structure of the scheme means that the rebate percentages (*i.e.*, the percentage of sales that Members must pay back to the Department of Health) increase in the later years of the scheme. 2022 is the penultimate year in the current VPAS cycle. While it is unsurprising that payment percentages have increased, the particularly sharp rise from 2021 (5.1%) to 2022 (15%) has caused concern for industry. Projections for 2023 suggest there could be a further sharp rise. The need to pay such high rebates is challenging the commercial viability of certain products where profit margins are typically low.

Statutory Scheme

Manufacturers or suppliers of branded medicines to the NHS who do not participate in the VPAS are, by default, subject to the so-called "Statutory Scheme" (set out in sections 262–264 of the NHS Act 2006).

The Government revised the Statutory Scheme significantly in 2018 through the Branded Health Service Medicines (Costs) Regulations 2018 (the "2018 Regulations"). The 2018 Regulations came into force on 1 April 2018 and have been subject to a number of amendments since. Currently, the Statutory Scheme includes the following features:

- Manufacturers or suppliers must pay a percentage of their net sales of branded products to the NHS on a quarterly basis. The percentage payable for 2021 was 10.9%. At the time of writing, the Department of Health has initiated a process to increase the percentage for 2022 to 14.3% and 24.4% in 2024. This mirrors sharp rises in VPAS rebate payments.
- There are also pricing controls, such as:
  - The maximum price of a product that was on the market on 1 December 2013 is capped to the price at that date, subject to any agreed increases.
  - Price increases and the price of new presentations require the agreement of the Secretary of State, who must take into account factors including: (i) the clinical need for the product; (ii) the cost of therapeutically equivalent or comparable products (including in other European Economic Area countries); (iii) whether the product contains a new active substance; and (iv) estimated profits and other financial parameters, *etc.*
- Unless the VPAS applies, the Statutory Scheme will encompass all biologic medicines supplied to the NHS, including biosimilars.

Despite having been historically different, the current versions of the Voluntary and Statutory Schemes are quite similar. Nevertheless, there are some notable differences. Pricing arrangements for products containing new active substances are more straightforward under the VPAS than the alternative.

Factors that affect pricing

A number of factors affect drug pricing in the UK, ranging from Government and NHS policies, commercial arrangements between companies and the NHS, and marketplace competition. The UK list price is often a benchmark for countries that operate reference pricing systems. This can be an important consideration for companies, which encourages providing discounts to the NHS under agreements that do not affect the reference price.

Companies must price branded products in accordance with the VPAS or Statutory Scheme. The schemes tightly control increases in the price of established branded medicines but provide more (though unlikely complete) flexibility when pricing new products. New, innovative products are very likely to be subject to a NICE appraisal and companies try to meet NICE's cost-effectiveness criteria as far as possible. If that is not feasible, companies often consider methods to provide better value for money to the NHS, such as through Patient Access Schemes or Managed Access Agreements. Traditionally, price control schemes and NICE appraisals had been the two major levers that affected the return a company might make from a branded medicine sale to the NHS.

However, there is a growing tendency for other factors (often driven by NHS policy) to affect net pricing and returns. Their significance is growing, reflecting the increasingly multi-layered landscape for drug pricing in the UK.

For example, NHS Hospital Trusts, CCGs and other NHS bodies use tenders, rebate agreements and other commercial arrangements to purchase products with additional discounts to list prices. Historically, this had been for generic medicines and/or medicines in secondary care. However, the NHS increasingly uses tendering for branded products (including those used in primary care) and biologics. In particular, the NHS uses Framework Agreements (structured agreements in which a consortium of NHS "buyers" can purchase products for centrally contracted prices), which can significantly affect the price a supplier receives. Framework Agreements are regulated under the UK Public Contracts Regulations 2015. The use of tendering for branded medicines has received criticism from various commentators who argue it undermines NICE, the VPAS and the Statutory Scheme by giving Government "two bites at the discount cherry". Though the UK Government has announced that it intends to reform its public procurement laws, the changes proposed thus far may not affect medicines procurement.

Recent years have witnessed the NHS in England adopting an increasingly centralised approach to procurement and achieving lower medicines costs. For example, the NHS has established several national and regional procurement groups to co-ordinate and support medicines procurement, sharing information and expertise. This may affect the ability to give local, volume-based discounts. Similar groups exist to align local formularies and prescribing policies to the most cost-effective options available, which can stimulate companies to offer keener prices to remain locally recommended or on a preferred formulary. The NHS often has a complex internal system to incentivise hospitals and local commissioning bodies to adhere to centrally negotiated formularies and price structures, which again erodes local autonomy.

As in most other markets, competition from generic and biosimilar products also affects the price of innovator products on the market. The NHS's policy has, for some time, been

to encourage clinicians to prescribe most products by their International Non-proprietary Name ("INN") to encourage generic prescribing and dispensing. Many NHS organisations (such as CCGs or Hospital Trusts) also run programmes to switch patients from innovative to generic or biosimilar products. These factors mean that once generic or biosimilar products enter the market, suppliers of innovative products can rapidly lose market share unless they reduce prices. However, it is important to note that NHS prescribing guidance requires prescribing by brand name, *e.g.* for some biotechnology products. In general, the UK prohibits generic or biosimilar substitution in pharmacies where prescriptions specify a brand name. However, certain exceptions apply. For example, substitution may be permitted in hospitals in some cases. Also, pharmacy-level substitution is lawful if provided for under a "Serious Shortage Protocol" (which is a statutory mechanism that amends pharmacy dispensing rules if the Department of Health considers there is a serious shortage of one or many medicines in the UK).

The NHS generally avoids intervening in the market for generic products, relying on market forces to regulate it. However, over the last five years, the NHS has experienced shortages in the supply of certain generic medicines. Reportedly, Brexit-related uncertainty has contributed to shortages, but a variety of other supply-side issues have persisted since the UK left the EU. These shortages have led to price increases and the NHS has, in some cases, reflected this by offering a higher reimbursement amount in the Drug Tariff, often on a temporary or *ad hoc* basis.

Policy issues that affect pricing and reimbursement

The NHS's medicines policies aim to balance a number of interests, including:

- obtaining value for money for taxpayers;
- balancing health spending, particularly in light of higher expenditure resulting from the COVID-19 pandemic;
- ensuring there is equitable access to treatment for NHS patients;
- facilitating rapid market access to products that treat debilitating and high-burden diseases and/or unmet clinical needs; and
- stimulating innovation in the life sciences industry.

Balancing these interests is not straightforward, meaning that health policies are increasingly polarised. On the one hand, established, high-volume branded medicines often face funding squeezes, while on the other hand, new, innovative, rare disease or high-disease-burden treatments can benefit from significant funding stimuli.

The UK's population is growing as well as becoming older. The Office for National Statistics projects the UK's population to increase from approximately 67.1 million people in 2020 to approximately 69.2 million people in 2030 (a 3.2% increase). The proportion of the population over the age of 65 in England is also projected to increase from approximately one in five in 2019 to one in four by 2050. The rising number of older people has increased the demand for healthcare and the volume of products dispensed, particularly those to treat age-related conditions, such as cardiovascular disease and diabetes.

Against this context, the volume and cost of drugs used in and/or reimbursed by the NHS is on a steady upward trajectory. The COVID-19 pandemic saw a significant spike in spending, which the Government is now seeking to manage. This has resulted in sharp increases in rebates payable from pharmaceutical companies to the Department of Health under the Voluntary and Statutory Schemes. Companies who were used to paying around 5%–10% now face the prospect of paying rebates of 14%–24% of net sales in 2022–23. The

growth in tendering for branded medicines (especially in primary care) means companies must offer additional discounts to secure NHS uptake. This sits alongside making higher rebate payments.

The NHS remains focused on delivering efficiencies and focusing on priority areas. The multi-layered landscape that affects drug pricing, uptake and procurement is likely to evolve and be further enhanced.

Emerging trends

The pricing and reimbursement landscape in the UK is constantly evolving. 2021 was a year of major change, with further key changes expected in 2022 and beyond. These include: a revised methodology for NICE Health Technology Assessments ("HTAs"); new pathways to licensing and funding; and reforms to the structure of the NHS. In the near future, negotiations between industry and Government for a new Voluntary Scheme are set to begin. The full impact of these changes is still unfolding.

A key headline trend is that pricing and reimbursement are becoming increasingly multi-layered. A company's financial return from branded products is in reality "chipped down" from various different angles (ranging from NICE's Budget Impact Test, patient access schemes, rebates under the Voluntary or Statutory Schemes, branded drug tenders and the NHS's own internal management and prescriber guidance).

Current trends

The longer-term effects of Brexit and COVID-19 on the NHS and the medicines funding landscape are beginning to become clear. There is a focus on innovation and access for diseases where there is unmet need or where the disease burden is especially high. This goes hand in hand with sharp reductions in funding and cost-control initiatives for established, higher-volume branded medicines.

Against this backdrop, it is difficult to overstate the impact of NHS tendering for the purchase of certain branded medicines. In a competitive tender, pharmaceutical companies find themselves under pressure to offer further discounts to the NHS (beyond those built-in through the NICE process, the VPAS and/or the Statutory Scheme). A successful bid with a significant discount can often result in the product receiving a higher ranking or recommendation within the NHS's internal formularies and guidance to prescribers. The announcement of a tender in a particular therapy area can have major commercial implications for a company. Many of these tenders are complex and highly co-ordinated, which sometimes leads to medicines procurement litigation.

The NHS's internal structure and policies often incentivise local organisations to purchase "best value" products, particularly generics and biosimilars. NHS organisations that fall short of this are potentially vulnerable to financial penalties or disincentives.

Linked to the move towards generics and biosimilars is the growing tendency for the NHS to support using unlicensed products (or licensed products off-label) to cut costs. Historically, the NHS has respected the principle of using licensed products within their label wherever possible, which is consistent with the MHRA's position and professional guidelines for doctors. Similarly, NICE takes the position that it cannot positively recommend unlicensed products or off-label use of licensed medicines in an assessment (though it sometimes takes this into account for cost-comparison purposes). Despite this, the NHS has in certain high-profile cases advocated using lower-cost, unlicensed or off-label products. This is highly controversial, having been the subject of High Court and Court of Appeal litigation in respect of reformulated bevacixumab for intra-ocular use.

NICE's review of its HTA methodology did not result in an uplift to its cost-effectiveness thresholds. Pharmaceutical companies who develop high-cost drugs increasingly must negotiate bespoke agreements with the NHS (*e.g.*, through Managed Access Agreements or Patient Access Schemes) to achieve a positive NICE recommendation. Usually, this involves significant discounts from the product's list price.

NICE's review appears to have introduced more flexibility within the HTA system. Through "modifiers", NICE is able to give additional weight to factors such as the severity of a disease and unmet clinical needs. NICE's Highly Specialised Technologies Program is in principle clearer and may benefit a greater number of products. The CDF and IMF also reflect a trend to speed up access to promising treatments in areas where the disease burden is especially great.

Flexing its post-Brexit ambition, the UK Government has stated its commitment to accelerating the approval of, and access to, new, innovative medicines. 2021 saw the launch of the Innovative Licensing and Access Pathway ("ILAP"). ILAP aims to reduce market-entry time for medicines that hold "innovation passports". These passports enable companies to engage with the MHRA and NICE at a very early stage to generate evidence for a cost-effective value-proposition and/or expediting managed access into the NHS. So far, the MHRA has awarded 59 such passports, with key therapy areas being oncology, neurology and respiratory diseases.

Bespoke NHS agreements go hand in hand with the NHS exercising its mandate to negotiate pricing and access deals with pharmaceutical companies either alongside or outside the parameters of a NICE appraisal. In March 2021, the NHS announced a "smart deal" with Novartis for its life-saving spinal muscular atrophy drug, Zolgensma.

On the horizon

The proposed structural changes to the NHS – including the replacement of CCGs with ICSs – are designed to nurture local-level commissioning, co-operation across health and care services, and reduced bureaucracy. In secondary care, there may be a shift away from the "payment by results" model, towards a more collaborative system to fund local population health. In practice, this may make it easier for the NHS to develop local-level funding and tariff structures. The proposals also create more flexibility over when the NHS must use competitive procurement processes to purchase healthcare services.

Successful market entry

Formulating a successful strategy for market entry will depend on the type of product in question, its place in the NHS's complex architecture and the outcome of proposed reforms to NICE and the NHS. The following are some general points to consider:

- **NICE appraisal**. A company should investigate whether its product will be subject to a NICE appraisal and, if so, whether it could meet NICE's cost-effectiveness criteria, including the Budget Impact Test. For high-cost products, companies should get ahead of the curve by planning Patient Access Schemes or some other commercial offer to the NHS.
- **Specialised categories**. Falling within the scope of the Highly Specialised Technologies Program, the CDF or the IMF could materially affect the likelihood of a high-cost product receiving a positive NICE recommendation. Companies should explore whether a product falls within these categories early on.
- **Innovative access pathways**. Innovative access pathways, such as ILAP, could significantly streamline regulatory approval and the NHS reimbursement process. Companies should assess whether they might benefit from such schemes.

- **Factoring in the NHS's multi-layered approach to commissioning and procurement**. It is critical to appreciate the NHS's multi-layered approach to medicines pricing and purchasing. The pricing and reimbursement framework in the UK often cumulatively "chips away" at the amount a company might receive for a product (*e.g.*, through the VPAS, the NICE process or tendering). Companies should therefore consider their pricing strategy in a holistic way, and be prepared for downward pressure from multiple angles. Companies should also be aware that the NHS is now likely to share pricing information internally.
- **Understanding NHS prescribing policies**. In the UK, market penetration is often a greater concern for companies than market entry. The NHS's prescribing policies (both local and national) have a significant impact on the uptake of a new product, so understanding them is important. The outcome of an NHS tender can significantly affect the NHS's policy for prescribing certain products, and the guidance issued to clinicians.
- **Watch this space**. The NHS's structural reforms are currently in process. Their outcome may affect the commissioning and procurement landscapes. This goes alongside watching how recent changes – particularly to the NICE process – turn out in practice. Adapting rapidly to change will be key.

* * *

Endnotes

1. Regulation 5 of the Human Medicines Regulations 2012.
2. See also Regulation 220 of the Human Medicines Regulations 2012.
3. "Conditions for which over the counter items should not routinely be prescribed in primary care: Guidance for CCGs", NHS, 29 March 2018.
4. Schedule 1 to the NHS (General Medical Services Contracts) (Prescription of Drugs, etc.) Regulations 2004.
5. Schedule 2 to the NHS (General Medical Services Contracts) (Prescription of Drugs, etc.) Regulations 2004.
6. Regulations 7(2)-(3) of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 (SI 2013/259) and as set out in the NHS Constitution.

Grant Castle
Tel: +44 20 7067 2006 / Email: gcastle@cov.com

Grant Castle is a partner in the London office of Covington & Burling LLP, practising in the areas of life sciences regulatory law, with an emphasis on pharmaceutical and medical device regulation and associated compliance issues. He has assisted clients with a variety of UK pricing and reimbursement issues, including representing suppliers of pharmaceutical products and medical devices and other interested parties in a number of successful NICE appeals and administrative proceedings in the UK and EU courts.

Grant speaks and lectures frequently on regulatory issues in both the pharmaceutical and medical device areas at the University of Surrey, the University of Wales and Cranfield University. He received a BSc in chemistry with first-class honours from Imperial College of Science, Technology and Medicine in London in 1991, and a Ph.D. in organic chemistry from Trinity College, University of Cambridge in 1994.

Brian Kelly
Tel: +44 20 7067 2392 / Email: bkelly@cov.com

Brian Kelly is a partner in the London Life Sciences group, whose practice focuses on EU food and drug regulatory law, public and administrative proceedings, public procurement matters, EU law and product liability and safety.

Mr. Kelly has advised and successfully represented a variety of clients in respect of NICE appeals. He has advised clients on establishing joint working and risk-sharing relationships with the NHS in England and Wales. Mr. Kelly has also successfully represented life sciences clients in judicial reviews and other administrative proceedings in the UK in respect of NHS procurements. Mr. Kelly holds a degree in neuroscience and is an honorary lecturer at University College London.

Raj Gathani
Tel: +44 20 7067 2266 / Email: rgathani@cov.com

Raj Gathani is an associate in Covington & Burling LLP's London office. Raj's practice includes advising clients on a variety of UK pricing and reimbursement matters, including Drug Tariff listing and the Voluntary and Statutory Pricing Schemes. He has first-hand experience of drug reimbursement matters, having spent eight years operating a pharmacy business prior to joining Covington & Burling LLP.

Covington & Burling LLP

22 Bishopsgate, London, EC2N 4BQ, United Kingdom
Tel: +44 20 7067 2000 / URL: www.cov.com

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