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ORIGINAL ARTICLE

Free-of-charge medicine schemes in the NHS: A local and regional drug and therapeutic committee's experience

Simon O'Callaghan[1] | Robin E. Ferner[2] | Andrew Barron[1] | Katherine Saxby[1] | Reecha Sofat[3]

[1]Formulary and Medicines Management Department, University College London Hospital NHS Foundation Trust, London, UK

[2]Institute of Clinical Sciences, University of Birmingham, Birmingham, UK

[3]Centre of Clinical Pharmacology and Therapeutics, Institute of Health Informatics, University College London, London, UK

Correspondence
Simon O'Callaghan, Formulary and Medicines Management Department, University College London Hospital NHS Foundation Trust, 250 Euston Road, London NW1 2PG, UK.
Email: simon.ocallaghan@nhs.net

Reecha Sofat, Centre of Clinical Pharmacology and Therapeutics, Institute of Health Informatics, University College London, 222 Euston Rd, London NW1 2DA, UK.
Email: r.sofat@ucl.ac.uk

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Introduction: Free-of-charge (FoC) medicine schemes are increasingly available and allow access to investigational treatments outside clinical trials or in advance of licensing or NHS commissioning.

Methods: We retrospectively reviewed FoC medicine schemes evaluated between 2013 and 2019 by a single NHS trust and a regional drug and therapeutics committee (DTC). The details of each locally reviewed FoC scheme, and any nationally available Medicines and Healthcare products Regulatory Agency Early Access to Medicines Scheme (MHRA EAMS) in the same period, were recorded and categorised.

Results: Most FoC schemes (95%) allowed access to medicines intended to address an unmet clinical need. Over 7 years, 90% were company-FoC schemes and 10% were MHRA EAMS that were locally reviewed. Phase 3 clinical trial data were available for 44% of FoC schemes, 37% had phase 2 data and 19% were supported only by phase 1 data, retrospective observational studies or preclinical data. Utilisation of company-FoC schemes increased on average by 50% per year, while MHRA EAMS schemes showed little growth.

Conclusion: Company-FoC medicine schemes are increasingly common. This may indicate a preference for pharmaceutical companies to independently co-ordinate schemes. Motivations for company-FoC schemes remain unclear and many provide access to treatments that are yet to be evaluated in appropriately conducted clinical trials, and whose efficacy and risk of harm remain uncertain. There is no standardisation of this practice and there is no regulatory oversight. Moreover, no standardised data collection framework is in place that could demonstrate the utility of such programmes in addressing unmet clinical need or to allow generation of further evidence.

KEYWORDS
access to healthcare, compassionate access schemes, early access schemes, evidence based medicine, expanded access schemes, drug and therapeutic committee, drug approval, Free of charge schemes, health policy, medicine governance, service provision

1 | INTRODUCTION

A pharmaceutical company may market a medicine in the United Kingdom (UK) for a specified indication or indications only after the Medicines and Healthcare products Regulatory Agency (MHRA) or the European Medicines Agency (EMA) grants a marketing authorisation (MA) on the basis of data submitted that demonstrate acceptable quality, safety and efficacy in the relevant indication(s). However, newly licensed products can only be widely used in the NHS if they are considered cost-effective and funding is approved by the National Institute for Health and Care Excellence (NICE) directly by NHS England (NHSE) or by equivalent bodies in the devolved nations (Figure 1). The standard time to process an MA application for a new medicine is 30 weeks[1] by the MHRA, 40–49 weeks for a single technology appraisal by NICE[2] and 48 weeks for specialised commissioning policy by NHSE.[3] While these bodies have "fast-track" appraisal processes for treatment for severe and life-threatening conditions, these are infrequently utilised.

A free-of-charge (FoC) medicines scheme can be defined as any arrangement where a medicine is supplied free of charge by a pharmaceutical manufacturer to a healthcare provider for treatment of a single patient or cohort of patients. In the UK, FoC schemes operate broadly as either early access to medicines schemes. which are overseen by the MHRA (MHRA EAMS), or independent of regulatory oversight and co-ordinated by a pharmaceutical manufacturer. The latter are described in a variety of ways (eg, compassionate access, expanded access) but hereafter are referred to as company-FoC schemes. FoC schemes allow accelerated access to new treatments still in development or in advance of regulatory/NHS approval, and can be desirable for both patients and their treating physicians, particularly where therapeutic options are not available or are of limited effectiveness.

What is already known about this subject

- Pharmaceutical companies offer free-of-charge (FoC) medicine schemes that allow clinicians to access novel treatments either not yet authorised for use in the UK or not yet commissioned for use within the NHS.
- The Medicines and Healthcare products Regulatory Agency (MHRA) currently provide a voluntary governance framework in which FoC medicine schemes can operate, called the Early Access to Medicines Scheme (EAMS).
- Outside the MHRA EAMS programme, pharmaceutical manufacturers can independently make available FoC medicine schemes that are not standardised or regulated in the UK.

What this study adds

- FoC medicine schemes direct from manufacturers are increasingly being utilised within the NHS, particularly for anticancer treatments.
- Medicines that are in early drug development are available via FoC schemes that bypass existing clinical trials and medicine licensing governance frameworks.
- We provide evidence and experience of a large NHS trust and a regional drug and therapeutics committee to quantify the number of schemes and for which conditions FoC schemes are available as a mechanism to establish the scale of schemes.

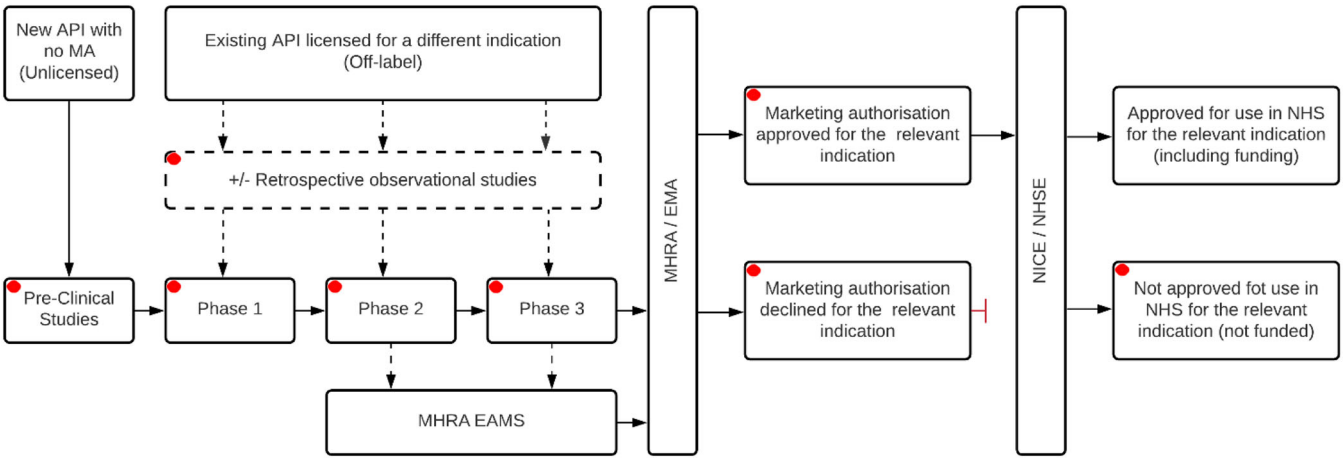

FIGURE 1 Drug development, licensing and typical NHS approval pathway in England. •Timepoints within the pathway in which company-FoC schemes are made available. API = Active Pharmaceutical Ingredient. MA = marketing authorisation. MHRA = Medicines and Healthcare products Regulatory Agency. EAMS = Early Access to Medicines Scheme. EMA = European Medicines Agency. NICE = National Institute for Health and Care Excellence

The MHRA EAMS process was introduced in 2014 to give patients with life-threatening or debilitating conditions early access to unlicensed or off-label treatments for which there is a clear unmet need.[4] MHRA EAMS is a voluntary process and is funded by the pharmaceutical company. The applicant must submit data (published or unpublished) demonstrating to the MHRA that the product is a Promising Innovative Medicine (PIM), fulfils a high unmet need in a serious condition, is likely to offer a major advantage over current treatments and has anticipated benefits that outweigh potential harms. Following submission of published or unpublished supporting data to the MHRA, this is reviewed in collaboration with NICE and NHSE, and a positive scientific opinion may be granted, allowing access to treatment until a marketing authorisation decision has been made, with an agreed clear exit strategy if the medicine is not licensed. Manufacturers can only apply for an MHRA EAMS scientific opinion for therapies with phase 3 data (phase 2 data in exceptional circumstances), and priority is given to medicines expected to be 18 to 24 months from MA approval. Locally, our practice is that all MHRA EAMS are subject to formal drug and therapeutic committee (DTC) review and approval for local use.

A pharmaceutical company can offer FoC access to treatments directly to an individual healthcare provider at the request of a prescriber. Unlike MHRA EAMS, there is no standardisation of company-FoC schemes with regards to the terms on which they are offered, the duration of access to FoC treatment, equity of access across the NHS and the approval criteria used. Company-FoC schemes are available for treatments at any stage of the drug development pathway, from early in development preclinical data to post-phase 3 randomised controlled trials awaiting licensing and NHS approval (Figure 1). There is no regulatory oversight or centralised assessment of company-FoC schemes, and it is for individual healthcare providers to assess their suitability before they are introduced into clinical practice. FoC schemes appear to be increasingly common, and are becoming viewed as a new standard of accessing treatments in the NHS outside traditional drug development via enrolment in clinical trials and regulatory approval pathways.

Local and regional DTCs are responsible for ensuring treatments offered within their organisation or region have sufficient evidence to support claims of efficacy, appropriately balanced with the known and potential unknown risks of novel treatments, and that treatment is cost-effective.[5] Here we report on the experience of a local and a regional DTC in England to determine the type, number and trends over time of FoC schemes encountered locally, including their origins, indications, what local decisions were made and any subsequent licensing or national approvals. We also compared our local experience with that of all nationally available MHRA EAMS during the same time period.

2 | METHODS

A data collection tool was designed to record and categorise FoC scheme applications received by a DTC according to how the FoC scheme was accessed (MHRA EAMS or company-FoC), whether the FoC scheme was for an individual exceptional patient request or for a defined patient cohort, what phase of drug development the treatment had reached for the proposed indication, the licensing status and whether the treatment displaced existing NHS commissioned therapies. The tool also recorded follow-up data of licensing status and NHS approval status at the time of data collection, noting if there had been any change in either status since original DTC review. The data collection tool and definitions of terms used can be found in Table 1.

All FoC scheme applications locally reviewed by DTCs at the University College London NHS Foundation Trust Use of Medicines Committee (UCLH-UMC) or the North Central London Joint Formulary Committee (NCL-JFC) over a 7-year period (1 January 2013 to 31 December 2019) were included in the data collection. NCL-JFC serves the NCL sector comprising eight hospital trusts and the NCL clinical commissioning group covering a population of approximately 1.3 million. Whilst UCLH is one of the hospitals that is a member of the NCL-JFC, schemes are not submitted to both, rather if an FoC scheme or EAMS is thought to be applicable to other members' services within the sector it is referred to the NCL JFC to be reviewed and, if approved, later ratified at each relevant provider trust.

DTC decisions for each FoC scheme application were recorded using the data collection tool. Licensing status at time of data collection was verified by referring to the MHRA,[6] EMA[7] approved products online databases and the electronic medicines compendium (eMC).[8] NHS approval status at time of data collection was verified by the technology appraisal (TA) status of the medicine and the approved or proposed indication on the NICE website[9] or if an NHSE commissioning policy existed on the NHSE website.[10] Original FoC scheme criteria were checked to establish if they aligned with subsequent licensing or NHS criteria, or were broader or more restricted.

Any medicines nationally available under the MHRA EAMS from its inception in April 2014 to 31 December 2019 were recorded using the same data collection tool, irrespective of whether local or regional DTC review had taken place, to compare the number of company-FoC schemes assessed locally with those assessed nationally by the MHRA as EAMS. The proportion of MHRA EAMS treatments that obtained a licence and NHS approval was also recorded. Specific information on PIM applications and negative or withdrawn scientific opinion applications is not published by the MHRA due to confidentiality agreements, therefore only information regarding MHRA EAMS with a positive scientific opinion could be recorded.

3 | RESULTS

3.1 | Locally reviewed FoC schemes

In total, 81 FoC schemes were locally reviewed by DTCs over a 7-year period. Company-FoC schemes accounted for 90% (n = 73) of schemes reviewed and 10% (n = 8) were MHRA EAMS. There were

TABLE 1 Free-of-charge scheme data collection categories and definitions

Factor		Definition
Access type	MHRA early access to medicines scheme (MHRA EAMS)	FoC access scheme co-ordinated by the MHRA and funded by the pharmaceutical manufacturer (only available as cohort FoC access schemes)
	Company-FoC scheme	FoC access scheme available independently from a pharmaceutical manufacturer (available as either individual or cohort FoC access schemes)
Scheme type	Individual FoC access scheme	A medicine is made available free of charge on a named patient basis only and does not represent a wider cohort
	Cohort FoC access scheme	A medicine is made available free of charge to a defined cohort of patients
Stage of supporting evidence	Preclinical	Preclinical studies for the treatment are available supporting a scientific rationale for the treatment but clinical trial data is not available
	Observational	Case reports and/or retrospective studies have been conducted for the treatment but no prospective clinical trial data are available
	Phase 1	Completed or interim data from phase 1 clinical trial(s) are available to support efficacy/safety of treatment
	Phase 2	Completed or interim data from phase 2 clinical trial(s) are available to support efficacy/safety of treatment
	Phase 3	Completed or interim data from phase 3 clinical trial(s) are available to support efficacy/safety of treatment
Displaces existing NHSE/NICE approved treatment(s)	Yes	Place in therapy for FoC scheme medicine displaces approved treatments within an existing NICE/NHSE treatment pathway (eg, proposed use as first line within an existing pathway)
	No	Place in therapy for FoC scheme medicine does not displace any approved treatments within an existing NICE/NHSE treatment pathway (eg, proposed as last line therapy or no approved treatments exist)
Licensing status a. At time of original DTC evaluation b. At time of data collection	Unlicensed	A medicine that has not been granted an MA by the MHRA or EMA for any indication
	Off-label	A medicine that has an MA from the MHRA or EMA but not for the proposed indication
	Licensed	A medicine that has an MA from the MHRA or EMA for the proposed indication
NHS approval status a. At time of original DTC evaluation b. At time of data collection	Approved	Treatment has been formally evaluated and approved for use within the NHS by NICE or NHSE due to sufficient evidence of efficacy, safety and cost-effectiveness for the proposed treatment
	Review pending	A review by NICE or NHSE has started for the proposed treatment but is still underway
	Not reviewed	A submission to NICE or NHSE has not been made and a review has not started
	Not approved	Treatment has been formally evaluated and not approved for use within the NHS by NICE or NHSE on grounds of insufficient evidence of efficacy, disproportionate risk of harm or unacceptable cost-effectiveness balance for the proposed treatment

DTC, drug and therapeutics committee; EMA, European Medicines Agency; FoC, free-of-charge; NHSE, NHS England; NICE, National Institute for Health and Care Excellence; MHRA EAMS, Medicines and Healthcare products Regulatory Agency Early Access to Medicines Scheme.

eight company-FoC schemes (10%) identified that displaced NICE or NHSE approved treatments. Of the 81 FoC schemes, 41 (51%) were utilised for individual patient requests and 40 (49%) were for a defined cohort. The majority of FoC schemes (75%) were for cancer treatments, with other schemes spread across various specialties (Figure 2). The number of locally reviewed FoC schemes grew on average by 57% per year, attributed to a 17-fold increase in FoC schemes for cancer treatments over 7 years, while noncancer

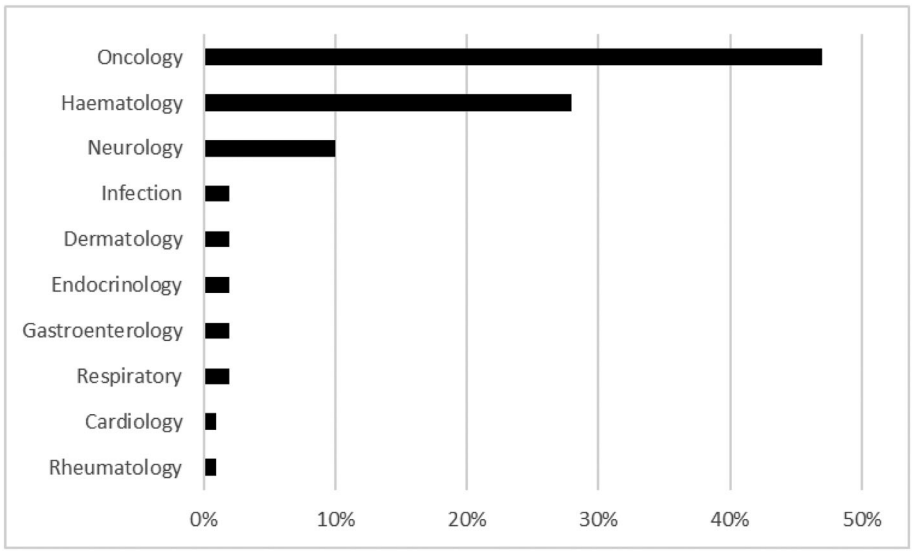

FIGURE 2 Free-of-charge schemes by clinical specialty locally reviewed by the University College London NHS Foundation Trust Use of Medicines Committee or the North Central London Joint Formulary Committee between January 2013 and December 2019

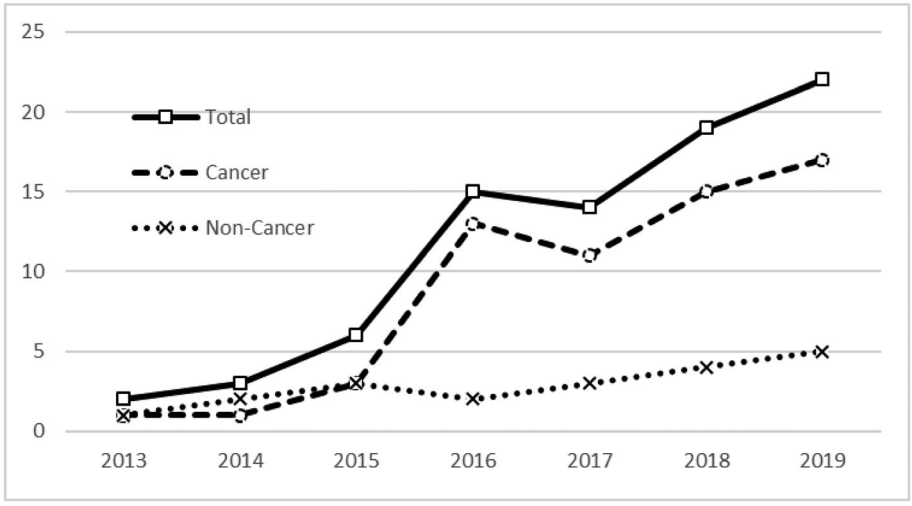

FIGURE 3 Number of free-of-charge schemes locally reviewed by the University College London NHS Foundation Trust Use of Medicines Committee or the North Central London Joint Formulary Committee between January 2013 and December 2019

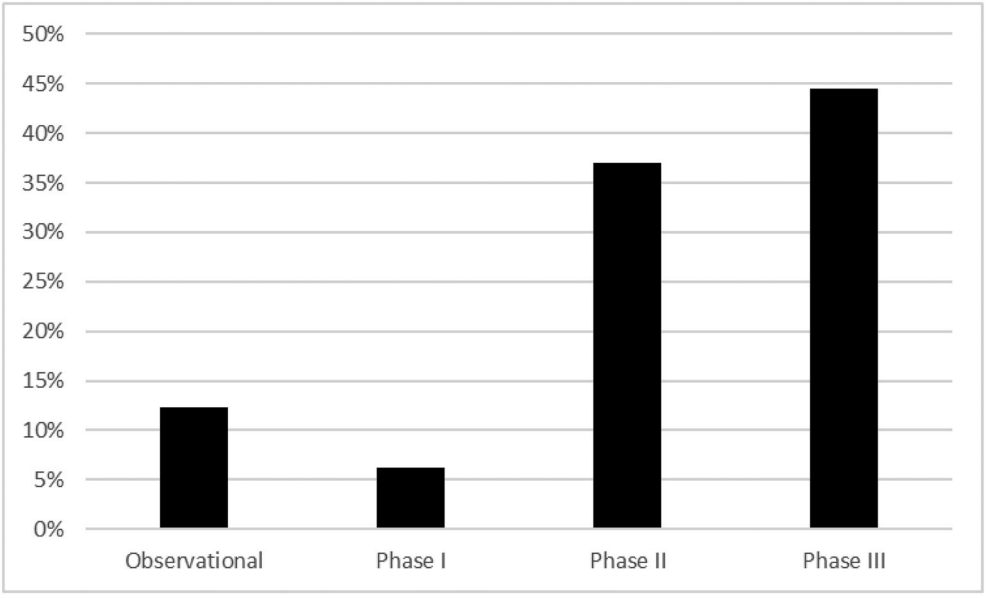

FIGURE 4 Drug development stage of free-of-charge schemes locally reviewed by the University College London NHS Foundation Trust Use of Medicines Committee or the North Central London Joint Formulary Committee between January 2013 and December 2019

FoC schemes remained consistent at one to five per year (Figure 3). FoC schemes were made available by 38 different pharmaceutical manufacturers.

The DTCs approved 95% of FoC scheme applications. FoC schemes were not approved as they either bypassed a NICE TA approved treatment with likely similar efficacy or proposed unacceptable terms, for example that the scheme was time-limited or limited the number of patients who could access. There were six schemes that bypassed NICE TA approved treatments but were approved for use due to one of the following reasons: the presence of a positive draft or final appraisal determination from NICE; pending commissioning implementation of a NICE TA; a cancer treatment specifically targeting a genetic mutation and the DTC concluded there was reasonable evidence that patients with the mutation had a lower response to standard of care treatment and/or may respond better to targeted treatment; or standard of care treatments were contraindicated.

At the time of DTC review, 36 (44%) FoC schemes were supported by phase 3 clinical trial data, with 30 (37%) supported by phase 2 data and five (6%) by phase 1 data; 10 (12%) relied solely on preclinical or retrospective observational data or both. There was a similar distribution of FoC schemes for licensed (27%), off-label (38%) and unlicensed (35%) treatments. All FoC schemes were for treatments that had not yet been approved by NICE or NHSE for use within the NHS. Figure 4 summarises the stage of drug development at the time of original DTC review.

The median elapsed time from original DTC review to time of data collection for this study was 23 months (range 0–78, interquartile range 11–43). At the time of data collection, of the FoC schemes for treatments that were off-label or unlicensed when initially reviewed by the DTC, 32% (19/59) had since been licensed in the UK for the proposed indication. However, the licensing criteria were more restrictive for 74% (14/19) of these than the criteria originally available under the FoC scheme. Of the FoC scheme treatments, 35% (28/81) were subsequently approved for use in the NHS but access criteria were more restrictive for 54% of these. Treatments not approved for use in the NHS had been reviewed and not approved (9%), or the review was still in progress (20%), or an application for use in the NHS had not yet been submitted by the manufacturer for the intended indication (37%) (see Table 2).

3.2 | Comparison between locally reviewed company-FoC schemes and nationally available MHRA EAMS

From the introduction of the MHRA EAMS programme in April 2014 to December 2019 there have been 28 nationally available MHRA EAMS. On average there were four MHRA EAMS approved nationally per year (range three to seven), with no indication of growth, and the majority were for cancer treatments (68%; n = 19) (Figures 5 and 6). In comparison, an average of 10 company-FoC schemes a year were

TABLE 2 Follow-up of UK licensing and NHS approval status of FoC schemes locally reviewed by the UCLH-UMC or NCL-JFC between January 2013 and December 2019

	Company FoC (n = 73)	MHRA EAMS (n = 8)	All FoC schemes (n = 81)
UK licensing status			
At original DTC review			
Licensed (for intended indication)	22	0	22 (27%)
Off-label (licensed for a different indication)	26	5	31 (38%)
Unlicensed	25	3	28 (35%)
At time of data collection[a]			
Licensed (for intended indication)	36	5	41 (51%)
Off-label (licensed for a different indication)	25	2	27 (33%)
Unlicensed	12	1	13 (16%)
NHS approval status[b]			
At time of data collection[a]			
Approved	24	4	28 (35%)
Not approved	6	1	6 (9%)
Review pending	13	3	15 (20%)
Not under review	30	0	26 (37%)

Abbreviations: DTC, drug and therapeutics committee; FoC, free-of-charge; MHRA EAMS, Medicines and Healthcare products Regulatory Agency Early Access to Medicines Scheme; NCL-JFC, North Central London Joint Formulary Committee; UCLH-UMC, University College London NHS Foundation Trust Use of Medicines Committee.

[a]Median time from original DTC review to data collection was 23 months.

[b]At time of original DTC review there were no FoC schemes available for treatments already approved for use in the NHS.

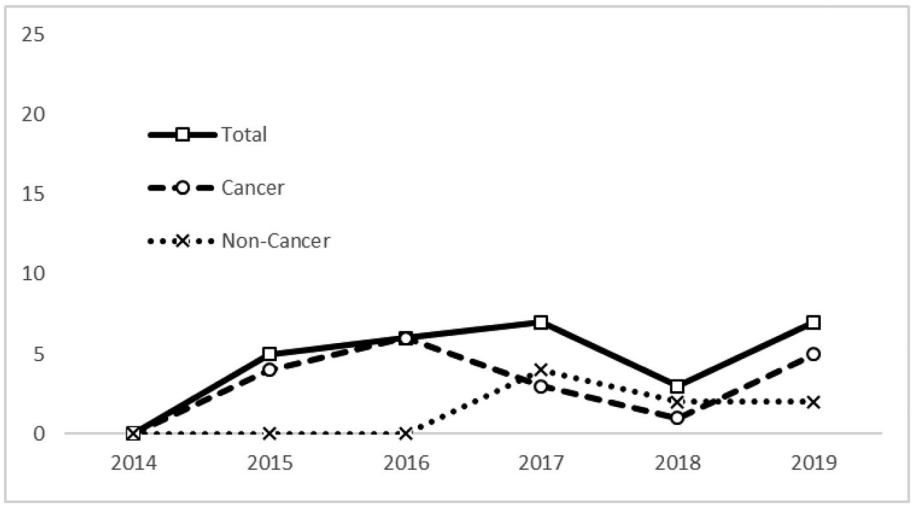

FIGURE 5 Number of nationally available Medicines and Healthcare products Regulatory Agency Early Access to Medicines Schemes between 2014 and 2019

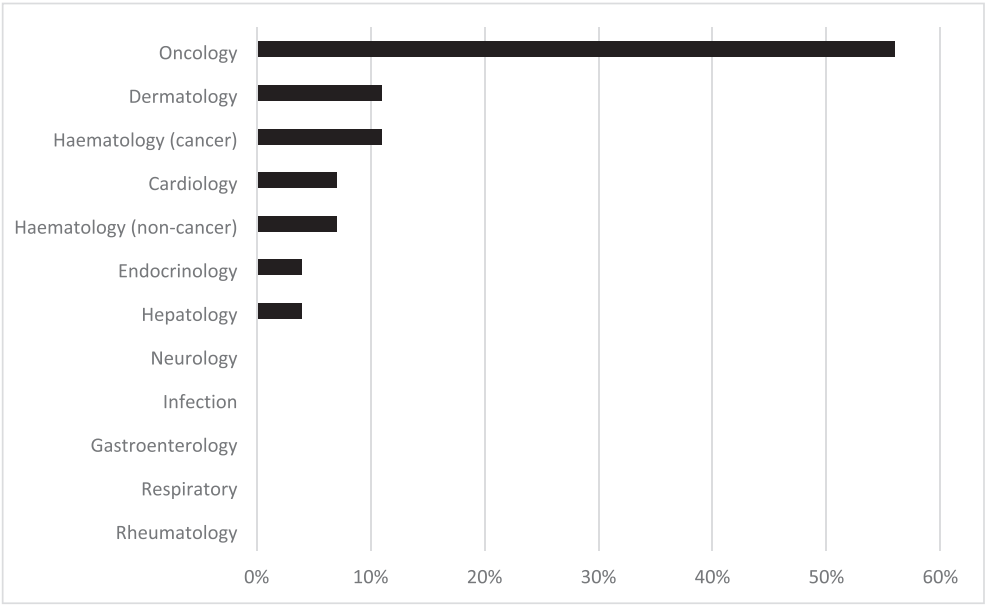

FIGURE 6 Nationally available Medicines and Healthcare products Regulatory Agency Early Access to Medicines Schemes between 2014 and 2019 by clinical specialty

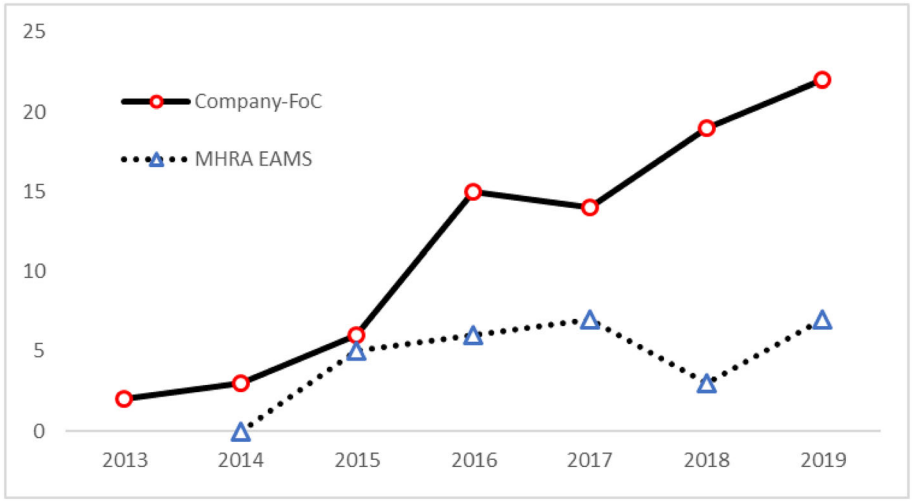

FIGURE 7 Number of company free-of-charge schemes (locally reviewed by University College London NHS Foundation Trust Use of Medicines Committee or the North Central London Joint Formulary Committee) compared with the number of nationally available Medicines and Healthcare products Regulatory Agency Early Access to Medicines Schemes in the UK between January 2013 and December 2019

locally reviewed during the same time period (range two to 19, average growth 50% per year) (Figure 7). The average duration of nationally available MHRA EAMS was 4.2 months (range 0.6 to 10.9 months), 18 were subsequently NICE/NHSE approved, one was not approved by NICE (cenegermin; for neurotrophic keratitis) and nine NICE TAs were still in development at data collection. The duration of company FOC schemes could not be compared as scheme closure dates are not publicly available. Of the 18 nationally available MHRA EAMS with a subsequent NHS approval decision, the average time from marketing authorisation (and MHRA EAMS closure) to NHS commissioning was 10.4 months (range 3.7 to 27.5 months). At the time of our data collections, there were three MHRA EAMS still open, and of the six NICE TAs still in development it had been 6.5 months (range 2.2 to 16.5 months) since the MHRA EAMS closed.

4 | DISCUSSION

We have described for the first time the number and characteristics of FoC schemes assessed by DTCs in a large NHS trust and in the NCL region. In a 7-year period, 90% of treatments locally reviewed were via company-FoC schemes and 10% were via the MHRA EAMS programme. Most schemes (95%) allowed access to medicines intended to address an unmet clinical need. Phase 3 clinical trial data were available for 44% of company-FoC schemes, 37% had phase 2 data and 18% were only supported by phase 1 retrospective observational studies or preclinical data. Locally reviewed MHRA EAMS comparatively were supported by phase 2 (25%) or phase 3 (75%) studies. The number of company-FoC schemes reviewed locally has increased almost 10-fold over a 7-year period, where MHRA EAMS utilisation nationally by pharmaceutical manufacturers and availability of treatments by this route has shown no indication of growth. Not all treatments initially available via FoC schemes went on to secure a UK marketing authorisation or NHS approval. Our data indicate that pharmaceutical companies are increasingly opting to independently offer FoC access that includes treatments immediately prior to licensing or NHS commissioning review but also early investigational treatments.

Early access to promising treatments where there is an unmet clinical need, particularly for life-threatening and debilitating diseases, is important to patients, clinicians and the overall NHS. The MHRA EAMS programme is a voluntary national process open to all providers with the intention of informing licensing and NHS commissioning, and ensuring equitable access to novel therapies. There is a governance framework which companies and providers must adhere to. By contrast, there is currently no standardised governance for company-FoC schemes, which introduce several unique clinical, administrative, financial and ethical challenges. Decisions are left to local healthcare providers and their DTCs. The methods and rigour of evaluation by which each DTC operates may differ but are nevertheless responsible for ensuring sufficient supportive evidence for treatment effectiveness is appropriately balanced against the risks of potential harm. There is also a requirement to sign a contract with the provider company, for which there is also no standardisation. The local DTC must ensure that the terms of any agreement ensure continued access for existing patients if the scheme is withdrawn or risk placing a cost burden on already constrained resources to continue treatments with unclear cost-effectiveness. Trusts should therefore ensure there is an appropriate exit strategy following the inevitable closure of a company-FoC scheme.

The motivations of pharmaceutical companies to offer FoC schemes are unclear, but they could include building early product demand and seeding the market in advance of regulatory or commissioning decisions. Growth in company-FoC schemes appears to be mainly driven by treatments for cancer. However, many noncancer conditions can also be life-threatening or severely debilitating and it is unclear why FoC access for emerging noncancer therapies are less likely to be offered by companies. Availability of company-FoC schemes creates a two-track system of access to drugs changing existing evidence-based treatment pathways within the NHS with the potential to destabilise commissioning processes for NHS services due to increased hospital attendance for monitoring, investigations or management of toxicities, without sufficient evidence of efficacy to support this increased activity. In our study, we identified eight company-FoC schemes that displaced existing NHS approved treatments within established pathways. Such schemes may also introduce inequity where only large centres with key opinion leaders receive approval from manufacturers for FoC access or where evidence review standards and processes differ between DTCs. There is a risk that FoC schemes may disrupt enrolment into randomised controlled clinical trials as a means of avoiding potential randomisation into a control arm. Earlier access to markets to form clinician experience may also provide an advantage over competitors who do not or are unable to offer FoC access.

The decision to approve an FoC scheme for treatments early in development to address an unmet need is extremely challenging, and is at least in part legitimised simply by their availability at no cost rather than an appropriate level of evidence. Evidence of proposed efficacy can be limited to a biological rationale based on a consensus of disease mechanisms, the presence of a genetic aberration or surrogate markers (eg, tumour response) in place of clinically relevant outcomes (eg, overall survival or quality of life). Early clinical trials may have small sample sizes and lack comparators, so can fail to detect serious adverse effects, thus exposing patients to unknown risks of harm which may be higher than any benefit gained. It remains ethically difficult to rationalise offering an experimental treatment outside of a clinical trial based on limited evidence.

Randomised controlled clinical trials are the gold standard for determining efficacy as well as enabling a longer-term therapeutic strategy for the given disease. Clinical trials operate under tightly regulated processes that include independent review of the trial protocol by an ethics panel, detailed informed patient consent and dedicated staff to ensure trials are carried out according to Good Clinical Practice. Notably, formal trials may not be feasible in very rare disorders or may not be required if treatment effects are large in observational studies. Our experience is that company-FoC schemes that make available treatments in early drug development do not provide

evidence of the same value or quality as formal clinical trials, and that NHS trusts are not currently equipped to mirror the safeguards provided within a clinical trial structure. A standardised governance process and data collection should be a requirement of FoC schemes to aid early evaluation of benefits and harms.

An independent review of the MHRA EAMS process[11,12] reported that industry valued a mechanism for dialogue with government about early uptake of new products, but companies reported the voluntary MHRA EAMS process was time-consuming and costly. Our study supports the apparent pharmaceutical industry preference to offer FoC schemes independently and outside the MHRA EAMS process (Figure 7). Availability of treatment via MHRA EAMS can create a new standard of care as they are required to address a high unmet clinical need, but access usually ceases for any new patients once an MA is granted and the MHRA EAMS subsequently closes. In our study, the average time from MHRA EAMS closure to an NHS commissioning decision was 10.4 months (n = 18), and others where assessment is still ongoing was up to 16.5 months. This gap in access creates inequity amongst patients as only those eligible during the limited time window of an MHRA EAMS were able to access treatment. This also puts trusts under pressure to continue to provide access to treatments for new patients previously available under an MHRA EAMS while awaiting an NHS commissioning decision.

The NHS Regional Medicines Optimisation Committee (RMOC) recently produced advice on company-FoC schemes to aid development of policy for local healthcare providers.[13] This was the first nationally produced advice on how company-FoC schemes should be considered within the NHS and a proposed framework in which they could be assessed. However, the advice provides little guidance on the assessment of clinical evidence for company-FoC schemes, particularly when considering informal FoC access agreements for unlicensed/off-label treatments earlier in the drug development pathway or for individual patient requests. The advice focuses on the over-arching principles of medicines optimisation, roles and responsibilities, and application processes, and highlights the administrative burden, the nondrug healthcare cost of FoC schemes and the potential imbalance introduced into the NHS commissioning process. Within NCL, a locally adapted version of the RMOC guidance on company-FoC schemes has been recently produced which aims to clarify the scope of company-FoC access arrangements and the framework in which they should be assessed.[14]

We suggest that a national body implement regulation and standardised assessment of company FoC schemes to ensure stronger governance, safeguards, uniform decision-making and equitable access to treatments across the UK. A register of FoC schemes could be maintained nationally and standardisation of FoC terms of supply agreed between industry and the NHS. A mechanism to collect patient outcome data enrolled in FoC schemes would benefit patients, clinicians, academia, industry and the NHS. This could be achieved through expansion of the MHRA EAMS framework to include medicines at any stage of drug development and for differing cohort sizes (similar to the FDA in the United States in which different pathways exist for early access schemes depending on whether treatment is for an 'individual', 'intermediate-size' or 'widespread' cohort).[15] Moreover, review of the MHRA EAMS process could address perceived or real barriers to industry engagement.

Our study has some limitations. The data presented here are limited to FoC schemes assessed by a single trust DTC and a regional DTC in England, and may not be representative of the national experience. Results in other trusts or regions will likely differ due to the services offered and may have different standards or processes by which to evaluate FoC scheme applications. We have not quantified the additional resource burden associated with implementation of FoC schemes, which includes administrative burdens such as FoC contracts and additional consent requirements, and also workforce and operational burdens. The details of treatments offered via FoC schemes cannot be disclosed due to confidentiality agreements as part of company-FoC scheme terms. We believe that company-FoC schemes operate widely within the NHS (assessed through personal communication with other DTCs), although they may be limited to centres where there are specialist services and risk creating inequity in accessing treatment across the NHS. We cannot be certain that we have captured all such schemes in our local health economy, and we have not estimated the prevalence of such schemes nationally. A register, maintained nationally, would allow the prevalence to be established. If FoC schemes are common, as we suspect, this would be a prelude to ensuring that they are operated within a standard governance framework. The median follow-up time in this study was 23 months and the licensing and NHS approval status of treatments available via FoC schemes may eventually change as more data become available and national review processes reach their conclusion.

5 | CONCLUSION

The effective regulation of medicines requires their independent assessment, based on robust evidence from tightly regulated clinical trials. This ensures that only effective treatments of acceptable quality are made available to patients and protects them from disproportionate harms. This information also forms the basis of rational health-economic assessments of new treatments. FoC medicines schemes increasingly enable access to treatments that have not yet undergone robust assessment in clinical trials or by independent regulators. Patients with life-threatening and debilitating diseases who have few or no treatment options may possibly derive benefit from accessing these treatments via an FoC scheme. However, FoC schemes are increasingly being offered by pharmaceutical manufacturers, bypassing established governance frameworks and safeguards, and risk exposing patients to harm potentially without any benefit gained. The clinical, administrative, financial and ethical implications of FoC schemes are increasingly challenging, and at present often must be evaluated by clinicians and DTCs based on limited evidence. Our experience highlights these increasing challenges, that the MHRA EAMS programme is not sufficient alone to address these and that company-FoC schemes should not remain wholly unregulated.

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COMPETING INTERESTS

The authors have no conflicts of interest to declare.

CONTRIBUTORS

S.OC. provided the collection of data, analysis and interpretation of data, and drafting of the manuscript. R.S., R.E.F., A.B. and K.S revised the manuscript critically for important intellectual content and gave final approval of the version to be submitted.

DATA AVAILABILITY STATEMENTS

Research data are not shared.

ORCID

Simon O'Callaghan https://orcid.org/0000-0001-7154-2593
Robin E. Ferner https://orcid.org/0000-0003-3769-1346
Andrew Barron https://orcid.org/0000-0002-6292-778X
Katherine Saxby https://orcid.org/0000-0002-3379-210X
Reecha Sofat https://orcid.org/0000-0002-0242-6115

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