No more, no less:

A guide to the appropriate prescribing of medicines and the role of industry

November 2024

About ABPI

The ABPI exists to make the UK the best place in the world to research, develop and access medicines and vaccines to improve patient care.

We represent companies of all sizes which invest in making and discovering medicines and vaccines to enhance and save the lives of millions of people around the world.

In England, Scotland, Wales and Northern Ireland, we work in partnership with governments and the NHS so that patients can get new treatments faster and the NHS can plan how much it spends on medicines. Every day, our members partner with healthcare professionals, academics and patient organisations to find new solutions to unmet health needs.

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Contents

Glossary

Adverse event	An unfavourable and unintended experience associated with the use of a medical product in a patient, which may or may not be causally related to the medicine
Adverse Drug Reaction	A response to a medicinal product which is noxious and unintended, where a causal relationship between the medicinal product and adverse event is either known or strongly suspected
Biosimilar	A biological medicine which has been shown not to have any clinically meaningful differences from the originator medicine in terms of quality, safety and efficacy
Code of practice	An ABPI document which sets out the requirements the industry must comply with and supports companies' commitment to self-regulation
Disclosure	Industry showing payments and benefits in kind made by the pharmaceutical company
Efficacy	The ability of a medicine to produce its desired effect
Indication	A reason to use a medicine
Licensed	Stipulates the medicine can be used to treat certain conditions
Medical Affairs	The part of a pharmaceutical companies which engages with healthcare professionals regarding the clinical aspects of products
Medicines Optimisation	Ensuring the best outcome from using or not using a medicine
Multimorbidity	The presence of two or more long term health conditions
Off-label	Using a medicine in a way that is different to described on the product license
Overprescribing	Potential harm outweighs the benefit of the medication but it is given anyway
Pharmacovigilance	Activities relating to the detection, assessment, understanding and prevention of adverse effects
Polypharmacy	Used to describe the situation when people are taking a number of medicines.
Post-marketing surveillance	The practice of monitoring the safety of a pharmaceutical drug after it has been approved for use
Real world evidence	the clinical evidence about the usage and potential benefits or risks of a medical product derived from analysis of real world data
Risk Management Plan	Submitted by companies when applying for their medicine to be able to be used, details how a medicines risks will be prevented or minimised in patients
Therapeutic class	A way of grouping medicines by their intended effect
Yellow Card Scheme	The system for recording adverse incidents with medicines and medical devices in the UK

1. Executive summary

Pharmaceutical companies have a key role to play beyond that of developing a medicine, in helping to navigate the complexity of the modern prescribing landscape. Within this report, we highlight recommendations, both for healthcare professionals and for the UK pharmaceutical industry as a whole, to enhance the visibility and the role industry has to play in the topic of appropriate prescribing.

Appropriate prescribing is a fundamental aspect of patient care and healthcare management. Appropriate prescribing means prescribing the right medicine, at the right dose, for the right duration and for the right patient. However, the prescribing options available to prescribers are ever-increasing, with, in some instances, increasing complexity. Therefore, navigating the prescribing ecosystem and making sure that the best possible treatment decision is made with a patient can become ever more challenging for prescribers.

Ahead of interactions within the prescribing landscape, pharmaceutical companies – working in conjunction with regulators – already play a key role in making sure that medicines that are approved for use are developed and manufactured with rigorous standards pertaining to quality, safety and efficacy. This rigour does not end with the approval of a medicine but continues with post-marketing surveillance and pharmacovigilance, risk-minimisation measures, and health-economic evaluation by bodies such as NICE, who determine whether the balance of benefits and risks of a medicine represents a good use of NHS resource for patients.

Pharmaceutical companies are experts with regards to the quality, safety and efficacy profiles of the medicines they research, develop and manufacture, and, accordingly, have resources available to prescribers to help guide appropriate prescribing – for example, the Summary of Product Characteristics. Beyond this, pharmaceutical companies have medical information and pharmacovigilance expertise, as well as medical advisers who can provide in-depth information and data upon request, and can help guide prescribers when making challenging prescribing decisions (including when it might be appropriate not to prescribe). These resources should be utilised by prescribers.

The pharmaceutical industry also has a vital role to play in ensuring that, when engaging with healthcare professionals about the development, promotion and supply of a medicine, any such relationship does not lead to an inappropriate bias in prescribing. The topic of transparency over industry payments to healthcare professionals was covered in both the 2020 ‘First Do No Harm’ report on patient safety by Baroness Cumberledge, as well as the 2021 National Overprescribing Review led by then NHS England Chief Pharmaceutical Officer, Keith Ridge. The ABPI and the pharmaceutical industry are committed to enhancing and promoting the importance of transparency and disclosure – and this paper sets out the continued progress in that area, which helps to underpin and support the other recommendations that are targeted at better outcomes for patients.

2. Summary of recommendations

Recommendations for pharmaceutical companies

1. Companies should consider whether their sales representatives could play a more holistic role in promotional calls, specifically considering the wider prescribing context confronting a typical patient. This would mean addressing not only the efficacy and safety of the medicine being promoted and who the medicine is appropriate for, but also giving reasonable weight in the conversation to who the medicine might not be appropriate for, as well as how the medicine fits into a broader polypharmacy scenario that a healthcare professional might be confronted with.
2. Pharmaceutical companies should ensure healthcare professionals are aware of company resources available to help guide appropriate prescribing, such as personnel in medical information, pharmacovigilance and medical affairs teams. This awareness should be encouraged and facilitated by companies, but without soliciting for enquiries on specific medicines.

Recommendations for prescribers

1. The Summary of Product Characteristics (SmPC) – a comprehensive reference document for a medicine, freely and easily available online, should be widely used by prescribers as the primary source for medicines information. This information can be supplemented by other sources, such as the British National Formulary (BNF) or the Monthly Index of Medical Specialties (MIMS). The BNF for Children (BNFC) is particularly helpful for prescribing paediatric medicines where the SmPC, which reflects the product licence, is unable to reflect the off-licence information available in the BNFC.
2. Healthcare professionals should engage with post-marketing surveillance strategies such as medicines risk management plans. This includes reporting any suspected adverse events to the relevant pharmaceutical company and/or via the Yellow Card scheme. Healthcare professionals should also be vigilant for suspected adverse events when switching between medicines within a therapeutic class or between brands.
3. Patients should be encouraged by prescribers and dispensers to be aware of the brand of medicine or manufacturer they are using.
4. Drug-drug interactions are a significant factor in adverse drug reactions, and clinicians should have a high degree of awareness of the potential relevance in hospital admissions, particularly in patients with polypharmacy and multimorbidity.

5. Healthcare professionals who have concerns about company promotion should not hesitate to raise their concerns directly with pharmaceutical companies. A formal complaint mechanism is available via the Prescription Medicines Code of Practice Authority (PMCPA).
6. Disclosure UK is the pharmaceutical industry's database of payments and benefits-in-kind from pharmaceutical companies to healthcare professionals and organisations. Almost 80 per cent of the relevant values on Disclosure UK are against a named healthcare professional. The minority of healthcare professionals who continue to decline to consent to being named, or object to publication, are strongly encouraged to embrace transparency in their relationships with the pharmaceutical industry. See the ABPI's leaflet 'Step up to Disclosure UK' and NHS England's guide to managing conflicts of interest (6.7).

Recommendations for the ABPI

1. The ABPI should continue to work with stakeholders and members to ensure that the industry can play its role in support of appropriate prescribing.

3. Introduction

The ABPI is committed to working with stakeholders and members to ensure that the industry can play its role in support of appropriate prescribing. Every year in the UK, well over one billion medicines are prescribed and dispensed, out of the more than 18,000 licensed preparations[1,2]. While no prescriber would have to choose from the thousands of options available, the growth in preventative and therapeutic options does illustrate the increasing complexity of prescribing.

Prescription medicines and vaccines have an enormous capacity to be a force for good, as most recently evidenced in the COVID-19 pandemic. Without medicines, modern clinical practice as we know it, with its capacity to prevent, treat and cure disease, would not exist in any meaningful way. However, they can also carry the potential for harm, so appropriate prescribing is necessary to make sure medicines are used correctly, in the right clinical situations where the benefits outweigh any risks to the patient.

Making this happen requires many aspects of the health system to function. Companies, as the experts who have developed and manufactured the medicine, want to help promote good, ethical, and evidence-based prescribing, so they should ensure there is the appropriate awareness and engagement in place to support prescribers to achieve this.

This paper explores specific areas where particular challenges exist and how pharmaceutical companies can – or already are – helping both prescribers and patients reach shared, evidence-based and proportionate decisions about what the best course of treatment is in different situations – which may include no treatment at all. It is in the interests of all – patients, the NHS and the life-science industry – for patients to be prescribed only the medicines that they need, no more, no less.

4. Principles and process of appropriate prescribing

Appropriate prescribing describes the scenario where the right medicine is prescribed for the right patient, as part of a shared decision-making process between healthcare professional and patient. Appropriate prescribing doesn't just describe the prescription of new medicines, it can also include where a medicine that is no longer right for a patient is discontinued, again as part of a shared decision-making process between clinician and patient.

The process of appropriate prescribing is usually based on the following principles:

- medicines should be prescribed only when they are considered clinically necessary as part of a holistic patient management plan, and in all cases, the benefit of administering the medicine should be considered in relation to the risk involved
- there must be a consultation between the patient and the healthcare professional to determine the most appropriate or right treatment choice for the patient
- the prescription of licensed medicines should be in line with the Summary of Product Characteristics (SmPC), which reflects the product licence. Clinicians are legally permitted to prescribe outside the SmPC in certain circumstances (the use of off-label and unlicensed medicines is covered in a separate ABPI position paper)
- following initiation of a prescription medicine, there should be a regular review of the medicine together with shared decision-making on continuation/ adjustment or stopping the prescription as appropriate
- stopping medicines requires careful consideration and shared decision-making with patients and is considered part of routine clinical care

There have been several reviews in recent years that have addressed the topic of appropriate prescribing. For instance, the first report of the Independent Medicines and Medical Devices Safety Review, 'First Do No Harm[3],' led by Baroness Julia Cumberlege and published in 2020, looked at several issues, including the issue of prescribing of the anti-epileptic medicine sodium valproate. One of the many recommendations within this report was proposed legislation for the mandatory reporting by pharmaceutical and medical device industries of payments made to teaching hospitals, research institutions and individual clinicians. The principle of mandatory public reporting at a self-regulation level has existed for many years for all companies abiding by the ABPI Code of Practice – ABPI-member companies and non-member companies agree to abide by the ABPI code.

Another report is 'Good for you, good for us, good for everybody' – a national overprescribing review, led by former NHS England Chief Pharmaceutical Officer, Keith Ridge.[4] This highlighted a potential 10 per cent rate of overprescribing in primary care and identified both systemic and cultural issues as the causes of overprescribing. Like the Cumberledge review, one of the cultural issues touched upon within the report is the importance of clinicians making unbiased decisions, undistorted by commercial influences, and the role that industry transparency initiatives such as Disclosure UK have to play here – which makes up a section of this paper.

Additionally, one of the suggested solutions within this overprescribing report is better guidance and support for clinicians – an area this report focuses on in terms of where industry has an important role to play.

5. Medicines regulation – how the regulatory process protects patients

Appropriate, up-to-date information about medicines must be provided to prescribers and patients, so medicines are managed appropriately and used only for the right patients for the right length of time. Pharmaceutical companies work with medicines regulators, such as the Medicines and Healthcare products Regulatory Agency (MHRA), to provide this important, evidence-based information, as set out below.

5.1 Licensing and monitoring of medicines

Medicines are developed and authorised for a specific indication or indications through a robust process of ongoing regulatory review and scrutiny to ensure patient safety and public health. The medicines licencing regime exists as a bridge between pharmaceutical companies and patients to assure that medicinal products are efficacious and of high quality. There is ongoing monitoring of the medicine and its safety profile to ensure the product information reflects how to use the medicine and the expected therapeutic effects and side effects.

Securing regulatory approval for a new medicinal product in the UK is a meticulous process that hinges upon the detailed evaluation of the benefits and risks. This process is closely monitored by the MHRA and is significantly informed by the valuable input of experts, ensuring a thorough and rigorous evaluation.

This includes assessing the quality, safety and efficacy aspects. The efficacy of the product is evaluated in rigorous clinical trials as part of a comprehensive clinical development program, amassing sufficient data to demonstrate to the MHRA that the product can elicit the anticipated effects in the intended patient population.

Concurrently, the safety of the product is evaluated. Here, the MHRA needs to be convinced that the benefit-risk balance of the product has been adequately assessed and that any significant specific risks have been clearly identified. This doesn't imply that a product must be risk-free, but rather that any potential risks should be manageable and outweighed by the therapeutic benefits it offers.

In some cases, such as sometimes seen in oncology or rare diseases where the benefit-risk balance may not be clearly defined at the point of approval, the MHRA may consider granting a conditional licence. This entails an obligation on the part of the manufacturer to continue gathering data post-approval to enhance understanding of the product's benefit-risk profile.

Actual approval or licensing of a product is typically contingent upon the implementation of a risk management plan. This plan imposes specific responsibilities on the pharmaceutical company to conduct activities designed to mitigate particular risks. These activities often encompass ongoing data collection and the creation and distribution of educational resources for both

patients and prescribers. The aim is to ensure that all stakeholders involved in the administration and use of the product are informed of any potential risks and how to manage them, and how to use the product correctly for maximum benefit.

As demonstrated, regulatory approval in the UK is a comprehensive, multistage process, designed to ensure that any medicinal product reaching patients is efficacious, of high quality and safe for its intended use. As healthcare professionals, it is important to be aware of this process as it underpins the therapies utilised daily in clinical practice.

The Risk Management Plan (RMP)

Companies must support the safe and effective use of their products. At the time of applying for a licence to the MHRA, companies must submit a Risk Management Plan (RMP), including any risk-minimisation measures that will be taken. RMPs play a vital role in maintaining the safety of medicines post-approval and are strategies designed to identify, characterise, prevent or minimise risks associated with medicinal products. They may include routine measures incorporated in the product information and additional risk minimisation measures when necessary, such as educational materials for healthcare professionals or patients, or controlled access programmes. These plans are continually updated based on emerging safety data and feedback from real-world use, as described below. In the UK, the MHRA evaluates and monitors these RMPs, ensuring they are effectively reducing identified risks while maximising the benefits of the medication for patients. By engaging in these proactive strategies, healthcare professionals can further contribute to the safety and efficacy of medicines in the post-marketing phase.

5.2 Pharmacovigilance and post-marketing surveillance

Post-authorisation safety studies

Post-authorisation safety studies, often referred to as phase IV trials or post-marketing surveillance studies, are an integral part of ongoing safety monitoring after a medicine has been granted marketing authorisation. These studies provide a crucial opportunity to observe the long-term effects of the medicine in a larger, more diverse patient population and real-world conditions, often detecting rare or late-onset adverse events that may not have been apparent in pre-approval clinical trials. Such studies may go on for many years. The results of these studies can lead to changes in the recommended use, dosage or safety information for a medicine, or even result in its withdrawal from the market if necessary. They are a critical component of the pharmacovigilance system, helping to ensure the continued safety and efficacy of medicines.

Pharmacovigilance

At the point of licensing, the benefit-risk profile for a new medicine will not be fully ascertained, particularly regarding rare adverse drug reactions (ADRs). Newer safety signals may well occur in populations under-represented in the clinical trial programme, for example in the very elderly or those with co-morbidities. Post-marketing surveillance, also known as pharmacovigilance, is crucial for ensuring the continued safety of medicines after they receive regulatory approval.

In the UK, the MHRA spearheads this effort, tracking and analysing reports of ADRs from healthcare professionals and patients through the Yellow Card scheme. Pharmaceutical companies also continually monitor and collect reports of adverse events, reporting this to the MHRA and looking for any signals that might suggest a previously unknown safety issue. All this spontaneous data is invaluable in identifying new or changing safety issues, which may lead to updates in product labelling (for example, the SmPC), warnings or even withdrawal from the market.

Healthcare professionals play a vital role in medicine safety by reporting suspected adverse events. This proactive vigilance helps to build a clearer picture of a medicine's safety profile in real-world conditions, outside of the controlled environment of clinical trials. It is vital that healthcare professionals actively participate in this process, reporting any suspected adverse events to the MHRA or pharmaceutical companies to help ensure the ongoing safety and efficacy of all medicines. Each report, no matter how insignificant it may seem, contributes valuable data to ongoing post-marketing surveillance, potentially revealing new, rare or serious side effects or interactions with other medicines, or identifying specific groups of people who may be more susceptible to certain side effects. As front-line observers, the active participation of healthcare professionals in adverse event reporting is crucial in ensuring the highest standards of patient safety and care.

Black triangle medicines

In the UK, medicines marked with an inverted black triangle symbol ▼ signify that they are under intensive monitoring by the MHRA because they are new to the market or have limited post-marketing exposure. This may include newly authorised medicines, biosimilars or medicines with a new active substance. Healthcare professionals are strongly encouraged to report all suspected adverse reactions with black triangle medicines, even if they are uncertain about the causality, as these reports can contribute vital information to the ongoing evaluation of their risk-benefit balance.

5.3 Medicines pricing, reimbursement and access

The UK employs an robust system of checks and balances to ensure responsible resource allocation and utilisation of taxpayer money, especially concerning the introduction and use of new medicines. At the heart of this system is the principle of cost-effectiveness, which is assessed using the cost per quality-adjusted life year (QALY). This critical metric evaluates the financial cost of a healthcare intervention relative to its potential to extend life and improve the overall quality of life.

Robust Health Technology Assessment (HTA) processes operate in each of the four UK nations, such as those of the National Institute for Health and Care Excellence (NICE) in England, the Scottish Medicines Consortium (SMC) in Scotland, and the All Wales Medicines Strategy Group (AWMSG) in Wales. The HTA process employs health economic modelling, a quantitative technique that combines information on health benefits and costs to assess the value for money of medical interventions. This modelling is primarily based on a combination of clinical evidence from clinical trials and anticipated NHS resource use/costs to treat the patients. Real-world evidence (RWE) may also be incorporated, providing a more comprehensive picture of a medicine's effectiveness and value outside the clinical trial environment. NICE evaluations require a substantial evidence package and decisions have to be made with some uncertainty around the data. If the uncertainty is deemed too high at the time of evaluation, NICE has an option to recommend use of a medicine within a managed access agreement, utilising temporary funding from the Cancer Drugs Fund or Innovative Medicines Fund (for non-cancer medicines) while additional evidence is collected.

Importantly, the HTA process values the input of a variety of stakeholders. This includes clinical experts who can provide a professional perspective on the efficacy and practicality of the medicine. The process also involves patients and representative patient organisations, who can provide essential insights into the lived experience of the conditions being treated, ensuring a human-centred approach to decision-making.

The NICE process includes specific cost-effectiveness thresholds, typically ranging between £20,000 and £30,000 per QALY. These thresholds help guide NICE's decision-making, to ensure that limited public funds are spent on treatments that provide the most health benefit relative to their cost. Exceptions can be made for treatment technologies that address an exceptional level of need or provide extraordinary value, such as 'highly specialised technologies' that treat very rare and severe diseases with high unmet need and technologies that treat larger numbers of patients with very severe diseases.

A budget impact test is also employed to manage the affordability of medicines that are expected to cost the NHS more than £20 million in any of the first three years of launch. In these instances, NHS England (NHSE) engages in commercial discussions with the company.

5.4 The ABPI Code of Practice and self-regulation

The pharmaceutical industry in the UK is committed to benefiting patients by operating in a professional, ethical and transparent manner to ensure the appropriate use of medicines and support the provision of high-quality healthcare. To demonstrate this commitment, more than 60 years ago in October 1958 the ABPI decided that certain activities should be covered in detail and thus agreed the first ABPI Code of Practice.

The ABPI Code:

- covers the promotion of medicines for prescribing to both healthcare professionals and other relevant decision-makers
- includes requirements for interactions with healthcare professionals
- sets standards for the provision of information about prescription-only medicines to the public and patients, including patient organisations

Administration and regulation:

The Prescription Medicines Code of Practice Authority (PMCPA) is the self-regulatory body that administers the ABPI Code of Practice for the pharmaceutical industry, independently of the ABPI. The long-established UK system of self-regulation is supported by the statutory role of the MHRA, with a memorandum of understanding setting out the arrangements for the regulation of the promotion of medicines for prescribing agreed between the PMCPA, the ABPI and the MHRA. The ABPI Code reflects and in many instances goes beyond UK law – it is intended to provide confidence to patients and the public by embedding high ethical standards and holding pharmaceutical companies accountable for compliance.

Some examples of how the ABPI Code practically guides how pharmaceutical companies communicate and interact with, and promote to healthcare professionals can be seen with the following examples:

- Hanging comparisons: must not be made whereby a medicine is described as being better or stronger or suchlike without stating that with which it is compared.
- Absolute risk and relative risk: referring only to relative risk, especially with regard to risk reduction, can make a medicine appear more effective than it actually is. In that regard, relative risk should never be referred to without also referring to the absolute risk.
- The word 'safe': cannot be used without qualification.
- Certification: all promotional materials (as well as many non-promotional materials) must be certified on behalf of the company by either a registered medical practitioner or a pharmacist registered in the UK or alternatively, in the case of a product for dental use only, a UK registered dentist.
- Prohibition on gifts and inducements to healthcare professionals or other relevant decision-makers.
- Call frequency: the number of calls made to a doctor or other prescriber by a representative each year should not normally exceed three on average.

The role of promotion in prescribing

The examples above serve to demonstrate some of the ways in which promotion, which should always be educational in nature, is carried out in a fair, balanced and appropriate manner. In the UK, companies are not permitted to advertise prescription-only medicines to the public, with the exception of vaccination campaigns approved by UK government health ministers.

Communication of information and data about a medicine by a pharmaceutical company falls broadly into one of two categories.

Promotional information

- Promotion means any activity undertaken by a pharmaceutical company or with its authority that promotes the administration, consumption, prescription, purchase, recommendation, sale, supply or use of its medicines. Many 'proactive' interactions – that is, interactions with a healthcare professional that are initiated by a company where a medicine is discussed – would usually be considered to be promotional. Typical examples of promotional information include medicine sales aids, presentations in company-sponsored symposia, journal advertising and the like. Visits to healthcare professionals by company medical sales representatives are a well-known example of a promotional interaction. Promotion of prescription-only medicines should always be educational in nature.

Non-promotional information

- Typical examples here would be replies made in response to unsolicited individual enquiries from healthcare professionals or other relevant decision makers, but only if they relate solely to the subject matter of the letter or enquiry, are accurate and do not mislead, and are not promotional in nature. Such information provided in a 'reactive' context – i.e. where the healthcare professional or other decision maker has initiated the request for information – may include off-label or off-licence information. Reference documents such as Summaries of Product Characteristics (SmPC) and patient information leaflets would not typically be considered as promotional information, unless used in a promotional context, for example, a sales representative visit.

Though this paper touches on company promotion and how this can more effectively meet the needs of healthcare professionals and, fundamentally, the patients they serve, the focus when discussing information is on non-promotional information – that is, exploring what information is available to healthcare professionals at their request to enable and empower them to make more informed prescribing decisions for their patients.

6. Transparency and disclosure

About Disclosure UK:

Disclosure UK is an online, public, searchable database that publishes certain payments and benefits in kind – known as transfers of value – made to healthcare professionals, other relevant decision makers (ORDMs) and healthcare organisations (HCOs) by ABPI member pharmaceutical companies and non-member pharmaceutical companies that have agreed to abide by the Code and accept the jurisdiction of the PMCPA in the UK.

It is designed to further increase the transparency of the important relationships between the pharmaceutical industry and the people it works with and is part of a Europe-wide pharmaceutical-industry-led initiative, laid out in the European Federation of Pharmaceutical Industries and Associations' Code of Practice and the ABPI Code of Practice for the Pharmaceutical Industry. Disclosure UK was launched in June 2016 with 2015 data and is updated annually.

Annual data publications on Disclosure UK cover the key areas of non-research and development collaboration between pharmaceutical companies and healthcare professionals, which includes:

- participation in advisory boards
- speaking at or chairing meetings
- working with and advising doctors and scientists in pharmaceutical companies
- speaking at conferences and symposia
- attending and contributing to national and international conferences
- participating in training funded by pharmaceutical companies

It also covers transfers of value provided to healthcare organisations, which includes the provision of grants and donations, and the sponsorship of events for the provision of medical education to healthcare professionals. More information can be found in How we work with HCPs and How we work with HCOs.

In addition, Disclosure UK covers the total amount that pharmaceutical companies provide to healthcare professionals and healthcare organisations annually on research and development activities.

In developing, researching, manufacturing, supplying, and promoting medicines to healthcare professionals, pharmaceutical companies have necessary and vital interactions with healthcare professionals at all stages in this process.

As pharmaceutical companies are developing and supplying medicines that will ultimately be prescribed by a healthcare professional and used by a patient, companies must engage appropriately with clinical experts.

Some of these activities include gaining advice and expertise from healthcare professionals on topics of clinical relevance or engaging healthcare professionals as expert speakers on topics of educational and clinical relevance. These activities might involve a payment to the healthcare professional for their time.

The principle of transparency of such payments made by companies to healthcare professionals is an important one in addressing the potential for bias in decision-making. Indeed, as stated in the National Overprescribing Review report, medicines optimisation depends on clinicians making unbiased decisions on the medicines they prescribe, and patients having confidence that these decisions are not distorted by commercial influences.

That is why the review recommended that the ABPI should ensure Disclosure UK becomes the global lead in transparency of pharmaceutical industry sponsorship.

Data privacy laws in the UK mean that for pharmaceutical companies to legally and publicly disclose on Disclosure UK the names and practising addresses of the healthcare professionals they have worked with, together with the values they received, companies must identify an appropriate lawful basis. The bases most relevant to Disclosure UK are 'consent' or 'legitimate interests'.

Practically, 'consent' means companies must ask each healthcare professional for permission to publish their name and principal practising address, together with the values received on Disclosure UK. Where consent is not provided, the company must publish the value in aggregate.

Under 'legitimate interests', a company asserts its transparency commitments over the data rights of the individual healthcare professional. In practice, this means a company does not ask the healthcare professional for permission to publish their name and practice address with the value received on Disclosure UK. While no longer asking for formal consent, the company has a responsibility to be clear about its intentions with the healthcare professional and offer individuals a mechanism to raise legitimate objections. Objections are duly considered via a formal framework under data protection requirements but do not necessarily mean the data is removed from publication. For more information, see 'What is Legitimate Interests?'

The ABPI champions companies' use of legitimate interests for Disclosure UK as a strong commitment to ethical and transparent collaboration. This position is supported by stakeholders across the UK life sciences sector, including the Academy of Medical Royal Colleges, The Royal College of Physicians, the British Medical Association, Department of Health and Social Care, MHRA and the Welsh Government.

In 2017, the NHSE published guidance on managing conflicts of interest[5]. In this guidance, the NHSE supports the development of Disclosure UK in bringing greater transparency to the relationships between healthcare professionals, ORDMs, HCOs and companies. The NHSE and the ABPI published a joint letter in 2017 in support of Disclosure UK[6].

Efforts are paying off. For the fourth year in a row, 2022 data shows an increase in the estimated percentage rate of healthcare professionals named on Disclosure UK who work with pharmaceutical companies on non-R&D collaborations – an estimated 78.8 per cent or nearly eight in 10, and an increase compared to 72.6 per cent in 2021, 68.1 per cent in 2020 and 55.9 per cent in 2019.

7. The role of the pharmaceutical industry in helping with appropriate prescribing

Through developing, researching, manufacturing, supplying and promoting medicines to healthcare professionals, pharmaceutical companies have necessary, vital interactions with healthcare professionals at all stages in this process.

7.1 Summary of Product Characteristics (SmPC)

The SmPC for a medicine or vaccine is effectively the reference document or 'instruction manual' for prescribers and is agreed upon by the regulatory authorities and pharmaceutical company based on evidence. SmPCs for the UK may be accessed through the electronic medicines compendium or individual company UK websites.

The SmPC sets out the specific indication or indications (i.e. diseases or conditions) to be treated, identifies the specific group of patients who may and may not be treated with the medicine, and carries important safety warnings, including interactions with foods and other medicines.

The SmPC is mentioned in this paper as a pharmaceutical resource that should be used by prescribers, because, though many prescribers will be well versed in using the BNF or the Monthly Index of Medical Specialties (MIMS) as a prescribing guide – both high-quality, important aides to prescribing – the SmPC usually represents the most comprehensive, up-to-date source of information for prescribers on a medicine or vaccine when used within its licensed indications.

7.2 Medical information services

Most pharmaceutical companies in the UK provide a Medical Information Service (MIS), which may be 'in-house' or 'outsourced' via a third-party provider. The MIS is, in many instances, the main interface between a pharmaceutical company and healthcare professionals and the public. MISs can be accessed by healthcare professionals, patients and the public via telephone or e-mail. MIS personnel aim to provide evaluated, balanced information and advice on all clinical aspects of medicines.

To do this, they use:

- the SmPC
- reference textbooks
- medical and pharmaceutical journals
- research papers (including clinical trials and systematic reviews)
- guidelines produced by expert bodies
- data on file, e.g. pharmacovigilance data

Case study

A senior advanced pharmacist in alcohol and drug recovery services contacted the MIS requesting publications or information on prescribing a medicine used in aiding alcohol abstinence to patients over 65 years old.

The response stated that, as per the SmPC, the medicine should not be used in older people, as the safety and efficacy has not been established in patients older than 65 years.

It was also pointed out that elderly patients may have some degree of renal impairment. As the medicine is excreted in the urine and there is a linear relationship between renal clearance and plasma half-life of the medicine, it is contraindicated in cases of renal insufficiency.

Information from the literature on the off-label use of the medicine in older patients was also provided. This included two open treatment studies (six male patients with alcohol dependence with an average age of 78 years, and 19 patients aged over 60 years). The studies reported on the effectiveness and safety of treatment in these patients. A case report describing a 72-year-old patient who developed extrapyramidal symptoms and acute-onset Parkinsonism following treatment with the medicine was also included.

A review article discussing strategies to prevent relapse and maintain abstinence in older adults with alcohol-use disorders was also referenced for the pharmacist's review.

Case study

An enquiry was received from an oncologist who had a metastatic urothelial carcinoma (mUC) patient who was starting treatment with a monoclonal antibody medicine (mAB). The patient also had ulcerative colitis and was receiving treatment with another monoclonal. The oncologist asked for any real-world evidence on interactions between the two.

A literature search was performed and no information was retrieved specifically on the use of the mAB in patients with mUC and ulcerative colitis treated with the other mAB.

However, a few case reports of other chronic inflammatory diseases were found for patients who were being treated with the two mABs for other cancer types. As well as these case reports, information from the European Society for Medical Oncology and American NCCN Clinical Practice Guidelines on managing toxicities from immunotherapy were included in the response. The oncologist was also reminded of the special warnings of immune-related adverse events associated with the mUC mAB, including colitis, from the SmPC.

7.3 Pharmacovigilance: The role of pharmacovigilance in answering medical queries

For certain types of complex safety-related healthcare professional queries, the MIS may choose to escalate an enquiry to the internal drug safety or pharmacovigilance department. Company pharmacovigilance departments collate adverse event reports on their medicines from around the world, both for marketed as well as investigational medicines, and report these events to regulatory agencies – in the UK, this is the MHRA. Pharmacovigilance departments receive and process a wide range of reports on the use of their products. These reports may be received via company clinical trial programs (solicited), scientific literature and regulators. However, by far the biggest source of information is spontaneous or unsolicited adverse event reporting by healthcare professionals and members of the public. These include reports relating to:

- adverse events
- serious adverse events
- off-label/off-licence use, e.g. in an unlicensed indication or an unlicensed population (e.g. paediatrics)
- use in pregnancy
- use of unapproved doses or routes of administration, including under/overdosing

This information goes into updating the safety profile or benefit-risk profile of the medicine. The company that is the licence holder for a product is essentially the custodian of the benefit-risk profile of that medicine and holds the most comprehensive information on this. Consequently, pharmacovigilance is a source of rich knowledge and data on the safety profile of their medicines, and as such can assist in answering more complex, safety-related queries, whether from internal safety data or published literature.

Case study

An enquiry was received from a hospital pharmacist about a patient who had begun to experience Parkinsonian symptoms (tremors). The patient had started several medications at the same time, one of which was a beta-blocker. The pharmacist was trying to establish whether any of the medications could be responsible for these symptoms and therefore requested any information, data or reports regarding the beta-blocker and adverse events of tremor or Parkinsonian symptoms.

Upon internal escalation of the enquiry to pharmacovigilance, the response provided stated that according to the latest Periodic Benefit Risk Evaluation Report (PBRER – a regulatory document prepared by the pharmaceutical company that updates authorities on the safety and effectiveness of a medicine), tremor has been reported to the company. However, as tremor is not listed as an undesirable effect in the product information for the beta-blocker, there is no established causal relationship based on current knowledge.

A literature search for reports of tremor with the beta-blocker was also conducted and did not retrieve any information. However, an abstract was identified that presented the results of a systematic review and meta-analysis showing that use of the beta-blocker does not significantly increase the risk of Parkinson's disease. The information was forwarded to the pharmacist to assist in their determination of the cause of the patient's symptoms.

7.4 Medical affairs and Medical Science Liaisons (MSLs)

Medical advisers in medical affairs help to ensure patient health and well-being are at the forefront of marketing decisions. This requires providing a clinical interpretation of the scientific and clinical trial data arising from the development process, which in turn ensures the promotional materials used in the marketing of a licensed medicine are medically accurate and in compliance with the product licence, ethical and legal requirements and industry codes of practice.

As part of their role, medical affairs personnel work cross-functionally with many other teams to ensure that the information about the safety and efficacy of the medicine is continually gathered and updated.

Though company structures will differ, broadly speaking there are two types of medical affairs personnel: head office-based personnel will be called medical advisers, usually headed by the company Medical Director, while field-based personnel are called MSLs or, sometimes called Field Medical Advisors. The latter role involves less interaction with internal colleagues, and more with healthcare professionals.

In response to a request for information on a company medicine, medical advisers and MSLs can meet healthcare professionals in person to answer detailed, data-driven questions and take the healthcare professional through relevant data. While the more simple, straightforward queries can be answered by the MIS, the use of medical advisers or MSLs is reserved for scenarios in which a more in-depth conversation is required by the healthcare professionals, in as much detail as is required. Medical advisers and MSLs are generally subject matter experts, and, therefore, able to engage in discussion with healthcare professionals in considerable detail and granularity. Such interactions are available only on request, for example via the MIS, or company sales representatives, and can be useful in helping a healthcare professional make an informed prescribing decision. It should be noted that the function of medical advisers, MSLs or the MIS is non-promotional. That is, their interactions with healthcare professionals are not designed to 'sell' or 'promote' a medicine, but are structured to be that of an objective, subject matter expert. They are also able to liaise internally to get more information if needed.

Again, these personnel are mentioned in this paper as a pharmaceutical resource that should be used by prescribers to help prescribing decisions and support improved patient safety.

Case study

A patient was receiving supply of a medicinal product to help with an inflammatory bowel condition. Following three months of successful treatment the patient fell pregnant and needed to make an informed decision about whether to continue with treatment. The treating physician reached out to his Medical Science Liasion (MSL) within the company to request further information on use in pregnancy in order to be able to council the patient appropriately and enable that decision.

The MSL liaised internally with the pharmacovigilance team on the request. While use in pregnancy was not contraindicated, there was limited information within the current product label and use in pregnancy was not recommended. The pharmacovigilance team reviewed the Periodic Safety Update Report – a report supplied to regulatory authorities that provides the worldwide safety experience of a product within a defined timeframe, as well as information on pregnancy-related outcomes through the pharmacovigilance database – and had a discussion with the global medical safety lead.

Following this, the pharmacovigilance team created a medical safety review report of data from pregnant patients, which was provided to the physician. This also provided the team with an opportunity to highlight to the physician the importance of completing the related pregnancy follow-up forms, as well as how this information is then used in the aggregate reporting process and how it can impact on the product label in the future. Provision of this data enabled the physician to discuss the information with their patient, and in this case the patient decided to continue with treatment, well informed of the benefits and risks of continued treatment.

7.5 Medical sales representatives

The role of a medical representative, or 'sales rep', involves promoting prescription products to GPs and hospital doctors, pharmacists and nurses. The ABPI Code of Practice requires medical representatives to pass an accredited examination covering their knowledge of the human body, pathology and pharmacology, body systems, and specialist topics including disease areas, immunology and pharmacology. The exam must be passed within two years of taking up a position as a medical rep in the UK. As well as the examination, medical representatives will be given extensive training on the medicines they are promoting as well as the relevant disease area. Though the role of a medical representative is promotional, they are nevertheless a good source of information for healthcare professionals and are expected to answer simple questions, as well as more in-depth ones, on the medicines they promote in a fair and balanced way. However, for more complex questions, medical affairs may be the more appropriate option.

As discussed in this paper, the role of promotion and education serves an important purpose, both in raising awareness of new pharmacological vaccines and therapies and educating, informing and, in some cases, enabling its use. However, it is fair to say that company promotion of medicines, like clinical guidelines, are often focused on a single condition, and do not always consider the wider, more holistic types of patient scenario confronting a healthcare professional. In this sense, there is a continued and future role for companies – through directing their sales representatives to play a more holistic role in promotional calls – in considering the wider prescribing context confronting a typical patient. This includes addressing not only the efficacy and safety of the medicine being promoted and who the medicine is appropriate for, but also giving sufficient weight in the conversation as to who the medicine might not be appropriate for, as well as how the medicine fits into a broader polypharmacy scenario in the multimorbid patient, including clusters of related conditions, which is a typical scenario a healthcare professional might be confronted with.

8. Summary

Prescribing the right medicine at the right dose for the right duration and for the right patient is a necessarily complex affair, with a complex interplay of influencing factors. This starts from the discovery and development of a medicine in clinical trials, continues to the assessment of its benefit-risk balance and approval by a regulator, as well as an assessment of whether the medicine is cost-effective, through to its ultimate destination – a patient – with the prescriber as the gatekeeper. The pharmaceutical company's responsibility starts with the development and manufacture of the medicine, and continues with the ongoing monitoring of the safety profile of the medicine, educational and information sources to help facilitate appropriate prescribing and promotional efforts in driving uptake of the medicine.

This position paper is an attempt to bring these disparate elements together in an easy-to-understand manner and shine a light on the resources available within pharmaceutical companies that can help healthcare professionals in their day-to-day practice. It is fair to say that the pharmaceutical industry does not always get this balance right – examples of poor conduct both past and present occasionally tarnish what is a highly regulated, highly scientific and highly ethical industry. However, the self-regulatory mechanisms that are in place in the UK to govern good conduct, which have developed and evolved over many years, have a reputation as some of the most robust in the world and play a pivotal role in protecting patients and helping prescribers make the right prescribing decision, for the right patient. However, there is more that can be done and the recommendations in this paper are a first step in progressing the conversation and the role of the pharmaceutical life-sciences industry in driving good or appropriate prescribing.

9. Challenging prescribing scenarios

9.1 Prescribing in pregnancy

Challenge:

When it comes to assessing the benefit-risk balance of a medicine, this is rarely more challenging than in use in pregnancy. Medicines may have harmful effects on the embryo or foetus, with the risk varying depending on the stage of gestation, and, of course, the medicine in question. It remains the case that most clinical development programmes for medicines do not include pregnant women. This challenge becomes particularly acute when a pregnant woman has a serious or life-threatening condition, such as cancer.

Current approach and existing guidance:

The tragic examples of thalidomide and diethylstilbestrol are well known. More recently, the Cumberlege report (Annex A) highlighted a healthcare system slow to respond to concerns around the prescribing of sodium valproate[7] in pregnancy[8]. Consequently, a conservative approach is taken with regards to exposure of the foetus to investigational medicines, with most of the knowledge on safety of a medicine in pregnancy gained as a result of exposure after the medicine is brought to market.

Prescribers will be familiar with the BNF and the BNFC, which have useful information on medicines that may have harmful effects in pregnancy and indicate the trimester of risk. It also identifies medicines that are not known to be harmful in pregnancy.

Further information on use of a medicine in pregnancy or during breastfeeding is available in Section 4.6 of the SmPC (fertility, pregnancy and lactation). Where pregnancy data in humans is not available, there will often be animal data provided, including in section 5.3 (preclinical safety data). However, the fact that most clinical development programs for medicines do not include pregnant women means that the information available to healthcare professionals around whether a medicine does or does not have teratogenic potential in humans is limited. Even where there is a known teratogenic potential for a medicine, this may not be routinely highlighted in prescribing systems or on the medicine packaging, for example, in the case of topical retinoids.

The Birmingham Health Partners report 'Healthy Mum, Healthy Baby, Healthy Future'[9] made a recommendation for companies to prioritise updates for existing medicines with the potential to be used in pregnancy – with regulators and industry working towards pregnancy-specific information on safety, dosing and effectiveness.

A useful resource on this topic is the Speciality Pharmacy Service, which has advice on safety of medicines in pregnancy – including signposts to guidance relating to treatment for several different conditions. Another potential source of information for healthcare professionals is the Public Assessment Report – a comprehensive document that reflects the scientific conclusions of the relevant regulatory committee at the end of the medicine assessment process, providing the grounds for the committee opinion on whether or not to approve a medicine licence application. A public assessment report is published for every medicine that has been granted or refused a licence since October 2005, and provides detailed background and context for much of the information contained within the SmPC.

Sodium valproate prescribing

Sodium valproate is an antiepileptic drug that is used to treat a range of conditions, including epilepsy and bipolar disorder. It is a highly effective drug, and cited on the WHO Model List of Essential Medicines, but it's teratogenic potential when taken by a woman in pregnancy is now well recognised.

Sodium valproate when taken during pregnancy can cause a range of birth defects, including:

- spina bifida
- cleft lip and palate
- heart defects
- learning disabilities
- autism

The risk of birth defects is highest if valproate is taken during the first trimester of pregnancy. There is no safe time to take valproate during pregnancy.

Additionally, the Medicines and Healthcare products Regulatory Agency (MHRA) has issued precautionary guidance regarding the of use of valproate in men. This follows a retrospective observational study which has indicated a possible association* between valproate use by men around the time of conception, and an increased risk of neurodevelopmental disorders in their children.

The Medicines and Healthcare products Regulatory Agency (MHRA) has put in place a number of measures to restrict the prescribing of valproate in women and girls of childbearing potential, and for male patients who may father children. These measures include:

- valproate should not be prescribed in female children or women of childbearing potential aged under 55 years unless two specialists independently consider and document that there is no other effective or tolerated treatment
- women and girls under the age of 55 who are prescribed valproate must be registered on the pregnancy prevention programme (PPP). The PPP provides support and advice to women and girls who are taking valproate and who are planning to become pregnant or who are already pregnant
- women and girls under the age of 55 who are prescribed valproate must use effective contraception. This is to prevent pregnancy and to minimise the risk of birth defects
- as a precautionary measure, GPs and specialists should inform male patients about this potential risk and recommend the need for male patients and their female partner to use effective contraception while using valproate and for at least 3 months after treatment discontinuation
- this advice is in addition to the existing requirements for oral formulations of valproate for two specialists to independently consider and document that there is no other effective or tolerated treatment or the risks are not applicable at initiation of treatment in male patients under 55 years. It is however noted that reproductive potential in male patients continues beyond 55 years and men older than 55 years on valproate should be counselled on the risk as appropriate.

Safety data, including teratogenic potential pertaining to other key anti-epileptic medicines has been reviewed by the Commission on Human Medicines (CHM), and should help inform treatment discussions with women.

*The study did not include an untreated group and background risk in this patient population is therefore unknown. An increased risk of neuro-developmental disorders in children of fathers treated with valproate in the 3 months prior to conception is possible however the causal role of valproate is not confirmed. As such this advice is precautionary.

The ABPI position:

Though data on exposure (accidental or otherwise) in pregnancy is collected continually via spontaneous reporting once a medicine is marketed, this data may only find its way into the SmPC after many years, and sometimes, depending on the validity and robustness of the data, not at all. This creates a dilemma for a treating physician when confronted with a pregnant woman who needs a medicine with limited information in the SmPC on use in pregnancy, or in the case of a patient who has already had exposure to a medicine and urgently wishes to know if there is the potential for an adverse impact on the developing foetus.

Though a pharmaceutical company can never provide clinical advice, they can assist with literature searches, and, in some circumstances, may be able to interrogate their pharmacovigilance databases for raw data that is not available in the public domain. One such example, provided by a pharmaceutical company, is below.

Case study

A question was received by a pharmaceutical company from a consultant neurologist regarding treatment with a company medicine for multiple sclerosis (MS). She wished to enquire about delaying treatment in year two due to pregnancy, and whether this would result in worse outcomes for the patient's MS.

The response reiterated that the medicine is contraindicated in pregnancy and that patients should be on effective contraception.

A literature search was conducted on the efficacy and safety of delaying treatment due to pregnancy. This retrieved one reference examining disease activity in patients who became pregnant with different intervals between the last treatment and pregnancy, but no outcome data regarding length of treatment or year of treatment were reported.

As there was no directly relevant data, information was then provided on delay of treatment for reasons other than pregnancy. This consisted of information from the SmPC and the supporting study (treatment in year two can be delayed for six months to allow for recovery of lymphocytes) and congress material presenting outcomes in patients who stopped the medicine after one year (due to a trial closure) and then restarted in a new clinical trial some time later. This identified 16 patients who had been re-dosed with intervals of more than one year and provided data relating to efficacy (Expanded Disability Status Scale) and safety (lymphocyte count) to inform the neurologist's decision for this patient.

9.2 Prescribing in paediatrics

Challenge:

The challenges with prescribing in pregnancy are, to some extent, mirrored in prescribing in a paediatric population. There are several areas of paediatric medicine where there is a lack of adequate medicines information and where off-licence use of medicines becomes routine. (A 2017 study by the Royal College of Paediatrics and Child Health[10] found that 25 per cent of all medicines prescribed to children in the UK were used off-label, followed by a 2018 study by the European Medicines Agency,[11] which found that 30 per cent of all medicines approved for use in children in Europe were used off-label.)

Unlike in pregnancy, the situation with licensed paediatric medicines has in some circumstances improved with the requirement for medicines being authorised to have a Paediatric Investigation Plan (PIP) – a development plan aimed at ensuring that the necessary data are obtained through studies in children, to support the authorisation of a medicine for children. All marketing authorisation applications for new medicines must include the results of studies as described in an agreed PIP, unless the medicine is exempt because of a deferral or waiver.

Nevertheless, there remain gaps, and this becomes particularly acute in areas of paediatric medicine, such as paediatric oncology.

Current resources:

The British National Formulary for Children is a well-known and excellent resource, which aims to provide prescribers, pharmacists, and other healthcare professionals with up-to-date information on the use of medicines in paediatrics. Information in the BNFC has been validated against emerging evidence, best-practice guidelines, and, crucially, advice from a network of clinical experts. Drawing information from company literature where appropriate, the BNFC also includes advice that goes beyond the product licence, as is sometimes necessary in this area of medicine. The primary use case for the BNFC is to support paediatric non-specialist clinical practice, and as such, less detail is given for specialist areas, such as malignant disease.

ABPI position:

As with prescribing in pregnancy, company medical information departments may prove a useful source of information in such challenging scenarios. Again, a pharmaceutical company cannot provide clinical advice, but should be able to assist with literature searches, and in some circumstances, may be able to interrogate their data on file, such as detailed clinical study reports and pharmacovigilance databases, for raw data that is not available in the public domain. One such example is provided below.

Case study

An enquiry was received from a healthcare professional who asked for any data on the use of a medicine in paediatric patients. The healthcare professional had a 17-year-old patient diagnosed with multiple sclerosis (MS), and they were considering giving this treatment to this patient.

As there was minimal information in the literature, a search of internal data was conducted. This included information from the PBRER on the use of this medicine in patients younger than 18 years that had been reported to the company. This information together with the label information was shared with the healthcare professional to support them in making a clinical decision for their patient.

The Independent Review of gender identity services for children and young people (The Cass Review)

Background:

The Independent Review of Gender Identity Services for Children and Young People, also known as The Cass Review, was commissioned by NHS England to make evidence-based recommendations on how to improve NHS gender identity services, and ensure that children and young people who are questioning their gender identity or experiencing gender dysphoria receive a high standard of care, that meets their needs and, is safe, holistic and effective. To scrutinise the existing evidence, the Review commissioned a robust and independent evidence review and research programme from the University of York to inform its recommendations. This included examining the evidence base for medical pathways i.e. the use of puberty blockers (GnRH analogues) and masculinising/feminising hormones in the management of gender dysphoria.

Approach to treatment:

The review recognises existing conflicting views about the clinical approach in gender identity services - and a divergence between some expectations, and usual clinical practice. It also highlights that the evidence base in relation to the use of puberty blockers and masculinising/feminising hormones has been shown to be weak - with the current understanding of the long-term health impacts of hormone interventions being limited. In discussion on individualised care planning, the review advises that most clinical teams would still see psychosocial interventions as the starting point in a care pathway, and that a medical pathway may not be the best way to achieve the addressing of distress.

Puberty blockers

The initial justification for using puberty blockers was to provide adolescents with "time to think" by delaying puberty, which could also enhance the likelihood of "passing" in adulthood. Later, it was suggested that puberty blockers might also improve body image and psychological well-being. However, a systematic review by the University of York found that while puberty blockers do effectively suppress puberty, they also compromise bone density during puberty suppression. The review did not find evidence of changes in gender dysphoria or body satisfaction. Additionally, the evidence on the impact of puberty blockers on psychological well-being, cognitive development, cardiometabolic risk, or fertility was either insufficient or inconsistent.

Furthermore, since the vast majority of young people who begin using puberty blockers eventually move on to masculinising or feminising hormones, there was no indication that the blockers provided meaningful "time to think." There is also concern that puberty blockers might alter the course of psychosexual and gender identity development.

In its July 2023 letter to NHS England, the Review recommended that puberty blockers be offered only within a research framework, given their clearly defined benefits in limited situations and the potential risks to neurocognitive development, psychosexual development, and long-term bone health. This has been taken forward by NHS England and National Institute for Health and Care Research (NIHR) with the NHS stopping the routine prescription of puberty blocker treatments to under-18s.

Subsequently, the Medicines (Gonadotrophin-Releasing Hormone Analogues) (Emergency Prohibition) (England, Wales and Scotland) Order 2024 has been passed which bans prescriptions of GnRH analogues written by UK private prescribers and prescribers registered in the EEA or Switzerland to those under the age of 18 years for the purposes of puberty suppression in those experiencing gender dysphoria or incongruence. This currently temporary ban, is expected to become indefinite. The new arrangements apply to GnRH analogue medicines that consist of, or contain, buserelin, gonadorelin, goserelin, leuprorelin acetate, nafarelin or triptorelin.

In addition, the government has also introduced indefinite restrictions to the prescribing of these medicines within NHS primary care in England, in line with NHS guidelines. It should be noted that the use of these medicines for the purposes of puberty suppression in those experiencing gender dysphoria or incongruence falls well outside of their product licenses, and consequently would not be allowed to be promoted by pharmaceutical companies.

Patients already established on these medicines by a UK prescriber for these purposes can continue to access them. They will also remain available for patients receiving the drugs for other uses, from a UK-registered prescriber.

Masculinising/Feminising hormones

The University of York also carried out a systematic review of outcomes of masculinising/feminising hormones. The review explains that overall, the authors concluded that there is a lack of high-quality research assessing the outcomes of hormone interventions in adolescents with gender dysphoria/incongruence, and few studies that undertake long-term follow-up. A recommendation from the review states that though the option to provide masculising/feminising hormones from age 16 is available, the Review would recommend extreme caution. There should be a clear clinical rationale for providing hormones at this stage rather than waiting until an individual reaches 18.

9.3 Prescribing in the elderly

Challenge:

In the context of an aging population in the Western world, the elderly patient with multiple morbidities will present an ever-larger proportion of the challenge when it comes to prescribing. There are several specific considerations for prescribers.

- Age-related changes in physiology and pharmacokinetics: as people age, their bodies change in ways that can affect how they absorb, distribute, metabolise and excrete medicines. This can lead to increased or decreased medicine levels, which can increase the risk of adverse effects and alter the effectiveness of treatment.
- Comorbidities and polypharmacy: elderly people often have multiple comorbidities and take multiple medications (polypharmacy). This can increase the risk of drug interactions and adverse effects, and affect compliance.
- Risk of adverse drug reactions: elderly people are at increased risk of adverse drug reactions (ADRs), due to the age-related changes mentioned above, as well as the presence of comorbidities and polypharmacy. ADRs can present in a non-specific way in the elderly, for example, confusion, constipation, postural hypotension and falls.
- The nervous system of the elderly is more sensitive to many commonly used medicines such as opioids, benzodiazepines, antipsychotics and antiparkinsonian medicines. Other organs may be sensitive to other medicines such as nonsteroidal anti-inflammatory drugs and antihypertensives.

Resources:

The STOPP/START criteria are a set of evidence-based criteria used to identify potentially inappropriate medications and potential prescribing omissions in the elderly.[12] STOPP stands for screening tool of older persons' prescriptions and START stands for screening tool to alert to right treatment. The STOPP/START criteria are regularly reviewed and updated to reflect the latest evidence. The most recent version of the criteria was published in 2019.

The STOPP/START criteria can be used by healthcare professionals to review the medication regimens of older patients and identify any potentially inappropriate medications or prescribing omissions.

ABPI position:

In addition to these general considerations, there are some specific things that doctors should keep in mind when prescribing medicines to elderly people. Some of these points are taken from NICE/BNF guidance on prescribing in the elderly:[13]

- Start with a low-licensed dose and increase gradually – this is especially important for new medications, as elderly people are more likely to experience ADRs.
- Use the fewest medications possible – this can help to reduce the risk of drug interactions and ADRs.
- Avoid medications that are known to be problematic in the elderly – this includes certain types of sedatives, pain relievers and antidepressants.
- Monitor patients closely for ADRs – this is especially important when starting a new medication or increasing the dose of an existing medication.
- Non-pharmacological measures may be more appropriate for certain symptoms such as headache and insomnia, especially when associated with social stress such as widowhood or loneliness.
- In some cases prophylactic medicines are inappropriate if they are likely to complicate existing treatment or introduce unnecessary side-effects, especially in elderly patients with poor prognosis or with poor overall health. As ever, the underlying principle is one of benefit-risk. However, elderly patients should not be denied medicines that may help them, such as anticoagulants or antiplatelet medicines for atrial fibrillation, antihypertensives, statins and medicines for osteoporosis.

9.4 Pharmacogenomics

Context:

The use of pharmacogenomics is an example of personalised prescribing, where an individual patient's genetic makeup and the effect this has on their clinical response to certain medicines is used to guide prescribing.

Many medicines are affected by pharmacogenomics. Examples include certain specific anticonvulsants, antidepressants, antipsychotics, statins, oncology medicines and warfarin.

It has recently been announced that a new research resource, known as a 'biobank', will be piloted by the MHRA to better understand how a patient's genetic makeup can impact the safety of their medicines.

Publications:

A recent report from the Royal College of Physicians (RCP) and British Pharmacological Society (BPS) on personalised prescribing highlighted the role that pharmacogenomic testing was starting to play in the NHS in guiding safe, effective treatment decisions, for example, for certain chemotherapy treatment in colorectal and breast cancers.[14]

ABPI position:

Pharmacogenomics has the potential to lead to improved outcomes in patients in terms of both safety and efficacy. It has the potential to reduce the trial-and-error approach to drug therapy by providing prescribers with actionable information about a patient's likely clinical response to a particular medication. This is a field that is still relatively new but is growing in importance and is likely to become part of treatment guidelines in the future.

The recommendations made in the RCP/BPS report, such as mainstreaming pharmacogenomic services throughout the NHS and supporting and educating clinicians and staff of different disciplines on pharmacogenomics, aligns with goals of the industry. These are: reducing health inequalities, speeding up diagnosis for patients and improving health outcomes in the population.

9.5 Online prescribing

Context:

Online prescribing generally refers to prescribing medicines to a patient based upon an interaction that has taken place online, without a face-to-face consultation, before a prescription is written.

Regulatory landscape and guidance:

There are requirements for operating legally when selling or supplying human medicines online as highlighted by the National Pharmacy Association, and regulators have issued guidelines to address the practice of issuing prescriptions online. These guidelines are outlined below.

As a healthcare regulator, the Care Quality Commission (CQC) aims to work alongside the users of online services, those who provide the services and regulatory partners to encourage improvement, stay abreast of technological developments and refine the regulatory approach. The CQC has published findings from a programme of inspections of primary healthcare services provided online in the independent sector.

There is also public information on the CQC website on choosing an online healthcare service with tips for users, including a section on receiving a prescription. The advice here for patients echoes the principles mentioned in this paper regarding clear information and consideration of interaction with other medicines.

The MHRA manages a system whereby the law requires sellers of medicines online to apply for a European-wide common clickable logo, which must be displayed on every page of the website that offers to supply medicines, including prescription-only medicines. This is explained in the MHRA's guidance on selling human medicines online (distance selling) to the public.

The General Medical Council (GMC) has published good practice in prescribing and managing medicines and devices guidance, which was updated in 2021 following a call for evidence on remote prescribing in early 2020 and responds to the huge increase in remote consultations resulting from the COVID-19 pandemic. The latest version of the guidance (effective April 2021) integrates information on remote consultations and prescribing throughout.

The General Pharmaceutical Council (GPhC) requires all pharmacies in Great Britain, including those providing internet services, to be registered with the GPhC and meet the standards for registered pharmacies. It operates a voluntary internet pharmacy logo scheme, which provides reassurance to patients and the public by indicating registered pharmacies that have met GPhC standards. There is also guidance for registered pharmacies providing pharmacy services at a distance, including on the internet to help meet the needs of patients and people who use pharmacy services, which may not take place in a pharmacy itself.

ABPI position:

Online prescribing may be helpful for patients in certain circumstances, including the recent pandemic where face-to-face consultation had associated risks. However, due to the potential risks associated with online prescribing, this must be done appropriately depending on the medicine and in compliance with the relevant regulatory standards. Although regulators have previously deemed that most medicines are prescribed and dispensed safely online, the risks are greater than standard prescribing and prescribers must therefore be mindful and take measures to ensure patient safety is not compromised.

9.6 Drug interactions

Context:

Medicines may interact with certain foods, alcohol, herbal remedies or other medicines. Such interactions become more likely in 'polypharmacy' patients, can be complex and often go unrecognised. A 2022 prospective observational study that analysed one month of medical admissions for adverse drug reactions, polypharmacy and multimorbidity showed that of 1,187 hospital admissions, 218 had an adverse drug reaction. Of these, 64 (29.4 per cent) were possibly or probably caused by a drug-drug interaction.[15]

Factors such as age, weight, renal and hepatic function, and genetic variations can affect how medicines are metabolised and eliminated, and therefore impact the likelihood of drug interactions. Information on interactions can be found in section 4.5 of the Summary of Product Characteristics.

Reports and guidance:

Polypharmacy may be appropriate for a person with complex or multiple conditions if their medicines are optimised and prescribed according to best evidence. NHS England has provided a series of resources in its 2023/4 medicines optimisation opportunity report, including case studies/examples of good practice, and resources to help support implementation such as clinical tools, e-learning courses and official guidance.

ABPI position:

Though certain drug interactions are investigated in the clinical trial program, this cannot be comprehensive, and the possibility of unknown interactions is always possible. If there is a high degree of clinical suspicion, company medical information departments may be able to help with additional information on interactions. Prescribers should remain alert to the possibility of drug interactions and, where practical, efforts to safely support deprescribing in polypharmacy patients should be made.

9.7 Prescribing generics and biosimilars

Context:

In 2023, around 81 per cent of prescriptions prescribed in primary care were for generic medicines.[16] Generic medicines go through an abridged licensing process, with the emphasis being on demonstrating bioequivalence to the originator product. European regulations state that generic products must be shown to have bioavailability within the range of 80–125 per cent of the reference product.[17]

Guidance:

The NHS Specialist Pharmacy Service provides a list of medicines it considers preferable to prescribe by brand name.

For patients with epilepsy, different oral anti-epileptic drugs (AEDs) vary considerably in their characteristics, often with a narrow therapeutic index, which influences whether switching between different manufacturers' products of specific medicines may cause adverse effects or loss of seizure control. As a result, the Commission on Human Medicines (CHM) has classified AEDs into three categories based on therapeutic index, solubility and absorption to help prescribers and patients decide whether it is necessary to maintain continuity of supply of a specific manufacturer's product.[18]

The CHM has advised that tacrolimus, an immunosuppressant medicine given orally to prevent or treat organ transplant rejection, should be prescribed and dispensed by brand name only, to reduce the risk of inadvertent switching.[19] Tacrolimus has a narrow therapeutic index and even minor differences in blood levels have the potential to cause graft rejection reactions.

Biosimilar medicines – biological medicines similar to a reference product – are not considered generic medicines, as they are large, complex, biologically derived medicines as opposed to small molecules. However, the MHRA considers biosimilars to be interchangeable with their reference product and with one another. However, they advise that all biological medicines, including biosimilars, should be prescribed by brand name.[20]

ABPI position:

As the packaging and appearance of a medicine may vary between the reference product and generic alternatives, it is good practice for healthcare professionals, whether prescribing or dispensing, to make these differences clear to a patient to promote adherence. It is worth noting that tablets or capsules often change colour and shape between different versions of the same medicine, which may be confusing to patients. In some situations, continued branded prescribing may be preferable for a particular patient, where there is a concern over confusion for the patient and a possible effect on adherence.

Prescribers are advised to consult the MHRA website for further details of this categorisation. In any case, if it is desirable for a patient with epilepsy to be maintained on a specific manufacturer's product, this should be prescribed either by specifying a brand name or by using the generic medicine name and name of the manufacturer (also known as the Marketing Authorisation Holder).

10. Specific classes of medicines

Appropriate prescribing is a particular focus for certain classes of medicines. The ABPI is monitoring and responding as necessary in the following areas in which there has been significant recent policy activity.

10.1 Opioids

Context:

Chronic pain is a complex condition to manage, and the choice of therapy needs to be decided based on the individual circumstances.

Several classes of medicines including opioids carry a risk of dependence and/or addiction as detailed in their Summary of Product Characteristics.

This class of medicines was included in a Public Health England (PHE) review[21] (see annex B).

Guidance:

A systemic review and meta-analysis showed that around 28 million people in the UK live with chronic pain at any time.[22] A NICE guideline on the assessment of all chronic pain and management of chronic primary pain was published in April 2021 (NG193).

The MHRA reviewed the evidence on the use of opioid medicines in the UK to make sure the information for patients and healthcare professionals helps minimise potential over-prescription and misuse of these medicines. The MHRA also undertook a piece of work regarding co-prescriptions of opioid medicines with benzodiazepines, highlighting the risk of respiratory depression.

The World Health Organisation (WHO) analgesic ladder is a well-established model that was originally developed to improve management of cancer pain but is also used for acute and chronic non-cancer pain.

ABPI position:

Opioid analgesics, mostly generic medicines in the UK, still have an important role to play in alleviating pain and suffering, but with a watchful eye by both the healthcare professional and patient for signs of overuse or addiction. The ABPI welcomed the advice from the MHRA on the new addiction label warnings for opioid-containing medicines and worked with the MHRA and other UK trade associations to develop a new opioid patient safety leaflet, which was finalised in late 2020.

The decision to use opioid analgesics should be taken by a healthcare professional in consultation with the patient, considering the patient's individual circumstances. Patients taking long-term opioid analgesics should be carefully monitored to ensure the ongoing benefits outweigh any risks. The right choice of treatment should be a joint decision between the doctor and the patient.

Chronic pain is difficult to treat – all therapies, including opioid analgesics, should be considered as part of a multi-disciplinary approach tailored to each individual patient.

10.2 Selective serotonin uptake inhibitors (SSRIs)

Context:

SSRIs are one of the most studied classes of medicines and continue to be recommended by NICE where medicinal treatment is required. SSRIs are mainly prescribed to treat major depressive disorder and are often used in combination with a talking therapy, such as cognitive behavioural therapy. Some SSRIs are also used as part of the management of other conditions, including generalised anxiety disorder, obsessive-compulsive disorder and others. Anti-depressants, including SSRIs, are not generally considered as first-line treatment unless that is the person's preference.[23] This class of medicines was also included in the 2019 PHE review (see annex B).

Guidance:

The MHRA has produced guidance on specific issues:

- cases of suicidal thoughts have been reported with SSRI use. This issue has been monitored by the MHRA and the Commission on Human Medicines (CHM) since these products were first licensed and is clearly labelled in the SmPC
- all SSRIs may be associated with withdrawal reactions,[24] such as anxiety, agitation and insomnia on stopping or reducing treatment

NICE issued guidance on discontinuing this medicine in June 2022. This guidance places importance on the pharmacokinetic profile and the duration of treatment when tapering a treatment – citing the prolonged duration of action of fluoxetine as an example.

To help clinicians and patients to withdraw antidepressants, the Royal College of Psychiatrists has produced information on stopping antidepressants. The college also has this position statement on antidepressants and depression.

ABPI position:

SSRIs are effective medicines, and the balance of risks and benefits in adults of all medicines in these medicine classes remains positive in their licensed indications.

Patients and their healthcare professionals must determine whether a treatment is the right one for the individual according to their specific needs. These discussions need to happen before prescribing an SSRI and will continue during treatment to ensure that the medicine remains right for the patient. As with all prescription medicines, SSRIs have known side effects and patients must be monitored to see whether to continue the medicine, adjust the dose or stop the medicine. Any reduction or discontinuation of SSRIs must be in consultation with a healthcare professional to reduce the risk of withdrawal.

10.3 Cannabis-based medicinal products

Context:

In August 2018, a review by the England Chief Medical Officer (CMO) recommended moving cannabis-based medicinal products out of Schedule 1 of the Misuse of Drugs Regulations 2001 into Schedule 2, thereby allowing them to be prescribed for medicinal purposes under controlled conditions by registered medical practitioners on the GMC specialist register.

Guidance:

There has been government guidance regarding cannabis-based products for medical use, which includes details of the current status of the small number of licensed cannabis-based or cannabinoid products. There is also MHRA guidance: the supply, manufacture, importation and distribution of unlicensed cannabis-based products for medicinal use in humans 'specials'.

There are several external publications on the use of cannabis. The RCP issued guidance in October 2018 looking at the evidence for chemotherapy-induced nausea and vomiting, as well as chronic pain, neuropathic pain and epilepsy. NICE published guidance on cannabis medicinal poducts in November 2019. The British Paediatric Neurology Society also provided guidance on the use of cannabis products in 2018.

A Health Select Committee Inquiry concluded that the reality of the change in law was that medicinal cannabis products were rescheduled, which allowed them to be prescribed. However, most medicinal cannabis products are unlicensed and therefore remain governed by a restrictive prescribing process.

ABPI position:

The ABPI position is that all cannabis products need to have proven quality, safety and efficacy that has been reviewed by regulators and licensed via the relevant regulatory process.

Where no licensed medicine is available for the indication being treated, unlicensed or off-label use of cannabis-based medicines may be an appropriate treatment choice for healthcare professionals in meeting the therapeutic needs of an individual patient only. This should be done according to the relevant professional and regulatory standards. Please see separate ABPI position paper on use of off-label and unlicensed medicines.

10.4 Antibiotics and antimicrobial resistance

Context:

Poor stewardship in the use of antibiotics has contributed to an acceleration in the natural ability of bacteria to develop resistance, to the point where the number of antimicrobial-resistant bacteria is rising faster than the development of new antibiotics to treat them. Sometimes described as a 'silent pandemic', the WHO has declared antimicrobial resistance (AMR) one of the top 10 global public health threats facing humanity. Currently, an estimated 1.2 million people globally die from infections that are resistant to antibiotics each year and the WHO predicts that by 2050, antimicrobial-resistant bacterial infections will result in 10 million deaths per year worldwide.[25] England alone saw more than 90,000 hospital admissions because of antibiotic-resistant infections in 2019/20.

In 2020, the AMR Action Fund was launched – a $1 billion pharmaceutical industry-led global investment fund, which aims to bridge the funding gaps facing antibiotic developers.

In the UK, the government has a 20-year vision for addressing antimicrobial resistance, which is being delivered via a series of five-year action plans. During its G7 presidency, the UK made antibiotic resistance a centrepiece of its agenda. In addition, the UK implemented a world-leading pilot project to test a reimbursement model that provided a fixed fee that delinked payment from the volume payment product used. This pilot is now being turned into a permanent model where transformative antibiotics will be reimbursed via an annual subscription fee paid over the patent lifetime – the fee is based on a value assessment as opposed to the volumes used. The aim is for other countries to implement similar models, which together will achieve a level of incentive that will increase investment in antibiotic R&D throughout the pipeline, resulting in an eventual increase in the number of antibiotics available that will treat resistant bacteria.

Guidance:

NICE guidance for HCPs on prescribing antimicrobials makes several recommendations, including following local or national guidelines on prescribing the shortest effective course and the most appropriate dose and route of administration. NICE also recommends reviewing intravenous antimicrobials within 48 hours (taking into account response to treatment and microbiological results) and considering stepping down to oral antimicrobials where possible.

ABPI position:

Antibiotics are the cornerstone of modern healthcare. They are essential for cancer care, routine and complex surgery, and for treating life-threatening infections such as meningitis and sepsis. Without antibiotics, treatment for many conditions would simply not be possible. One of the biggest problem areas is that due to the coupling of high cost of research and development and low returns, there are very few new antibiotics in clinical development – only around 40 globally. The high R&D costs are due to the scientifically difficult nature of developing antibiotics that avoid the resistance mechanism developed by bacteria that leads to high rates of failure. The lack of return is a result of a desire to preserve the effectiveness of new products, meaning that they are often used very little.

It will be several years before the antibiotic pipeline recovers, so it will be key to ensure responsible stewardship of existing antibiotics to minimise the emergence of further AMR strains of bacteria and to responsibly steward any new antibiotics to reduce the emergence of new resistance mechanisms. A key area of this is responsible prescribing to ensure antibiotics are only used to treat bacterial infections and that patients are informed of the importance of completing the course and disposing of any spare medication in a responsible fashion.

Annex A

‘First Do No Harm’ The Independent Medicines and Medical Devices Review, 2020

The ‘First Do No Harm’ report, chaired by Baroness Julia Cumberlege, was published in July 2020 as part of the Independent Medicines and Medical Devices Safety Review. The report was commissioned in February 2018 by then Secretary of State for Health Jeremy Hunt and was tasked with examining three specific medical interventions: Primodos (a hormone pregnancy test), sodium valproate (an antiepileptic medicine), and vaginal mesh. The report primarily focused on how the health system responds when patients and their families raise concerns about the safety of treatments.

The report made nine strategic recommendations and suggested 50 actions for improvement:

1. Apology: the report suggested that the government should apologise on behalf of the healthcare system for the time taken to respond to concerns raised by affected patients. The government accepted and actioned this recommendation within one day of the report’s publication.
2. Patient Safety Commissioner: the report recommended the appointment of a Patient Safety Commissioner. The government accepted this recommendation and a Patient Safety Commissioner for England, Dr Henrietta Hughes is now in the role.
3. Independent redress agency: the report proposed the establishment of an independent redress agency. However, the government did not accept this recommendation.
4. Care and support scheme: the report suggested a scheme to meet the costs of additional care and support for those who experienced avoidable harm from pelvic mesh. This recommendation was not accepted by the government.
5. Specialist centres: the report recommended the establishment of a network of specialist centres to provide comprehensive treatment, care and advice for those affected by implanted mesh. This recommendation was accepted and actioned, resulting in the creation of eight specialist centres in England.

6. MHRA improvements: the report recommended improvements to the MHRA, especially in terms of adverse event reporting and medical device regulation. This recommendation was accepted and work is underway to improve MHRA's patient response process.
7. Central patient identifiable database: the report suggested the creation of a central database with details of implanted devices. The government accepted this recommendation and has begun work to establish a UK-wide medical device information system.
8. GMC register expansion: the report proposed the expansion of the GMC register to capture financial and non-pecuniary interests for all doctors. The government partially accepted this recommendation, opting to require all registered healthcare professionals to declare their relevant interests at the employer level.
9. Taskforce: the report recommended setting up a task force to implement the recommendations. The government partially accepted this recommendation, establishing a patient reference group to work with the government to develop a response, but deciding against the creation of a separate independent task force.

The 50 actions for improvement included measures such as improving informed consent, with doctors being encouraged to be open about uncertainties and share all relevant information about potential benefits and harms with patients. They also involved giving patients time and opportunity to digest information and ask questions, with potential support from patient decision aids and other tools for shared decision-making.

Annex B

Public Health England review of prescribed medicines, 2019

The Parliamentary Under Secretary of State for Public Health and Primary Care commissioned Public Health England (PHE) to review the evidence for dependence on, and withdrawal from, prescribed medicines. Withdrawal is more accurately defined as discontinuation syndrome in relation to anti-depressants. The review launched on 24 January 2018 and was published on 10 September 2019. The ABPI engaged with PHE throughout the process and welcomed the report when it was published. The ABPI subsequently met PHE who stated it recognised industry efforts and encouraged continuing work in this area under the ABPI Code of Practice.

This was the first evidence review of dependence and withdrawal problems associated with five commonly prescribed classes of medicines in England. The review assessed the scale and distribution of prescribed medicines and made recommendations for better monitoring, treatment and support for patients. It used available prescription data (April 2015 to March 2018), a literature review and reports of patients' experiences. A total of five classes of medicines were included in the review: benzodiazepines (mainly prescribed for anxiety and insomnia); Z-drugs (insomnia); gabapentinoids (neuropathic pain); opioid pain medications (for chronic non-cancer pain such as low back pain and injury-related and degenerative joint disease); and antidepressants (depression).

The main findings included:

- one in four adults had been prescribed at least one of these classes of medicines in the year ending March 2018
- in March 2018 half of those receiving a prescription (of these classes of medicine) had been continuously prescribed for at least the previous 12 months. Between 22 per cent and 32 per cent (depending on the medicine class) had received a prescription for at least the previous three years
- long-term prescribing of opioid pain medicines and benzodiazepines is falling but still occurs frequently, a finding not in line with the guidelines or evidence on effectiveness

Links to deprivation included:

- prescribing rates and duration of prescription are higher in some of the most deprived areas of England
- a similar pattern is also seen for the number of medicines co-prescribed (for example, at least two of the drugs)
- for opioids and gabapentinoids, the prescribing rate in the most deprived quintile was 1.6 times the rate in the least deprived quintile
- the co-prescribing rate in the most deprived quintile was 1.4 times higher than in the least deprived quintile (30 per cent compared to 21 per cent)

The review made several recommendations focusing on education and treatment, including:

- giving NHS commissioners and doctors better access to data, improving insight of prescribing behaviour in their local area and enabling GPs to follow best practice
- updating clinical guidance for medicines that can cause dependence and withdrawal, and improving training for clinicians to ensure their prescribing adheres to best practice
- developing new clinical guidance on the safe management of dependence and withdrawal problems
- providing better information to patients on the benefits and risks with these medicines
- doctors should have clear discussions with patients and where appropriate offer alternatives, such as social prescribing
- commissioners ensure appropriate support is available locally for patients experiencing problems
- a national helpline for patients to be set up
- ensuring high-quality research around dependence and withdrawal is undertaken

Annex C

'Good for you, good for us, good for everybody' National Overprescribing Review, 2021

The 'Good for you, good for us, good for everybody' National Overprescribing Review, 2021, commissioned by the UK government, was led by Dr Keith Ridge, Chief Pharmaceutical Officer for England. The review was aimed at studying the use of medication and overprescribing, with a goal of reducing inappropriate prescribing.

The review was guided by a short-life working group, which included senior stakeholders from across the healthcare system, patients and third-sector representation. The group examined the role of digital technologies, research, culture change, social prescribing, repeat prescribing and transfer of care.

The review outlined a series of practical and cultural changes to ensure patients receive the most appropriate treatment for their needs while also ensuring clinicians' time is well spent and taxpayer money is spent wisely. This includes better use of technology, how to review prescriptions more effectively, and how to offer alternatives to medicines where they would be more effective.

Though evidence was limited, the review estimated that potentially at least 10 per cent of the total number of prescription items in primary care need not have been issued. The review found overprescribing is a serious problem in health systems internationally – one that has grown dramatically over the past 25 years – and has two main causes:

- systemic: key factors are single-condition clinical guidelines, a lack of alternatives to prescribing a medicine, a need for ongoing review and deprescribing to be built into the process of prescribing, inability to access comprehensive patient records, the lack of digital interoperability and pressure of time
- cultural: a healthcare culture that favours medicines over alternatives and in which some patients struggle to be heard

The report identified several situations where overprescribing can occur:

1. a better alternative is available but not provided
2. the medicine is appropriate for a condition but not the individual patient
3. a condition changes and the medicine is no longer appropriate
4. the patient no longer needs the medicine but continues to be prescribed it

Dr Keith Ridge emphasised that the report was not about taking treatment or services away from people where they are effective, but also pointed out that medicines can cause harm and can be wasted.

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