

# Pharmaceutical Medicine

## 1. Description of the specialty

### Overview

Pharmaceutical medicine is a medical specialty concerned with the discovery and development, evaluation, licensing and monitoring of medicinal products, for the benefit of patients and public health. Pharmaceutical physicians work in the pharmaceutical industry, drug regulatory authorities, contract research organisations and academia. They have a close affinity with their medical colleagues in primary and secondary healthcare.

The basis of pharmaceutical medicine is founded on the knowledge and understanding of how drugs work, the limitations and variability of response to treatments, and how therapies can be used optimally in clinical practice. In addition to expertise in basic research, drug development and evaluation, clinical trials and registration, pharmaceutical physicians also need a good understanding of pharmacoeconomics, medical aspects of the marketing of medicines, business administration and the social impact of healthcare on patients and public health.

### The roles of pharmaceutical physicians

Some pharmaceutical physicians are involved in defining the biological mechanisms of disease, enabling medicines to be identified that specifically target the illness. However, the majority of doctors in the specialty are responsible for the design, management and implementation of clinical trials and work with a team of clinical investigators and supporting clinical staff. They are either directly employed by industry, or work as independent consultants. Their work contributes to all stages of clinical trials as described below:

- A small number of pharmaceutical physicians are involved in phase 1 trials, which are conducted in dedicated clinical pharmacology units and involve the first dosing of a drug to (usually healthy) humans for safety and tolerability testing, measurement of

pharmacological effects and pharmacokinetic profiling. Depending upon the treatment indication and the type of drug being evaluated, phase I studies may also be performed in patients, e.g. in oncology studies.

- A larger number of physicians are involved in phase 2 and 3 trials. Phase 2 trials are generally the first conducted in patients and are small scale trials that give an indication that the drug works effectively and safely. Pharmaceutical physicians choose suitable disease targets, design trials using appropriate measures of clinical efficacy, pharmacodynamic end-points and safety.
- Phase 3 trials are of larger scale, involving hundreds or thousands of patients and are required to prove the clinical efficacy and safety of a drug. Due to the patient numbers required and the international nature of many pharmaceutical companies, phase 3 trials are often carried out globally, requiring pharmaceutical physicians to adapt their practice significantly depending on location and circumstance.
- Pharmaceutical physicians also consult on the implementation of phase 4 clinical studies. Once a marketing authorisation for a new medicine is granted and the drug opened to a wider patient group, post marketing and continued safe prescribing needs to be closely monitored. Clinical doctors and pharmacists work closely with the pharmaceutical physicians responsible for drug safety to ensure full, timely and complete analysis of unexpected adverse drug reactions alongside the regulatory agencies, to comply with their necessary reporting regulations.

All trials are strictly governed by regulations designed to protect the safety of patients. Many pharmaceutical physicians work within the regulatory agencies, such as the Medicines and Healthcare products Regulatory Agency (MHRA) and the European Medicines Agency (EMA), to ensure that trials are being carried out to utmost ethical and safety standards and in the best interests of the patient<sup>1,2</sup>.

Some physicians are involved in medical affairs, which includes the marketing of medicinal products. These doctors conduct market support studies, provide medical input to marketing strategy, support sales staff in the field, review drug advertising

and the safety (pharmacovigilance) of marketed drugs and ensure that the information materials for both prescribers and patients are as accurate and as easy to understand as possible.

### Pharmaceutical physicians and patients

As mentioned previously, those participating in clinical trials are usually either patients suffering with the particular condition under investigation, or can be healthy members of the public who volunteer (and can receive remuneration) to take part in trials. However, apart from phase 1 clinical trials, direct patient contact is rare for pharmaceutical physicians. Phase 1 trials are carried out in independent 'clinical research units' and here the pharmaceutical physicians have medical responsibility for the safety of the participants and must have up-to-date knowledge of resuscitation techniques and treatment of medical emergencies. These physicians regularly conduct physical examinations for fitness, take blood, give injections etc. Phase 2 and 3 trials are usually carried out with patients 'in-the-field' and pharmaceutical physicians are more involved in monitoring the overall safety of patients, rather than day-to-day contact. All clinical trials require the informed consent of the participants who take part and pharmaceutical physicians will be involved in developing the requisite consent forms. Pharmaceutical physicians who work for regulatory agencies have almost no direct patient contact.

Despite the fact that pharmaceutical doctors have very little direct patient contact compared with typical hospital doctors or GPs, the medicines and vaccines that they develop can ultimately affect the lives of millions of people across the world. Thus, working for the benefit of the public is still very much at the heart of a pharmaceutical physician's endeavours. Despite this, relations between the pharmaceutical industry, the NHS and patients are often strained. The report in 2009 by the RCP 'Innovating For Health: Patients, Physicians, the Pharmaceutical Industry and the NHS'<sup>3</sup> suggested that many patients remain concerned that they do not enjoy equal access to medicines, nor do they believe that the full range of innovative medicines that are available is brought to their attention, thus undermining their confidence in the entire prescribing process. The report also indicated that patients in the UK are usually very willing to participate in clinical trials but that patients report a lack of opportunity.

The working party that produced this report is now coordinating the activities which will address these issues.

### Areas of work

Pharmaceutical physicians are involved in studies concerned with the research and development of new medicines in almost all disease areas and will have specialist knowledge in their chosen field of research. There are globally ~5000 medicines and ~350 vaccines currently in development (although only a small percentage of these will successfully make it to market), with the majority of research efforts being directed into new treatments for cancers, heart disease and stroke, diseases of the central nervous system and tackling the burden of infection in developing countries (Source: CMR International).

### 2. Organisation of the service and patterns of referral

As the majority of pharmaceutical physicians work outside the NHS and in such a wide variety of roles it is impossible to crystallise how the service they provide is organised. Pharmaceutical physicians are to be found at all levels of service in commercial, academic and government institutions.

Pharmaceutical physicians do not operate in the standard referral channels of GPs and hospital doctors. Although they are involved in designing the protocol for patient selection etc., they are not involved in individual patient referral to a site conducting a clinical trial.

### 3. Working with patients: patient-centred care

As mentioned previously, very few pharmaceutical physicians have direct contact with patients, though their work is always for the benefits of patients and the public.

Although the pharmaceutical physician does not deliver the information regarding trials directly to the patient, they are involved in coordinating all the relevant information concerning the patient's participation; including why the trial is being carried out, why this patient is involved and what the potential or expected benefits and risks are. One of the main sources of information for clinical trials patients is the NHS website 'Involve'<sup>4</sup> which is managed by the National Institute for Health Research (NIHR). Many of the disease-specific charities also provide advice and information for patients who are already undergoing or thinking about becoming involved in clinical trials.

The issue of post-trial patient information is considered to be an integral part of patient rights and has been mentioned as part of the World Medical Association's Declaration of Helsinki on the Ethical Principles for Medical Research Involving Human Subjects<sup>5</sup>, where paragraph 33 states...

*'At the conclusion of the study, patients entered into the study are entitled to be informed about the outcome of the study and to share any benefits that result from it...'*

Despite this, patients are still not routinely kept up to date with the outcomes of trials they have been involved in. The main reason for this is that often many months or years have elapsed before the analysis of a trial is complete and the communication channels between the investigators and patients and their consultants have often broken down. Clinical trial participants are coded and thus the responsible pharmaceutical physician doesn't have access to individual patients. At the end of the trial, the outcomes are reported to the investigators involved and it is their responsibility to pass this information on to the participants from their centre.

#### 4. Inter-specialty and interdisciplinary liaison

Although their contact is often limited, pharmaceutical physicians work with clinicians across almost the entire spectrum of medicine. They are available to talk to

clinicians working in a particular field and to discuss the use of medicines in a particular condition. Clinical doctors always have a route of contact with a company's medical information department when issues around medicinal products arise, and these circumstances are likely to involve a pharmaceutical physician. Increasingly, pharmaceutical physicians are also acting as direct sources of expert information on the medicines that their companies provide to doctors working in the NHS. This interaction is usually initiated by the consulting clinician and can act to greatly enhance patient care but is currently an underused relationship.

## 5. Delivering a high-quality service

### What is a high-quality service?

Due to the diverse nature of their roles, it is difficult here to define precisely what constitutes a high-quality service as delivered by pharmaceutical physicians. Beyond phase 1, the running of a safe and efficient clinical trial requires close collaboration between the trial sponsor, the hospital or clinic where the patients are located and the consultant or GP responsible for them, the chief investigator and other healthcare professionals supporting the research and the ethics committee responsible.

To ensure a safe, rigorous and well-executed trial the sponsor or chief investigator must go through several authorisation procedures before, during or after a clinical trial:

1. The sponsor or investigators must first apply to the MHRA for Clinical Trial Authorisation (CTA). They then usually register the trial for an International Standard Randomised Controlled Trials Number (ISRCTN) and although this is not compulsory it ensures that the trial complies with the requirements of the International Committee of Medical Journal Editors (ICMJE) – a pre-requisite for publishing trial data in most journals.
2. Ethical approval for the trial must be sought by the Principal Investigator through a Research Ethics Committee (REC), part of the National Research Ethics Service (NRES).

3. Once a trial is underway, safety and progress reporting must be carried out to the appropriate REC both on a periodic basis (both six-monthly and annually) and also whenever there is an unexpected or dangerous event, known as a Suspected Unexpected Serious Adverse Reaction (SUSAR).
4. When a trial is finished it must be reported to the MHRA and the relevant REC (within 90 days of its conclusion or within 15 days of early termination) and a summary of the final report on the research should be sent to the main REC within 12 months of the end of the project.

Those pharmaceutical physicians who work for the regulatory agencies have a very different remit and therefore different definitions of a quality service. Their prime responsibility is to protect public health.

#### Maintaining and improving the quality of care

Pharmaceutical physicians are predominantly employed by private companies which will have their own strict codes of conduct, ethical principles and protocols for ensuring the ongoing high quality of work carried out under their sponsorship. These practices are further supported by professional codes of practice<sup>6</sup> and statutes that enshrine Good Clinical Practice (GCP) and the safety and well-being of the patient and/or research subject.

The majority of pharmaceutical physicians in the UK are members of the Faculty of Pharmaceutical Medicine (FPM), a Faculty of the Royal Colleges of Physicians of the UK. The FPM conducts Postgraduate Medical Specialty Training (PMST) which enables qualified doctors to obtain specialist registration in Pharmaceutical Medicine with the General Medical Council (GMC). The overall aim of PMST is to produce accredited pharmaceutical physicians, who are equipped with specialist knowledge and comprehensive skills and competencies to practise to the highest ethical and professional standards, for the benefit and safety of patients and the public, in the development and maintenance of medicines. The earliest entry point into PMST is at ST3 level.

The FPM also coordinates the continuing professional development (CPD) of its members, though it does not currently provide modules for CPD accreditation. The FPM is currently developing the framework for the revalidation of pharmaceutical physicians and recommends that all practising pharmaceutical physicians registered with the GMC should have a Licence to Practise and therefore make themselves available for revalidation. Because of the diverse nature of pharmaceutical physicians' roles, coupled with the fact that they work outside the NHS and that the majority of their work does not involve direct patient contact, their revalidation process is going to be very different to the majority of doctors. It is vitally important that the revalidation of pharmaceutical physicians is carried out in a manner which is as objective, transparent and robust as possible. The FPM will continue to develop guidance on revalidation and to work closely with the GMC.

#### 6. Clinical work of consultants

Apart from the few pharmaceutical physicians who continue to work part time in a wide variety of other specialties and general practice, the profession is not engaged in clinical work.

#### 7. Opportunities for integrated care

This does not directly apply to pharmaceutical physicians, but contact between nurse and pharmacist prescribers and pharmaceutical physicians will occur where the healthcare professional is seeking information or advice from the sponsor of the product.

#### 8. Workforce requirements for the specialty

The FPM has just under 1000 UK-based members, but has estimated that there are over 1500 pharmaceutical physicians currently practising in the UK. It is difficult to give a more precise figure for this, again due to the diverse and extra-NHS nature of the profession. There are currently 215 postgraduate trainees in pharmaceutical

Medicine with a National Training Number, undertaking training in 104 organisations, and 118 pharmaceutical physicians now have a Certificate of Completion of Training.

#### 9. Consultant work programme/specimen job plan

Pharmaceutical physicians can be self-employed, work for a multi-national pharmaceuticals company or a regulatory agency or in academia. Their work involves developing medicines and vaccines in almost all disease areas, both at home and abroad. Because of this huge diversity it is almost meaningless to produce a 'typical' work programme or job plan for a pharmaceutical physician.

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<sup>1</sup> European Union. *EU Clinical Trials Directive 2001/20/EC*, 2001

<sup>2</sup> UK Government. *Medicines for Human Use (Clinical Trials) Regulations (SI 2004/1031)*, 2004.

<sup>3</sup> Royal College of Physicians. *Innovating for Health: Patients, Physicians, the Pharmaceutical Industry and the NHS*. Report of a working party. London: RCP, 2009.

<sup>4</sup> <http://www.invo.org.uk/>

<sup>5</sup> WMA Declaration of Helsinki - *Ethical Principles for Medical Research Involving Human Subjects*. Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964. Most recently amended by the 59th WMA General Assembly, Seoul, October 2008

<sup>6</sup> Association of the British Pharmaceutical Industry. *ABPI Code of Practice for the Pharmaceutical Industry* 2008 (and references therein).