My medicine: From laboratory to pharmacy shelf

This section aims to help you find out more about the life cycle of medicines from their first scientific discovery through to licensing and ongoing monitoring.

The pages set out to explain:
- How and why medicines are developed
- How the process is regulated and monitored
- How potential problems can be reported and what you can do to help
- Why not all medicines are widely available in the NHS.

Each one covers a different stage in the life cycle of a medicine, with links to other relevant articles in the series and useful websites where you can obtain further information.

You may also find this glossary of terms helpful:

Glossary of MHRA terms

An overview of each of the pages is available below. Each page is also available in pdf format, should you prefer this format - these documents are available in the 'Featured publications' section at the right of this page and on each of the individual pages. The entire section is also available in pdf format.

From laboratory to pharmacy shelf

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It takes an average of 10 years for a chemical compound to make the journey from the laboratory to reach the pharmacy shelf as a medicine.

The development of any new medicine requires a great deal of skill and expertise and costs millions. Thousands of promising compounds never make it out of the laboratory. On average, only one in 5000 will end up as a prescription medicine.

A new compound or new area for drug treatment needs to differ in some way from what has gone before, so that the unique recipe can be protected (patented) while development is taken forward.

Patents last for 20 years to enable drug companies to recoup the huge costs involved in developing their medicine. After this other companies can legitimately develop cheaper versions of the same medicine. These are called generics.

The first medicine of its type may be a trail-blazer. However, it is likely to be overtaken by other similar, but more effective versions.

**Who regulates medicines?**
Whether it’s cough mixture or cancer drugs, all medicinal products have to be licensed—given a marketing authorisation—before they can be put on the market.

A licence means that a medicine has been thoroughly tested and quality controlled, to make sure that it is acceptably safe and works as intended.

In the UK, licensing falls to the medicines regulator, the Medicines and Healthcare products Regulatory Agency (MHRA).

The MHRA works closely with the European regulator, the European Medicines Agency (EMEA) (external link), which sits at the centre of a collaborative network of national regulatory bodies within the European Union (EU),
plus Liechtenstein, Norway and Iceland.

The EMEA is responsible for licensing “high-tech” medicines, such as gene therapy, and those that meet EU public health priorities, such as those for diabetes. This guarantees that these treatments are available across Europe rather than just in individual countries.

The regulation of medicines in the UK is covered by an Act of Parliament and European Directives.

The pharmaceutical industry also regulates itself through a code of practice, which sets out how companies can behave when they sponsor research and training, and how they can promote their products to healthcare professionals and the media.

**What does “acceptably safe” mean?**
Every medicine has some side effects (risks), ranging from minor to severe. In a life threatening condition, such as cancer, severe side effects may be an acceptable trade-off for the benefits the treatment brings. But severe side effects will not be acceptable in a medicine used to treat a minor ailment, such as hay fever.

Ultimately, with the help of healthcare professionals, patients have to decide whether they are prepared to put up with certain side effects in return for relief from painful symptoms, the slowing of a disease, or a cure.

**The life cycle of a medicine**
A medicine starts life as a chemical substance or compound. Many promising compounds turn out to be unsuitable—sometimes many years into development. This is because they have too many unwanted side effects or because they simply don’t work as well as at first thought.

Broadly, the life cycle of a medicine consists of:
- The **discovery stage**, when a compound is screened for its potential to be developed further and its make-up assessed in detail.
- Promising compounds are then tested in the laboratory and in living tissue in **pre-clinical research**. Thousands of compounds never go beyond this stage.
- Those that do are then tested on gradually increasing numbers of people in phased **clinical trials**, a stage of development that usually takes around six years.
- The manufacturers then apply to the regulator for a **marketing authorisation** (licence) so that the medicine can be put on the market.
- Once licensed, the effectiveness and safety of the medicine continue to be carefully tracked by the manufacturers, regulators, healthcare professionals, and the public. This **monitoring** may include further research, which can be carried out many years after a licence has been granted.
- Sometimes there will be **changes in the use of a medicine**, when it is shown to work well in different groups of patients or for different conditions.

**Who decides which medicines can be prescribed?**
Not every new medicine will be widely available to all patients across the UK. This is because different national bodies are responsible for recommending which treatments should be used in the National Health Service (NHS).

In England this is the job of the [National Institute for Health and Clinical Excellence (NICE)](https://www.nice.org.uk) (external link).

In Scotland, the [Scottish Medicines Consortium](https://www.smcond.org.uk) (external link) and the [Scottish Intercollegiate Guidelines Network (SIGN)](https://www.sign.ac.uk) (external link) take on this role.

Wales tends to follow NICE guidance, and the [Department of Health, Social Services, and Public Safety (DHSSPNI)](https://www.gov.wales) (external link) adapts it for patients in Northern Ireland.

Not all medicines will be assessed by these bodies. And the availability of certain medicines on the NHS will be influenced by other factors, such as local treatment priorities and budgets.
Drug companies are continually searching for new compounds to develop into acceptably safe and effective medicines that can:

- Relieve troublesome symptoms
- Prevent disease from taking hold
- Slow down the course of a disease
- Potentially cure disabling and/or lethal conditions

Finding suitable compounds, which stand the best chance of becoming effective medicines, is a process of elimination. This discovery phase takes several years and requires a wide range of skills and expertise.

**Ideas for drug development**

Many different factors influence the development of new medicines. These include:

- Advances in the understanding of human biology and healthcare, such as stem cell research and gene therapy, which help scientists piece together how a disease is caused and what processes in the body are involved
- Government treatment priorities—diabetes and heart disease, for example
- An ageing population, among whom diseases, such as Alzheimer’s disease and cancer, are more common
- Global initiatives, such as those to halt new cases of malaria and HIV infection, for example
- The availability of research funding and sponsorship
- The costs and effectiveness of existing medicines
- Chance findings, which shift the focus of research. For example, Viagra was originally developed to relieve the chest pain of heart disease. But during tests, men said it helped them with erectile problems, and it was subsequently developed for this purpose instead.

**The search for a new compound**

Scientists start by either targeting a known step in the disease process or working out how a disease is caused. They then pinpoint a stage that can potentially be altered or interrupted.

This might be interfering with the production of a particular chemical, or the way in which certain cells interact, or a process that switches a gene on or off, for example.
Once the “target” has been identified, the hunt begins to find suitable compounds. These can be sourced from:

- An existing reserve of chemical compounds built up over many years
- Design changes to the make-up of an existing medicine
- Combining compounds to make a new one

Special tests to screen for the unique properties of the compounds also need to be developed.

**Weeding out unsuitable compounds**

Millions of compounds will be tested to see if they have any impact on the intended target(s). Many won’t. But of every 1000 that do, called hits, just 30 will be suitable for testing further at varying strengths, on different cells and under different conditions to see if they still have an effect. Those that do are called lead compounds.

Scientists will want to know if a new entity is likely to:

- Be stable under different conditions
- Behave consistently
- Be harmful
- Pass into cells efficiently
- Reach its chosen target effectively
- Be selective rather than indiscriminately knocking out several other related targets

Commercial factors also come into play. The drug company will want to know if the compound is unique so that its originality can be protected (patented) and if it is going to be suitable for manufacture on a large scale.

Usually only a dozen entities will meet all these criteria, to be developed further—a process known as lead optimisation—with the aim of being subsequently tested in pre-clinical research.
Before a promising compound can be safely tested on people, a great deal more detailed research must be done to answer vital questions about its chemical properties and ability to treat a particular disease or symptom.

This is known as pre-clinical research. It’s carried out in the laboratory in test tubes, known as in vitro research, and in living organisms, known as in vivo research. Computer technology is also used.

Pre-clinical research involves a wide range of complex technical tests to find out much more about what chemical groups the compound contains, how these behave in water and fat, for example, and how they react with other chemicals and in different cells and tissues.

Similar versions (analogues) are made in a bid to uncover side effects and hone the effective (active) ingredients.

What the research can tell us

All this research shows whether the compound has the potential to act like a medicine by answering the following questions:

- How much of the compound is likely to be absorbed?
- Where is it likely to work?
- Is it likely to reach the target cells/tissues?
- How much is it likely to be changed by organs, such as the liver, kidneys, skin or lungs?
- What harmful chemicals and break-down products is it likely to produce?
- Will it do more harm than good? Could it potentially cause cancer or harm an unborn child, for example?
- How quickly will it be cleared from the body?
- Will it stay in the body long enough to do its job, but without causing other problems in the process?

If it becomes clear that the compound is potentially unsafe or unlikely to work, no further tests will be done and it will not be developed further.

For compounds with real potential to become medicines, pre-clinical research results decide the starter range of doses to be tested in people, as well as the format to be used—syrup, capsule, pill or injection, for example.

Why are animals still used?
The international Helsinki declaration and a European Directive require every new potential prescription medicine to be first tested in animals before it can be tested and used in people.

This is because test tube results may not always be the same when tested in living tissues, and no matter how sophisticated the technology, it is still very difficult to predict how a compound will work in the complex environment of the human body.

Animal research in the UK is tightly controlled and the animals used are bred for the purpose. It can’t go ahead without a licence from the Home Office. In 2006 more than 80% of animal research was carried out in mice, rats, and other rodents.

Before a licence can be granted, researchers have to prove that the use of animals is justified, and stick to clearly defined and strict regulations, designed specifically for this purpose. The regulations set out the circumstances under which animal experiments can take place, as well as standards relating to welfare, humane treatment, staff qualifications, and facilities.

Find out more...

- The Medical Research Council (MRC) (external link)
- Coalition for Medical Progress (external link)
- The Association of the British Pharmaceutical Industry (external link)
- Home Office statistics (external link)
Once researchers know that a new compound could be useful as a potential treatment, and it has passed safety tests in pre-clinical research, it needs to be tested thoroughly in clinical trials.

Trials for new medicines are largely funded by the pharmaceutical industry. But funding may also come from research institutions, the NHS, and publicly funded bodies, such as the Medical Research Council (MRC) (external link).

**Why are trials needed?**
Clinical trials are the start of the process that ends with a medicine being licensed and used for treatment.

These aim to find out if it:

- Works well in people
- Has an acceptable level of side effects
- Is at least as effective as existing treatments

**Who takes part?**
Clinical trials involve healthy volunteers or patients (research participants), depending on the type of treatment under test and its stage of development. All participants must agree to take part by giving informed consent before being given any treatment.

Larger numbers of participants take part in each trial phase, to uncover side effects that have not come to light before, and confirm the effectiveness, or otherwise, of the compound.

**The Northwick Park incident**
Side effects are common when a new compound is tested in people for the first time. But those of the severity
experienced by six people in the Northwick Park Hospital trial in 2006 are, fortunately, exceptionally rare.

These volunteers were helping to test a compound (TGN1412) for its potential to treat leukaemia, multiple sclerosis, and arthritis, but became seriously ill and had to be admitted to hospital.

The report into the incident by an independent expert scientific panel is available below:

Expert Group on Phase One Clinical Trials: Final report (external link)

The episode illustrates the unpredictability of medicines development and the need for rigorous testing of any new compound.

**Trial phases**

Trials run in phases I to IV, and a compound will only go forward to the next phase if it has passed the safety and effectiveness tests of the previous one.

- **Phase I** trials usually involve small numbers of healthy people. They are designed to find out how the treatment works in the body and how those treated react to it. This type of trial also aims to find out the lowest dose at which the treatment is effective, known as the minimum therapeutic dose, and the highest dose at which it can be taken without causing harm.
- **Phase II** trials test the treatment in several hundred people with a given disease or condition. They aim to find out how well the treatment works in larger numbers, identify common side effects, and refine the dose and length of treatment.
- **Phase III** trials typically compare the treatment on several thousand patients, to gather more detailed information on how well it works and in which groups of patients, as well as its safety. The results influence the prescribing and patient information of a medicine once it is marketed.
- **Phase IV** trials are carried out after a medicine has been licensed, put on the market and prescribed to patients. Part of the monitoring process, these trials are designed to find out more about the long term harms and benefits of a medicine, and to discover new uses for it.

**The different types of trial**

There are several types of clinical trials. For example:

- Randomised controlled trials aim to compare doses or treatments in two or more different groups. Participants are randomly assigned to their group, but matched for factors, such as age and sex, so that the results are comparable. These trials may compare two similar treatments or an active treatment and an inactive treatment (placebo).
- Blind trials aim to eliminate bias. Patients don’t know what treatment they are getting. They might be given an inactive treatment, for example.
- Double blind trials mean that neither the treating doctors nor the participants know which treatment they are being given.

It’s possible to have a combination of trial types, such as a randomised controlled double blind trial, for example.

**Quality safeguards for trials**

To protect the safety and wellbeing of participants and ensure that quality standards are maintained, a clinical trial for a medicinal product must be approved by the appropriate medicines regulator before it can be given the go ahead.

For UK trials, this is the Medicines and Healthcare products Regulatory Agency (MHRA). The MHRA issues licenses for trials of new compounds and medicines that have already been marketed, but for which the manufacturers are seeking a change in use.

All UK clinical trials are legally required to meet the standards laid down by the European Union Clinical Trials Directive (May 2004). And they are regularly inspected by the MHRA to make sure they are meeting these standards.

A trial must also have ethical approval from an independent body called a Research Ethics Committee. This is to ensure that the purpose of the trial can be justified on ethical grounds, and that the rights and privacy of the participants have been fully protected.
Find out more...
If you are interested in taking part in a clinical trial, you can contact the Clinical Contract Research Association (external link) for details of trials in your area.

More information on clinical trials is available below:
- The National Research Register (external link)
- The UK Clinical Research Network (external link)
- The UK Clinical Research Collaboration (external link)
- The World Health Organization International Clinical Trial Register (external link)
My medicine: Licensing (marketing authorisation)

In this section...

- Why is licensing important?
- Weighing up the pros and cons of a medicine
- "Off label" or "unlicensed" prescribing
- The role of the European regulator

By law, before a medicine can be placed on the market, it must be given a marketing authorisation (product licence) by a medicines regulator. The UK regulator is the Medicines and Healthcare products Regulatory Agency (MHRA).

A specially trained panel of medicines assessor reviews all the available evidence arising out of the pre-clinical research and clinical trials. Manufacturers may also be asked to supply additional information.

The MHRA also inspects the factory where the medicine is to be made, to make sure that supplies will be of a uniformly and consistently high standard.

Why is licensing important?
The licensing system is designed to:

- Guarantee that all those involved are answerable for their actions
- Ensure that processes, supplies, and quality can be thoroughly monitored
- Enable swift corrective action to be taken when needed

It is not influenced by the cost effectiveness or value for money of a medicine. These issues are considered by the relevant UK bodies who decide which treatments to recommend to their respective health systems.

Weighing up the pros and cons of a medicine
Every medicine has side effects, ranging from minor to severe. And some rare side effects may not come to light until the medicine has been used millions of times. If the regulators waited for every side effect to be identified before licensing a medicine this would deny patients useful treatments.

Before granting a licence the MHRA needs to know whether the medicine:

- Works well with minimal harm for most people who will be taking it
- Is acceptably safe.

A high level of side effects in a medicine used to treat a life threatening condition, such as cancer, may be an acceptable trade-off, but not in one used to treat a minor ailment, such as hay fever.
In general, side effects are considered to be very common when they occur in at least one in 10 cases and uncommon when they occur in between one in 100 and one in 1000 cases. Side effects occurring in one in 10,000 cases are regarded as very rare.

The MHRA will also want to know:

- What impact a treatment will have on quality and length of life
- If the evidence backs up its use in ordinary circumstances, rather than those of a clinical trial
- If all the evidence on the known and expected side effects has been made available

Under new legislation companies must also provide a risk management plan when applying for a licence for a new medicine. The plan includes:

- Known side effects, interactions with other drugs, and the types of patients not included in the clinical trials to date (safety specification)
- Additional research needed to fill in the gaps in knowledge about potential harm (pharmacovigilance)
- How the company intends to limit the risks to patients of the known side effects, including restricting access (risk minimisation)

Only when the MHRA is satisfied that a medicine meets high standards of safety and quality, and that it works for the purpose intended, will the licence be granted. This is denoted by a product licence or marketing authorisation number.

Such careful scrutiny takes time to complete, and explains why a new medicine cannot immediately be prescribed to large numbers of patients.

This level of scrutiny does not end after licensing. Monitoring continues throughout the life of a medicine as more becomes known about it.

“Off-label” or “unlicensed” prescribing
Sometimes doctors find that a licensed medicine works well for a certain condition, age group, or at a dose for which it has not been licensed by the regulator.

They prescribe it, based on their own and their colleagues’ experience, published studies, and findings presented at professional meetings. This is called “off label” prescribing.

It is more likely to happen when there are either no alternatives, or where access to effective alternatives is restricted.

Sometimes doctors will also ask the MHRA to import a medicine that has been licensed outside Europe if they think this might help a particular patient, on what is known as a named patient basis or “unlicensed” use.

The role of the European regulator
Some medicines used in the UK are licensed by the European Medicines Agency (EMEA) (external link) rather than the MHRA. Herceptin, used to treat patients with a certain type of advanced breast cancer, and the flu drug, Tamiflu, are two such examples.

Certain medicines can only be licensed through the EMEA. These include:

- “High tech” biotechnology treatments, such as gene therapies
- Medicines to treat HIV/AIDS, cancer, diabetes, and neurodegenerative diseases, such as multiple sclerosis and Alzheimer’s disease
- Orphan drugs—medicines that would not normally be commercially viable, because they have been developed for rare diseases, occurring in fewer than five in 10,000 people

This is to make sure that these important medicines are automatically available in every European Union member state rather than just in individual countries.

Manufacturers who want their medicines to be used across the European Union can also apply to the EMEA for a single licence, rather than having to apply to each country’s regulator separately. This speeds up patient access to these treatments.
It is impossible to know everything about all the side effects and benefits of a medicine when it is first licensed. A new drug is tested on thousands of people, but can end up being used by many millions.

Different people react to the same medicine differently, depending on their age and sex, and what other treatments they might be taking. And some rare and unexpected side effects may only emerge after a medicine has been in use for several years.

At other times, manufacturing problems may arise, which affect the quality and effectiveness of a medicine. And sometimes fake (counterfeit) medicines may enter the supply chain as a result of criminal activity.

Regulators and pharmaceutical companies know this and work together to continuously monitor the safety and quality of medicines after they have been licensed, so that swift and appropriate action can be taken to protect patients, should the need arise.

Who is involved?
There are several routes through which potential problems can be flagged up:

- Information supplied by manufacturers, including from research carried out during Phase IV clinical trials
- Reports on side effects associated with taking a medicine or herbal remedy made by healthcare professionals and the public to the Yellow Card Scheme
- Alerts raised by healthcare professionals on newly marketed drugs through the Black Triangle Scheme
- Research carried out using records from which patients’ names have been removed and stored in the General Practice Research Database (external link)
- Quality checks on products, including labelling and packaging carried out by MHRA inspectors. Every year they sample around 3000 medicines at manufacturers’ premises, wholesalers, and pharmacies
- Tip-offs about criminal activity, such as the sale of fake (counterfeit) medicines

What action is taken?
The regulators are committed to acting promptly and responsibly to protect patients from potential harm.
They warn healthcare professionals and wholesalers about quality or safety concerns by issuing alerts, which are graded according to the seriousness of their threat to the public’s health.

Healthcare professionals will in turn pass on this information to their patients in cases where continuing to take the medicine poses a serious risk.

- Class 1 life threatening: immediate recall required, for example, fake supplies of blood thinner drug Plavix 75 mg, in June 2007
- Class 2 harmful: recall is required within 48 hours, for example, quality concerns over the effectiveness of the active ingredient in the antibiotic amoxicillin in June 2007
- Class 3 unlikely to harm patients: action required within 5 days, for example, certain batches of a cream/pessary, used to treat fungal infections, such as thrush (Gyno-Pevaryl), because of errors in the patient information leaflet in August 2006
- Class 4 no threat to patient safety: caution advised, for example, fake batches of Sensodyne toothpaste in July 2007

The regulator can also:

- Set up expert panels to review concerns
- Commission further research to look into issues
- Suspend production or sale of a medicine
- Withdraw a medicine from use
- Take legal action against manufacturers and wholesalers when regulations have been breached

New medicines “on probation” (Black Triangle Scheme)

All new and existing medicines being used in a new way are put “on probation” after they are licensed to make extra sure that they work as intended and are acceptably safe.

An upside down black triangle symbol appears in prescribing manuals and adverts, to prompt healthcare professionals to be extra careful when prescribing them and to report any potential side effects.

There is no set time for this probationary period, but the performance of a new medicine will usually be assessed after two years.

Manufacturers also keep a close watch on their newly marketed products, and by law must inform the regulators of any unexpected side effects or quality concerns as soon as reliable information becomes available.

If you want to check on whether a medicine you are taking carries this symbol, you can look under Black Triangle Scheme on the MHRA website.

Using research to check on safety

Researchers, pharmaceutical companies, and drugs regulators can tap into the General Practice Research Database (external link) to carry out research on licensed medicines.

This contains the treatment records of patients, registered at more than 450 GP practices across the UK, and is a rich source of information on the safety and effectiveness of licensed medicines. All names are removed from these records to protect patients’ identity.

More than 500 studies have been published using the information the database contains. And it has been used to assess the safety of the Pill, MMR vaccine, antidepressants and hormone replacement therapy (HRT).

What to do about side effects associated with a medicine

- If you have new or worsening symptoms while taking a medicine always tell the healthcare professional who is treating you
- Speak to your local pharmacist
- You may also find it helpful to call NHS Direct (external link) for advice on 0845 4647 in England and Wales, or NHS24 if you live in Scotland on 08454 242 424
- Use the Yellow Card Scheme to report them to the regulator
Tackling fake (counterfeit) medicines
Sometimes fake versions of a medicine enter the supply chain, as a result of criminal activity by counterfeiters. Fake medicines may contain no active ingredient, so don't work, or may even contain harmful substances.

The production of counterfeit medicines is a growing problem, and has shifted from lifestyle drugs, such as those for weight loss and erectile dysfunction, to life saving medicines, such as those for cancer and heart disease.

Between 2004 and 2006, the Medicines and Healthcare products Regulatory Agency (MHRA) dealt with 14 cases of fake medicines. This compares with just one case in the previous decade.

Fake medicines can also come from internet pharmacies. The World Health Organization estimates that half of all sales made through internet sites without a return address are for fake medicines.

You can help stamp out the problem by using a dedicated hotline if you have been offered, bought, or have seen for sale, what you suspect might be fake medicines. Call: (0) 207 084 2701 or e-mail: counterfeit@mhra.gsi.gov.uk
The more widely a medicine is prescribed, the more becomes known about its effects, and a change in use may be required. This is because:

- New scope for treatment or increasing confidence in the safety record of an effective medicine can prompt it to be used more widely
- Concerns about the safety or quality of a medicine can prompt the regulator to restrict its use or change its status

Changes are usually requested by the manufacturer, but sometimes healthcare professionals or the regulator will ask for them.

Reports to the Yellow Card Scheme or research carried out using the information supplied to the General Practice Research Database (external link) can pinpoint patterns in the use of a medicine, which may affect how, and to whom, it is prescribed.

What changes can be made?
Changes can include:

- The addition of different conditions or age groups for which the medicine can now be prescribed
- Restrictions to the dose, length, or frequency of treatment as a result of unexpected side effects coming to light
- Limits on the quantity available—for example, paracetamol containers are now limited to 16 tablets in supermarkets and 32 in pharmacies, to cut the risk of serious liver damage when taken in large amounts
- A switch in legal status—from prescription only medicine (POM) to over the counter use under the direction of a pharmacist (P). Sumatriptan (50 mg tablets), for the relief of migraine symptoms, is now P status, for example
- Sometimes a medicine will be switched from P to GSL (General Sales List), which means it can be bought at a supermarket or corner shop, to boost its availability. Nicotine replacement lozenges are one such example
- Rarely, withdrawal of a medicine from sale because of serious safety concerns

Switching the legal status of a medicine
The legal status of a medicine will be changed only if the regulator is completely satisfied with its safety record, and after healthcare professionals and the public have been widely consulted.

Healthcare professionals are quickly advised of any changes in the use of a medicine by the manufacturer and the regulator, and these changes are then added to:

- Product information
- Patient information leaflets
- Prescribing reference manuals for healthcare professionals

**Withdrawing a medicine**

Before deciding to withdraw a medicine from sale, or restrict its use, the regulator carefully assesses all the available evidence for and against. This includes the impact its decision will have on patients who respond well to the medicine.

Independent expert advice is sought, and where appropriate, the public is also consulted. Decisions are based on the need for openness and honesty, and must be backed up by sound evidence and reasoning.

The pain-killer co-proxamol was withdrawn in 2005, for example, after earlier research had shown that it was involved in almost a fifth of all drug related suicides.

Most medicines work well and are acceptably safe. And the licensing process is so rigorous that few medicines are taken off the market because of safety concerns. Only 20 medicines have been withdrawn in the past 10 years from the 30 000 or more medicines licensed in the UK.

**Reporting side effects and symptoms (Yellow Card Scheme)**

Healthcare professionals and now patients can report as yet unidentified side effects and symptoms they suspect may be associated with a particular medicine or herbal remedy to the Yellow Card Scheme.

This is a confidential reporting system run by the Medicines and Healthcare products Regulatory Agency (MHRA), which aims to help build up a broader picture of how a medicine is working.

It provides invaluable feedback and enables the MHRA to pick up any problems that may be associated with taking a medicine and to take swift corrective action, if required.

And it can make a real difference. For example, in 2003, patients taking the blood thinning drug warfarin were advised not to drink cranberry juice, after it was found that the combination of the two boosted the risk of internal bleeding (haemorrhage).

Reports, including those on behalf of a child or adult in a person’s care, can be made by:

- Filling in a yellow card, available from GP surgeries or local pharmacies
- Completing a form online available in our Reporting suspected adverse drug reactions section.
- Calling 0808 100 3352.

Remember, a symptom that occurs while taking a medicine does not necessarily mean that it has been caused by that medicine. But it is always worth reporting it to the Scheme, none the less, in case it is part of a wider pattern and needs further investigation.
When licensing a new medicine, the regulators focus on quality, safety, and how well it works. They do not take into account the cost effectiveness or value for money of a medicine, or its impact on NHS budgets.

But the rising costs of development often mean that new medicines tend to be more expensive than existing treatments—at least until their patent runs out and cheaper versions, called generics, can be made.

With so many treatments in use, and new ones becoming available all the time, it can be difficult for busy healthcare professionals to know which ones work the best and are most suitable for their patients. And those in charge of limited healthcare finances need to know which ones offer the best value for money.

To help them weigh up the health and financial pros and cons of a treatment, independent agencies in each of the UK countries recommend which treatments to use, based on what is known about how well they work and how much they cost to prescribe.

Which agencies are responsible?

- In England, this role falls to the National Institute for Health and Clinical Excellence (NICE) (external link)
- The Scottish Medicines Consortium (SMC) (external link), NHS Quality Improvement for Scotland, and The Scottish Intercollegiate Guidelines Network (SIGN) take on this role in Scotland
- The All Wales Medicines Strategy Group (external link) is the responsible agency in Wales, but tends to follows NICE guidance
- The Department of Health, Social Services and Public Safety (DHSSPNI) adapts NICE guidance for patients in Northern Ireland

They aim to:

- Clear up any confusion about similar medicines used for the same condition
- Find out whether a new and expensive medicine offers value for money
Advise on how a particular and/or neglected condition should best be treated
Make sure that all patients with the same condition are treated equally, irrespective of where they live

Which treatments are reviewed?
Broadly speaking, criteria include the need to:

- Tackle emerging public health issues, such as obesity
- Reduce differences in the health of different groups according to sex, race, or wealth, for example
- Treat a disease with high levels of disability and/or death
- Improve patients’ or carers’ quality of life
- Assess a wide range of similar treatments
- Improve care

In the case of NICE, the Department of Health draws up a list of topics from among its own priorities for the NHS and suggestions from healthcare professionals and the public. These can be made:

- Online at topicsuggestions@nice.org.uk
- By phone on 0845 003 7781

Before narrowing down the list, a wide range of organisations is consulted, including those representing healthcare professionals, carers, and patients.

Not all medicines will be assessed. The availability of certain medicines in the NHS will be influenced by other factors, such as local treatment priorities and budgets.

Sifting through all the evidence takes time, but NICE now has a fast track process for life saving drugs that have already been licensed and for new medicines that are about to come on to the market.

The principles involved
Each agency has its own procedures, but they are all guided by the need to be thorough, independent, open and fair. They involve variously:

- Independent review of the evidence
- Expert panels
- Evidence from specialists, patients, carers, and manufacturers
- Public consultation
- Stated time frame to revisit the topic

Patients and other interested parties can challenge the final recommendations NICE intends to issue, for example, by lodging a formal appeal. This facility is built into the process.

Understandably, patients for whom a particular drug could mean extended or improved quality of life, and manufacturers who have worked hard to develop a new medicine, don’t always agree with recommendations to restrict the availability of a medicine or treatment in the NHS.

Decisions are reviewed after a couple of years to take account of new information on the usefulness and value for money of a particular medicine or treatment.

Putting the recommendations into practice
Once recommendations have been issued, local health organisations should put them into practice within three months, if they are not already doing so.

If you are not able to receive a medicine or treatment that is recommended by one of these national assessment bodies, you should contact the Patient Advice and Liaison Service (PALS) of your local primary care trust (PCT) in England and Wales, or your health board if you live in Scotland.

The equivalent in Northern Ireland is the Health and Social Services Board (external link).

Special cases
In certain circumstances, doctors may feel that they can best help their patients by prescribing a medicine that is
not licensed for use in the UK, but which has been licensed for use in another country, such as the USA, for example.

In these cases, the doctor applies to the MHRA to import it on an individual named patient basis.

**Find out more...**

- [The Association of the British Pharmaceutical Industry](#) (external link)
- [UK Medicines Information](#) (external link)
- [Department of Health](#) (external link)
- [Royal Pharmaceutical Society of Great Britain](#) (external link)
- [Scottish Health on the Web](#) (external link)
- [National Institute for Health and Clinical Excellence](#) (external link)
- [Scottish Medicines Consortium](#) (external link)
- [NHS Quality Improvement for Scotland](#) (external link)
- [The Scottish Intercollegiate Guidelines Network](#) (external link)
- [The All Wales Medicines Strategy Group](#) (external link)
- [Department of Health, Social Services and Public Safety (DHSSPS) Northern Ireland](#) (external link)