This briefing outlines both the process for licensing a new medicine in the UK (Part 1) and the process for issuing guidance and advice to the NHS in Scotland on its use (Part 2). It describes the role of the various bodies involved at a Scottish and UK level. It also provides information on the pricing of medicines and the operation of risk sharing schemes for specialised medicines (Part 3). It should be noted that this briefing does not cover the licensing of medical devices, which operates under a separate system.

This briefing is an update to, and supercedes, Briefing SB 08-17: ‘Licensing of Medicines in the UK and their Use in the NHS’.
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## GLOSSARY OF ABBREVIATIONS

Below is a list of abbreviations used throughout this briefing:

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<thead>
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<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ADTC</td>
<td>Area Drug and Therapeutic Committee</td>
</tr>
<tr>
<td>CHM</td>
<td>Commission on Human Medicines</td>
</tr>
<tr>
<td>DoH</td>
<td>UK Department of Health</td>
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<tr>
<td>EMA</td>
<td>European Medicines Agency</td>
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<tr>
<td>IPTR</td>
<td>Individual Patient Treatment Requests</td>
</tr>
<tr>
<td>MHRA</td>
<td>Medicines and Healthcare products Regulatory Authority</td>
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<tr>
<td>MTA</td>
<td>Multiple Technology Appraisal (issued by NICE)</td>
</tr>
<tr>
<td>NDC</td>
<td>New Drugs Committee (part of SMC)</td>
</tr>
<tr>
<td>NICE</td>
<td>National Institute for Health and Clinical Excellence</td>
</tr>
<tr>
<td>NSD</td>
<td>National Services Division</td>
</tr>
<tr>
<td>NSS</td>
<td>NHS National Services Scotland</td>
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<tr>
<td>PAS</td>
<td>Patient Access Schemes</td>
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<tr>
<td>PPRS</td>
<td>Pharmaceutical Price Regulation Scheme</td>
</tr>
<tr>
<td>QALY</td>
<td>Quality Adjusted Life Year</td>
</tr>
<tr>
<td>SMC</td>
<td>Scottish Medicines Consortium</td>
</tr>
<tr>
<td>STA</td>
<td>Single Technology Appraisal (issued by NICE)</td>
</tr>
<tr>
<td>VBP</td>
<td>Value Based Pricing</td>
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EXECUTIVE SUMMARY

Introduction

Whilst the process of licensing (or 'market authorisation') of a new medicine is a matter reserved to the UK Parliament, the development of guidance to the NHS on their use or otherwise is a devolved issue. It is important to note that despite the licensing procedures and guidance for the use of new treatments or a new use of an existing treatment, it is ultimately the decision of clinicians to decide whether or not a drug should be used in the treatment of their patient, using certain criteria.

Part 1: The Regulation of Medicines

There has been a form of regulation medicines in England (and subsequently the United Kingdom) since the times of King Henry VIII, but it was not until the 1960s that a comprehensive system of regulation was developed, including the coming into force of the Medicines Act 1968. Since then, the UK has worked with other European nations to develop a European-wide system of medicines regulation, preceding the Medicines Act 1968, which itself been amended to be consistent with EU regulations.

There are two competent authorities for the regulation of medicines – one at UK level and the other at a European level. The competent authority for the regulation of medicines in the UK is the Medicines and Healthcare products Regulatory Authority (MHRA). It is responsible for ensuring that medicines and medical devices work, and are acceptably safe. The European Medicines Agency (EMA) coordinates the evaluation and supervision of medicinal products throughout the EU.

The regulation of medicines starts as soon as they are first discovered and tested, all the way through to when a company wants to change the conditions its products are approved for, from changing the colour of a tablet, to what it is used for. Before a medicine gets to the stage of being considered for a license it will, typically, have undergone 12 years of research and development. The purpose of the licensing process is to consider whether the medicine has a measurable effect against a comparator in a clinical trial (referred to as “efficacy”) and, whether, on balance, the drug is likely to have an acceptable level of safety and quality. There are two ways of obtaining a licence for the UK:

- applying for a licence in the UK through the national procedures of the MHRA
- applying for a licence through the EMA, which relates to all EU Member States, known as the 'centralised procedure'

Once a medicine has been licensed there is on-going monitoring undertaken at UK as well as European level. In the UK the MHRA itself inspects good and safe practice, but it also counts on health professionals and the public reporting defects, side-effects and mis-leading information. In addition, manufacturers must report any issues that come to their attention. The action taken is determined by the scale of the threat posed to the public’s health.
Part 2: Approving a medicine for use in the NHS

Once a medicine has been licensed in the UK it is available for general use by prescribers in the NHS, though many NHS bodies and prescribers will prefer to await official guidance on its use. The purpose of the guidance for the NHS is different to that of licensing, which considers efficacy and safety. Whilst NHS guidance does consider the efficacy of the medicine, it also reflects on its clinical effectiveness (i.e. how the medicine fits with what is currently being used) and its cost effectiveness (i.e. whether or not it is good value for money).

There are different arrangements across the UK for producing this guidance, and this can cause confusion and debate. Guidance over the use of licensed drugs in the NHS in Scotland is a devolved matter. However, there is a level of joint working that takes place between the organisations responsible for issuing guidance across the UK.

In Scotland, Healthcare Improvement Scotland is the body with statutory responsibility for producing guidance on all technologies, including medicines. However, for new medicines, the Scottish Medicines Consortium (SMC) is responsible for issuing advice. In England and Wales the equivalent body for both functions is the National Institute for Health and Clinical Excellence (NICE). There are circumstances where NICE’s ‘Multiple Technology Appraisal’ guidance can be validated in Scotland.

The SMC was established in October 2001. Its role is to advise NHS Boards and their Area Drug and Therapeutic Committees (ADTCs) on the use of new medicines as soon as they are licensed by MHRA or EMA. The SMC is made up of representatives of all ADTCs, other health professionals, the pharmaceutical industry and patient representatives.

NICE is responsible for providing national guidance on the promotion of good health and the prevention and treatment of ill health in England and Wales. As part of its role it produces technology appraisals, which offer guidance on the use of new and existing medicines and treatments within the NHS in England and Wales. It generally only reviews medicines referred to it by Ministers (which is unlike the situation with the SMC which appraises all new medicines when they receive a license). The NHS in England and Wales is obliged to adhere to NICE guidance.

Processes for assessing medicines for use in NHS Scotland

The SMC monitors when manufacturers launch new medicines and proactively asks them to make a submission on the product, including results of clinical trials and cost effectiveness data. The SMC’s role is to undertake an evaluation of the medicine’s clinical efficacy and cost effectiveness, and then determine whether the medicine should be recommended for use in the NHS in Scotland. It does this through a two stage process (see ‘Process for assessing medicines for use in NHS Scotland in the main briefing).

The health economics tool used to measure the benefit of a medicine is the quality-adjusted life year (QALY). This takes into account how a treatment affects a patient’s quantity of life (how long they live for) and the quality of life (the quality of their remaining years of life). These factors are then combined into a single measure that puts a figure on the health benefits for a medicine. The resulting QALY can then be used to benchmark the benefits each medicine is likely to offer. Then, to consider the cost effectiveness of the medicine, the QALY is combined with the cost of the medicine to produce a ratio called the cost per QALY.

On completion of the SMC assessment process, it publishes its advice for NHS Scotland. NHS Boards are required to consider this advice. It is important to note that NHS Boards will consider all SMC accepted advice as a matter of course but can still decide not to include such medicines on their own local formulary i.e. where the medicine does not represent sufficient
added benefit to other medicines already on the formulary for the same indication. The Scottish Government recently issued guidance to Boards on this issue.

NHS Boards are expected to fund the cost of SMC accepted medicines from within their resource allocations, according to their local formulary/approved lists.

SMC advice may be superseded when:

- in the case of ‘not recommended’ advice, a pharmaceutical company makes a resubmission which subsequently leads to recommended advice
- NICE publishes a Multiple Technology Appraisal which is then adopted by Healthcare Improvement Scotland

The NICE process for assessing medicines and its applicability to Scotland

NICE assesses the clinical and cost effectiveness of a medicine through one of two appraisal processes:

a) the Single Technology Appraisal (STA) process, which is similar in nature and timing to the SMC process, and as a result has no formal status in Scotland, though Healthcare Improvement Scotland publishes them on its website for information.

b) the Multiple Technology Appraisal (MTA) evaluation, which is more in-depth and takes considerably longer. A MTA will normally cover more than one technology, or one technology for more than one indication. Given the more in-depth nature of the MTA process, they do have status in Scotland. Healthcare Improvement Scotland is involved in the NICE MTA process with one Scottish expert being assigned to an MTA throughout the whole process. Any resultant draft guidance is then reviewed by a group of experts in Scotland. Healthcare Improvement Scotland will then determine the applicability of the guidance for Scotland. Where it validates a NICE MTA recommendation, NHS Boards in Scotland are required to consider it. The NICE MTA advice supersedes any relevant SMC advice.

Accessing medicines not recommended for use

Prior to April 2011, there was no formal guidance for NHS Boards to make decisions on requests by patients to be treated with a medicine not recommended for use within NHS Scotland. However, it was generally the case that in order for a Board to agree to such a request, the patient would need to be: a) significantly different to the general population of patients with the condition in question; and, b) likely to gain more benefit from the medicine than the average patient. These criteria were referred to as “exceptional circumstances”. NHS Boards had their own procedures for dealing with such decisions.

Following from the issues raised by petition PE1108, concerning the provision on the NHS of cancer treatment medicines, the Scottish Government published guidance in May 2010, which set out a framework for the development of NHS Board written policies for dealing with such requests, now known as Individual Patient Treatment Requests (IPTRs). Further guidance has been subsequently published. The Scottish Government (2012a) expects these processes to be used though accepts there will need to be a degree of flexibility.

Each Board’s written policy should have been in place by 1 April 2011, and they should be available on the Board’s website. It is expected that NHS Boards are monitoring and collecting data on IPTR requests and their outcome (including Appeals). In addition, the Scottish Government is keen that the rationale behind each decision is being recorded, which, it believes
will help Boards to share good practice in relation to the IPTR process. Boards have also been asked to consider reviewing GP prescribing of SMC “not recommended” medicines as part of on-going reviews of primary care prescribing. It should be noted that there is no central database with records of IPTR decisions.

Part 3: Further considerations

Pharmaceutical Price Regulation Scheme

The Pharmaceutical Price Regulation Scheme (PPRS) is the mechanism which the Department of Health (DoH) in England, on behalf of the four UK health departments, uses to regulate the prices of branded medicines. It is a voluntary scheme, usually negotiated every five years, between the DoH and the pharmaceutical industry though is underpinned by statutory powers. It seeks to achieve a balance between reasonable prices for the NHS and a fair return for the industry to enable it to research, develop and market new and improved medicines.

The 2009 PPRS introduced Patient Access Schemes (PAS) - an agreement reached with a pharmaceutical company where discounts or rebates are offered to reduce the costs of a medicine to the NHS. This then improves its cost-effectiveness, and thus enhances the likelihood of availability. In Scotland, the manufacturer would propose a PAS when making a submission for a new medicine to the SMC. The PAS Assessment Group (established under the auspices of NHS National Services Scotland) will carry out an assessment of the PAS in a process independent of the SMC. Where a PAS is considered feasible, the SMC is then able to take account of the discount offered under the terms of the PAS. Where a PAS is not considered feasible, SMC appraises the drug on its standard costs.

The UK coalition Government stated, in its programme for government, its intention to reform arrangements for the pricing of branded medicines and to introduce a new system of value-based pricing (VBP). It is argued this would create a closer link between the price the NHS pays and the value that a medicine delivers. Following a consultation in 2011 negotiations between the UK Department of Health (DoH) and stakeholders are due to begin in 2012. One of the key issues with the DoH’s proposals is that they would have an effect on the way medicine technology appraisals are undertaken, which as discussed above is a devolved matter. A recent statement by the DoH and the Association of the British Pharmaceutical Industry discussed the importance of working with the devolved administrations to ensure a coordinated and coherent approach.

Risk sharing schemes

Some medicines, such as orphan medicines, which are deemed highly specialised may be commissioned nationally through a risk sharing scheme operated by National Services Division (NSD) of NHS National Services Scotland. A NHS Board will make a submission asking for a medicine to be placed in the scheme. NSD then establishes whether the medicine has been considered by the SMC and gathers information on the likely numbers of patients who might be assessed as requiring the therapy, and likely total costs to NHS Scotland. NSD then submits this information to the NHS Board Chief Executives’ Group for consideration and decision on inclusion (or otherwise) of the medicine. To be included, the medicine in question must have been accepted for use by the SMC. There is a range of criteria used by NHS Boards to decide which services or therapies fall within the risk share (see ‘Risk Sharing Schemes’ in the main briefing).
INTRODUCTION

There is significant interest in the licensing of new medicines in the UK, and how they are approved for use in the NHS in Scotland. Whilst licensing is a matter reserved to the UK Parliament, the development of guidance to the NHS on their use or otherwise is a devolved issue. Figure 1, below, outlines the process for licensing medicines in the UK, and then the process for issuing guidance to the NHS in Scotland compared to England and Wales. These processes are discussed in more detail in the following sections.

Since 2007 the Scottish Government has sought to clarify the various processes involved, to ensure that decisions taken on medicines at a local level are based on national guidance. These occurred principally as a result of Petition 1108 to the Scottish Parliament which was lodged in January 2008 by Tina McGeever, on behalf of her husband Mike Gray. This called for greater equity on the appropriateness, effectiveness and availability of medicines, particularly those for cancer. The then Public Petitions Committee undertook an inquiry into the issues raised by the petition and published its report in June 2008. This has led to the publication of the following pieces of guidance by the Scottish Government:

- ‘Arrangements for NHS patients receiving healthcare services through private healthcare arrangements’ (March 2009) – covers situations where NHS patients may wish to include elements of private healthcare, including medicines, in the management of their clinical conditions (Scottish Government, 2009)
- ‘Introduction and availability of newly licensed medicines in the NHS in Scotland’ (May 2010) - sets out the policy framework with regard to the introduction and availability of newly licensed medicines in the NHS in Scotland (Scottish Government, 2010)
- ‘Guidance to further strengthen the safe and effective use of new medicines across the NHS in Scotland’ (February 2012) (Scottish Government, 2012a)

Primacy of Medical Practitioners

It is important to note that despite the licensing procedures and guidance for the use of new treatments or a new use of an existing treatment, it is ultimately the decision of clinicians to decide whether or not a drug should be used in the treatment of their patient, using certain criteria, which include:

- that the treatment is not a controlled drug
- if the treatment does contain a controlled substance that the product has been granted a license for importation by the UK Home Office under the Misuse of Drugs Act 1971
- that the clinician has consulted with and gained the consent of the patient

If a clinician feels that a particular unlicensed product would benefit their patient then they have to be prepared to take the full clinical and legal responsibility for the prescription, and as a result many clinicians will not prescribe a medicine that has not been licensed. Should they be prepared to prescribe the drug then it is also up to them to secure a supply and funding for their patient. In some cases the patient may choose to fund it themselves. However, for the NHS to fund such a treatment, the NHS Board which employs the practitioner, would have to be prepared to fund the prescription. Nevertheless, even if there is advice produced for a particular medicine, it does not override the individual responsibility of the clinician to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.
Figure 1: The process for licensing a medicine and the issuing of guidance to the NHS

Marketing Authorisation (License) sought for medicine via either

Medicines and Healthcare products Regulatory Authority (MHRA)  European Medicines Agency (EMA)

Approved  No

Yes  Medicine goes no further, or is re-submitted after further work

Process in Scotland  Process in England and Wales

Scottish Medicines Consortium (SMC) Assessment of ALL newly licensed medicines (18 weeks)  NICE considers medicines referred by UK Ministers

Approved

Yes  SMC publishes “accepted” advice. Advice remains extant unless HIS advises that a subsequent NICE MTA for the same product and indication is valid for Scotland

No  SMC publishes “not recommended” advice. Medicine goes no further or is resubmitted for SMC appraisal. Advice remains extant unless Healthcare Improvement Scotland advises that a subsequent NICE MTA for the same product and indication is valid for Scotland

NHS Boards required to consider SMC advice and make the medicine (or its equivalent) available

NHS Boards required to consider SMC advice. However, Boards can consider individual patient treatment requests

NICE Multiple Technology Appraisal (MTA)

Approved

Yes  Final NICE MTA Appraisal Guidance issued for England and Wales. There is an appeals process for negative NICE MTA decisions

No  Healthcare Improvement Scotland reviews NICE MTA for applicability in Scotland. If validated this advice supersedes any SMC advice on the medicine

NICE Single Technology Appraisal (STA)

Approved

Yes  NICE STA Appraisal Guidance issued for England and Wales (has no formal status in Scotland)

No
PART 1: THE REGULATION OF MEDICINES

Within the British Isles, the regulation of medicines is not new. A form of it has been in existence in England (and subsequently the United Kingdom) since the time of King Henry VIII. However, it was not until the 1960s that a comprehensive system of regulation was developed. This followed the outcry over the prescribing of thalidomide in the 1950s and 1960s to relieve morning sickness in early pregnancy, but which caused serious birth defects. The result was the creation of the Committee on Safety of Drugs in 1963 (now known as the Commission on Safety of Medicines) and the coming into force of the Medicines Act 1968 (the 1968 Act), which provided the legal framework for the control of medicines in the UK, including the licensing of medicines (Medicines and Healthcare products Regulatory Authority, 2008).

Since then, the UK has worked with other European nations to develop a European-wide system of medicines regulation, primarily provided for through Directive 2001/83/EC on the ‘Community code relating to medicinal products for human use’ (as amended)¹. This now precedes the Medicines Act 1968, which has itself been amended to be consistent with EU regulations. (Medicines and Healthcare products Regulatory Authority).

WHAT IS A MEDICINE?

Under current legislation, a medicine is defined as something used in:

- disease management (whether it is used to prevent, treat or diagnose it)
- anaesthesia
- investigating conditions
- interfering with the normal operation of the body

Numerous factors are considered in deciding whether a product is actually a medicine, including:

- what it contains
- what it’s advertised or used for
- the way it will be used
- any particular targeting of the marketing information
- what the promotional literature says

Claims that a product “supports” health or a healthy lifestyle is not usually considered as medicinal.

COMPETENT AUTHORITIES

There are two competent authorities for the regulation of medicines – one at UK level and the other at a European level.

The competent authority for the regulation of medicines in the UK is the Medicines and Healthcare products Regulatory Authority (MHRA). It is an executive agency of the UK Department of Health, and is responsible for ensuring that medicines and medical devices work,

¹ Further information on the EU regulation of medicines is available on the European Medicines Agency website here.
and are acceptably safe. The Commission on Human Medicines (CHM) provides independent expert advice to the MHRA. The MHRA has its own procedures for licensing medicines, which are not covered through the ‘centralised procedure’ of the European Medicine’s Agency (see ‘Licensing’, below).

The European Medicines Agency (EMA) coordinates the evaluation and supervision of medicinal products throughout the EU. It is responsible for the licensing according to the ‘centralised procedure’ (see ‘Licensing’, below). It is a decentralised body of the European Union and its main responsibility is the “protection and promotion of public […] health through the evaluation and supervision of medicines for human […] use”. It is considered to be the ‘hub’ of a European medicines network comprising over 40 national competent authorities in 30 EU and European Economic Area-European Free Trade Association (EEA-EFTA) countries, the European Commission, the European Parliament and a number of other decentralised EU agencies. It works with a network of over 4,500 ‘European experts' who serve as members of the Agency’s scientific committees, working parties or scientific assessment teams. These experts are made available to the Agency by the national competent authorities of the EU and EFTA states i.e. MHRA in the UK.

**Licensing**

The regulation of medicines starts as soon as they are first discovered and tested, all the way through to when a company wants to change the conditions its products are approved for, from changing the colour of a tablet, to what it is used for.

Before a medicine gets to the stage of being considered for a license (also referred to as a ‘marketing authorisation’) it will, typically, have undergone 12 years of research and development. In this long process, the substances that were identified in basic research need to pass pre-clinical & clinical tests. Pharmaceutical companies quite often research and test 10,000-30,000 different substances before one can be successfully licensed for use.

Following the development process the pharmaceutical company will seek a licence for the medicine. The purpose of the licensing process is to consider whether the medicine has a measurable effect against a comparator in a clinical trial (referred to as “efficacy”) and, whether, on balance, the drug is likely to have an acceptable level of safety and quality. The MHRA (2008, p 2) notes that no product is 100% safe, as all medicines have side effects and different people respond differently to them. The question posed by the MHRA and EMA is whether those side effects are acceptable – whilst a high level of side effects may be acceptable in the treatment of a life endangering illness, it will probably not be in the case of a common ailment.

There are two ways of obtaining a licence for the UK:

- applying for a licence in the UK through the national procedures of the MHRA
- applying for a licence through the EMA, which relates to all EU Member States, known as the centralised procedures

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2 The appointment of the Chairman and members of the CHM are carried out by the NHS Appointments Commission in accordance with Nolan procedures and the approval of UK health ministers.
3 The EMA also has responsibility for animal health and medicines for veterinary use.
4 Distinct from institutions of the EU, decentralised agencies are set up to deal with specific tasks, as a way of supporting Member States and their citizens.
5 The official permission from the regulatory authority to market/sell a product in the UK. This defines the indications for use as well as any contra-indications and cautions to the use of the product.
National authorisation procedure

As with the other member states of the EU and EFTA, the UK has its own procedures for assessing applications to have a medicine licensed, as long as that medicine is not within the scope of the ‘centralised procedure’ (see below). In the UK a number of licenses are required before a medicine is licensed to be sold in the UK. New products which are still in development will need a licence before they can be used in clinical trials on human subjects. In addition, the companies that are involved in all stages of the manufacture and distribution of the medicine require a manufacturer’s and wholesale dealer’s licence.

The MHRA takes independent advice from its various Committees when making a decision, including from the CHM. If a license is granted then the product will receive its marketing authorisation for the UK and can be ‘launched’ i.e. introduced to the market.

If a company wishes to seek a license in several countries simultaneously, it can do so in the following ways:

- **Decentralised procedure**: companies can apply for the simultaneous authorisation in more than one EU country of a medicine that has not yet been authorised in any EU country and that do not fall within the mandatory scope of the centralised procedure (see below)
- **Mutual-recognition procedure**: companies that have a medicine authorised in one EU Member State can apply for this authorisation to be recognised in other EU countries.

If a dispute arises it can be referred to the EMA for arbitration.

Centralised procedure

The EMA is responsible for the centralised procedure, which can result in a single license that is valid in all European Union countries, as well as in Iceland, Lichtenstein and Norway. In terms of human medicines, the centralised procedure is compulsory for:

- the treatment of HIV/AIDS, cancer, diabetes, neurodegenerative diseases, auto-immune and other immune dysfunctions, and viral diseases
- medicines derived from biotechnology processes, such as genetic engineering
- advanced-therapy medicines, such as gene-therapy, somatic cell-therapy or tissue-engineered medicines
- officially designated 'orphan medicines' (medicines used for rare human diseases)

If a medicine does not fall within these categories, companies can still submit an application under this procedure as long as the medicine concerned is “a significant therapeutic, scientific or technical innovation, or if its authorisation would be in the interest of public [...] health” (EMA, online).

Applications through the procedure are handled directly by the EMA. Evaluation can take up to 210 days and is undertaken by its scientific committees, after which the committee will adopt an opinion on whether the medicine should be licensed or not. This is then relayed to the European Commission, which has the ultimate authority for granting licenses in the EU. If a license is granted, the holder can then begin make the medicine available in all EU countries.
Orphan medicines

One issue of recent interest in the debate over the approval of medicines for use in the NHS, has been in regards to orphan medicines. As referred to above, the process for licensing an orphan medicine takes place through the EMA’s centralised procedure. The use of this procedure for orphan medicines was introduced in the EU in 2000 in an attempt to improve the availability of medicines for rare diseases. The EMA states that in order for a medicine to qualify for orphan designation, a medicine must meet one of two criteria:

- it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting no more than 5 in 10,000 people in the EU at the time of submission of the designation application
- it is intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition and without incentives it is unlikely that the revenue after marketing of the medicinal product would cover the investment in its development

In both cases, there must either be no satisfactory method of diagnosis, prevention or treatment of the condition concerned, or, if such a method does exist, the medicine must be of significant benefit to those affected by the condition. It is also worth noting that a single license cannot cover both orphan and non-orphan indications i.e. an individual medicine with different indications for its use cannot have orphan status for only one indication. Therefore if one of the indications is not an orphan indication the medicine loses its orphan status.

Given orphan medicines are intended for small numbers of patients, the pharmaceutical industry is less likely, in normal market conditions, to develop and market such medicines. Therefore, the European Commission offers a number of incentives to pharmaceutical companies to encourage the development of these medicines, including fee reductions, access to the centralised procedure and ten years of market exclusivity once licensed. There may also be a range of other incentives at EU and Member State level.

ON-GOING MONITORING

Once a medicine has been licensed there is on-going monitoring undertaken at UK as well as European level. The MHRA (2008, p 10 & 13) states that it regularly inspects good and safe practice itself, but also counts on health professionals and the public reporting defects, side-effects and mis-leading information. In addition, manufacturers must report any issues that come to their attention. The action taken is determined by the scale of the threat posed to the public’s health. Reports prompt investigations, which can result in the issue of warnings and alerts. In addition, the MHRA has the power to prosecute when regulations have been breached. The courts can impose fines or prison sentences when the law has been broken, and the Agency can withdraw unlicensed/ illegal products from the market. Similar processes are in place within the EMA for dealing with medicines which have been given a license under the centralised procedure.

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6 In medicine, an “indication” is a condition which makes a particular treatment or procedure advisable.
PART 2: APPROVING A MEDICINE FOR USE IN THE NHS

Once a medicine has been licensed in the UK it is available for general use by prescribers in the NHS, though many NHS bodies and prescribers will prefer to await official guidance on its use. This guidance is often referred to as a “technology appraisal”. The purpose of the guidance for the NHS is different to that of licensing, which considers efficacy and safety. Whilst NHS guidance considers the efficacy of the medicine, it also reflects on its clinical effectiveness (i.e. how the medicine fits with what is currently being used) and its cost effectiveness (i.e. whether or not it is good value for money). The resulting NHS guidance has no effect on the medicine’s licence status.

It is the fact there are different arrangements across the UK for producing guidance to the NHS that causes the most confusion and debate. Guidance over the use of licensed drugs in the NHS is a devolved matter. However, there is a level of joint working that takes place between the organisations responsible for issuing guidance across the UK. This briefing is particularly interested in the structures affecting the NHS in Scotland – principally the Scottish Medicines Consortium (SMC) and the National Institute for Health and Clinical Excellence (NICE) for England and Wales. However, it is useful to note that there are particular structures in Wales and Northern Ireland (see Box 1).

KEY ORGANISATIONS

In Scotland, Healthcare Improvement Scotland is the body with statutory responsibility for producing guidance on all technologies, including medicines. However, for new medicines, the Scottish Medicines Consortium (SMC) is responsible for issuing advice. In England and Wales the equivalent body for both functions is the National Institute for Health and Clinical Excellence (NICE). There are circumstances where NICE’s ‘Multiple Technology Appraisal’ guidance can be validated in Scotland.

Healthcare Improvement Scotland

Healthcare Improvement Scotland can be described as a Non-Departmental Public Body. It was created by the Public Services Reform (Scotland) Act 2010, and is a health body corporate responsible to Scottish Ministers. It came into being on 1 April 2011. It took over the functions of NHS Quality Improvement Scotland and the Care Commission as regards the regulation of the independent health care sector. It provides a national service, but rather than managing health services directly, it works with and supports organisations that do. Healthcare Improvement Scotland is the lead organisation in NHS Scotland for improving the quality of

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Box 1

**Northern Ireland**

The Department of Health, Social Services and Public Safety in Northern Ireland has links with NICE. It reviews any guidance issued by NICE and decides whether it is applicable for Northern Ireland.

**Wales**

The All Wales Medicines Strategy Group (AWMSG) takes decisions about which medicines should be available within the NHS in Wales. It aligns its work to NICE and will not usually review a medicine if NICE are planning to look at the medicine within the following 12 months. AWMSG issues interim guidance to the NHS in Wales, which is then superseded by any NICE guidance. Thus, if AWMSG says a medicine should be made available but then NICE issues guidance to say that the medicine should not be made available, then the NICE guidance stands.

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7 It is worth noting that the Scottish Intercollegiate Guidelines Network (SIGN) develops evidence based clinical practice guidelines for the NHS in Scotland. Although SIGN does not specifically focus on individual medicines it does suggest how and when types of medicines should be used.
healthcare delivered. Its roles include providing clear advice and guidance to NHS Scotland on effective clinical practice. This includes assessing new technologies through its Scottish Health Technologies Group. The organisation also hosts the Scottish Medicines Consortium (SMC) which assesses the clinical and cost effectiveness of newly licensed medicines.

**Scottish Medicines Consortium**

The SMC was established in October 2001. Its role is to advise NHS Boards and their Area Drug and Therapeutic Committees (ADTCs) on the use of new medicines as soon as they are licensed by MHRA or EMA. Prior to this such decisions were taken at a local level by NHS Board ADTCs. This resulted in the possibility of wide variation in the provision of new medicines across Scotland and involved a duplication of effort. Thus, the SMC was created to help reduce “postcode prescribing”. The SMC is made up of representatives of all ADTCs, other health professionals, the pharmaceutical industry and patient representatives. It is important to note that the SMC does not issue advice on medical devices, vaccines, branded generic drugs, non-prescription-only medicines, blood products, plasma substitutes and diagnostic drugs.

**National Institute for Health and Clinical Excellence**

NICE was first set up in 1999 with the aim of reducing the variation in the availability and quality of NHS treatments and care. Its role was reviewed and expanded in 2005. It is responsible for providing national guidance on the promotion of good health and the prevention and treatment of ill health in England and Wales. As part of its role it produces technology appraisals, which offer guidance on the use of new and existing medicines and treatments within the NHS in England and Wales (these are discussed in greater detail below). It generally only reviews medicines referred to it by Ministers (which is unlike the situation with the SMC which appraises all new medicines when they receive a license). The NHS in England and Wales is obliged to adhere to NICE guidance.

NICE is currently a Special Health Authority i.e. an arms-length Body funded by the Department of Health. The Health and Social Care Act 2012 provides for NICE to become a Non-Departmental Public Body with its remit expanded to include the production of quality standards for the social care sector.

**PROCESSES FOR PRODUCING GUIDANCE**

The relevant bodies in Scotland and England have their own structures for developing guidance, but, as shown in Figure 1, above, there is a level of cooperation between the two bodies. Thus to describe the process for developing advice for NHS Boards in Scotland it is important to discuss both processes.

**Process for assessing medicines for use in NHS Scotland**

The SMC monitors when manufacturers launch new medicines and proactively asks them to make a submission on the product, including results of clinical trials and cost effectiveness data. The SMC’s role is to undertake an evaluation of the medicine’s clinical efficacy and cost effectiveness, and then determine whether the medicine should be recommended for use in the NHS in Scotland.
In coming to a determination, the SMC has a two stage process, which is outlined in Figure 2, below. Firstly, its New Drugs Committee (NDC) evaluates the submission using the advice of medical, pharmaceutical, and health economics experts. The NDC then makes a provisional recommendation that is shared with the pharmaceutical company concerned. The advice from NDC, together with feedback from the company is then considered by the SMC committee. The submissions from patient interest group are also considered at this stage. These submissions focus on the difficulties the disease presents for patients. (SMC, 2011a). The SMC (2012a) has stated that the Patient Interest Group submissions often supply useful additional perspectives on new medicines, which are helpful in formulating the SMC’s conclusions. It also notes that it will consider special issues related to health care provision in Scotland (e.g. those related to rural communities), and any relevant societal issues.

Figure 2: SMC processes and timelines

The health economics tool used to measure the benefit of a medicine is the quality-adjusted life year (QALY) (see SMC, 2011b). This takes into account how a treatment affects a patient’s quantity of life (how long they live for) and the quality of life (the quality of their remaining years of life). These factors are then combined into a single measure that puts a figure on the health benefits for a medicine. The resulting QALY can then be used to benchmark the benefits each medicine is likely to offer. Then, to consider the cost effectiveness of the medicine, the QALY is combined with the cost of the medicine to produce a ratio called the cost per QALY. Some medicines have a low cost per QALY and these are considered to offer good value for money. Medicines with a high cost per QALY would not be considered good value for money. The SMC (2011a) has stated that a cost per QALY of under £20,000 is generally considered acceptable value for money. Adding that for a medicine with a cost per QALY between £20,000 and £30,000 SMC might accept this if the medicine gives significant benefits over existing treatments. In addition, the SMC can consider using modifiers for any medicine under
assessment where the estimated cost per QALY is relatively high. Thus, if a medicine has an estimated cost per QALY of more than £30,000, and the Committee is confident that the company’s clinical and health economic case is robust, then the Committee can consider whether one or more of the modifiers would allow it to be accepted (see SMC (2012a) for further information).

On completion of the SMC assessment process, it publishes its advice for NHS Scotland. NHS Boards are required to consider this advice. Where a medicine is accepted by the SMC, NHS Boards are expected to make it (or its equivalent) available. It is important to note that NHS Boards will consider all SMC accepted advice as a matter of course but can still decide not to include such medicines on their own local formulary i.e. where the medicine does not represent sufficient added benefit to other medicines already on the formulary for the same indication. The Scottish Government (2012a) recently issued guidance to Boards on this issue. Such decisions will be taken by the NHS Board’s ADTC and they should normally make this clear within 90 days of the SMC issuing advice on an accepted medicine. NHS Boards are expected to fund the cost of SMC accepted medicines from within their resource allocations, according to their local formulary/approved lists. (See Scottish Government (2010 and 2012a) for further information). SMC advice may be superseded when:

- in the case of ‘not recommended’ advice, a pharmaceutical company makes a resubmission which subsequently leads to recommended advice
- NICE publishes a Multiple Technology Appraisal which is then adopted by Healthcare Improvement Scotland (see below)

The NICE process for assessing medicines and its applicability to Scotland

The NICE work programme is developed by the UK Department of Health. This means that NICE does not produce guidance on every newly licensed medicine, unlike the SMC.

NICE assesses the clinical and cost effectiveness of a medicine through one of two appraisal processes: a) the Single Technology Appraisal (STA) process, which is similar in nature and timing to the SMC process, or, b) by undertaking a Multiple Technology Appraisal (MTA) evaluation, which is more in-depth and takes considerably longer.

Single Technology Appraisal process

This is a fairly recent development that only started in mid-2006. Prior to this, there was no such procedure, and this meant newly licensed had to wait for the full MTA process to be undertaken. Given the SMC structure in Scotland for dealing with newly licensed medicines this often led to advice being issued in Scotland a significant time before that in England, which could mean new medicines being made available in Scotland before England. As a result of this and other factors NICE introduced its STA process, which is a more rapid process for assessing drugs and other treatments to sit alongside its standard process. A STA can only be used for a single indication, and its evaluation process is similar to that of the SMC (see ‘Developing NICE single technology appraisals’ for further information). NICE STAs have no formal status in Scotland, though Healthcare Improvement Scotland publishes them on its website for information.

Multiple Technology Appraisals

The Multiple Technology Appraisal process undertaken by NICE is briefly outlined in Appendix 1. A MTA will normally cover more than one medicine, or one medicine for more than one indication. The process itself can take up to 54 weeks to be completed, though in some cases it has taken much longer than this depending on whether the decision of NICE is appealed.
Given the more in-depth nature of the MTA process, they, unlike STAs, do have status in Scotland. The Scottish Government (2010) explains that Healthcare Improvement Scotland is involved in the NICE MTA process with one Scottish expert being assigned to an MTA throughout the whole process. Any resultant draft guidance is then reviewed by a group of experts in Scotland. In determining the applicability of the guidance for Scotland, HIS will consider:

- the principles and values of NHSScotland
- epidemiology (frequency, distribution and stage at presentation)
- structure and provision of services
- other implications (e.g. rural issues, predicted uptake and existing advice from SMC)

When this process has been completed Healthcare Improvement Scotland publishes advice on its website. Where it validates a NICE MTA recommendation, NHS Boards in Scotland are required to consider it. The NICE MTA advice supersedes any relevant SMC advice.

**ACCESSING MEDICINES NOT RECOMMENDED FOR USE**

Prior to April 2011, there was no formal guidance for NHS Boards to make decisions on requests by patients to be treated with a medicine not recommended for use within NHS Scotland. However, it was generally the case that in order for a Board to agree to such a request, the patient would need to be: a) significantly different to the general population of patients with the condition in question; and, b) likely to gain more benefit from the medicine than the average patient. These criteria were referred to as “exceptional circumstances”. NHS Boards had their own procedures for dealing with such decisions.

Following on from the issues raised by petition PE1108, concerning the provision on the NHS of cancer treatment medicines, the Scottish Government published guidance in May 2010, which set out a framework for the development of NHS Board written policies for dealing with such requests, now known as Individual Patient Treatment Requests (IPTRs). In March 2011, the Chief Medical Officer for Scotland set out good practice guidelines on the process Boards should seek to apply in dealing with IPTRs. This was followed up in February 2012 by additional guidance, which included measures designed to assist NHS Boards further in their consideration of IPTRs. The process for the eligibility, referral and consideration of IPTRs are detailed in Appendix 2. The Scottish Government (2012a) expects these processes to be used though accepts there will need to be a degree of flexibility:

“NHS Boards are expected to apply common principles and processes in the introduction of newly licensed medicines in order to facilitate consistency of approach to local decision-making. However, IPTR decisions will be based on local clinical opinion on a “case by case” basis for individual patients and, as such, cannot be generalised.” (p 12).

Each Board’s written policy should have been in place by 1 April 2011, and they should be available on the Board’s website. Boards were expected to involve patients and the public in the development of their policies through their patient focus and public involvement arrangements. In addition, it is expected that NHS Boards are monitoring and collecting data on IPTR requests and their outcome (including Appeals). The Scottish Government (2012a, p 12) is also keen that the rationale behind each decision is being recorded, which, it believes will help Boards to share good practice in relation to the IPTR process. Boards have also been asked to consider reviewing GP prescribing of SMC “not recommended” medicines as part of on-going reviews of primary care prescribing. It should be noted that there is no central database with records of IPTR decisions.
PART 3: FURTHER CONSIDERATIONS

There are two key issues related to the assessment of new medicines which are worth outlining in this briefing. The first concerns the pricing of medicines and the second concerns the commissioning of highly specialised medicines through risk share schemes.

PRICING OF MEDICINES

Pharmaceutical Price Regulation Scheme

The Pharmaceutical Price Regulation Scheme (PPRS) is the mechanism which the Department of Health (DoH) in England, on behalf of the four UK health departments, uses to regulate the prices of branded medicines. It is a voluntary scheme, usually negotiated every five years, between the DoH and the pharmaceutical industry though is underpinned by statutory powers. It seeks to achieve a balance between reasonable prices for the NHS and a fair return for the industry to enable it to research, develop and market new and improved medicines.

Patient Access Schemes

The 2009 PPRS sought the introduction of more flexible pricing options to enable drug companies to improve the value of specific medicines to the NHS. One of these options was the creation of Patient Access Schemes (PAS). A PAS is an agreement reached with a pharmaceutical company where discounts or rebates are offered to reduce the costs of a medicine to the NHS. This then improves its cost-effectiveness, and thus enhances the likelihood of availability.

PAS were introduced in Scotland following consideration by a Short Life Working Group convened by the SMC. It was agreed they could bring benefits to patients by enabling access to medicines that are not, or might not be initially, considered to be cost-effective by the SMC.

In the context of the process for appraising medicines in Scotland, the manufacturer would propose a PAS when making a submission for a new medicine to the SMC. The PAS Assessment Group (established under the auspices of NHS National Services Scotland) will carry out an assessment of the PAS in a process independent of the SMC. Where a PAS is considered feasible, the SMC is then able to take account of the discount offered under the terms of the PAS. Where a PAS is not considered feasible, SMC appraises the drug on its standard costs. It is worth noting that that whilst the PAS and SMC processes are separate, it is not possible to have a PAS in isolation from SMC advice. In addition, when the SMC accepts a medicine with a PAS the acceptance is reliant on the implementation and continuing availability of the PAS.

The Scottish Government (2012b) has stated that the introduction of these schemes has played an important role in helping more patients to access drugs that would not otherwise be assessed as cost-effective by the SMC.

Value based pricing

The UK coalition Government stated, in its programme for government, its intention to reform arrangements for the pricing of branded medicines and to introduce a new system of value-based pricing (VBP).
On 16 December 2010, the UK Department of Health (DoH) published a consultation on the proposal. The DoH noted that the current PPRS, introduced in 2009, did introduce more flexible pricing options, which enabled drug companies to improve the value of specific medicines on offer to the NHS e.g. Patient Access Schemes. However, despite such developments it did not believe that these were long term solutions to the problem that having freedom of pricing in new medicines “puts the NHS in the position of either having to pay high prices that are not always justified by the benefits of a new drug, or having to restrict access” (2010, para 2.14). It added:

“There must be a much closer link between the price the NHS pays and the value that a medicine delivers. The Government is determined to create a system that gives patients access to the most effective medicines. If companies decline to supply a medicine at a price that relates to its value, it will be their responsibility to explain why.” (2010, para 2.15).

In addition, the DoH outlined how it believed a new system would provide more stability to the pharmaceutical industry, recognise and reward innovation and deal better with new medicines where the benefits are more limited.

Ultimately, the goal of VBP can be said to better align price with value delivered. The UK Government sees VBP as addressing a broad set of objectives:

- improve outcomes for patients through better access to effective medicines
- stimulate innovation and the development of high value treatments
- improve the process for assessing new medicines, ensuring transparent, predictable and timely decision-making
- include a wide assessment, alongside clinical effectiveness, of the range of factors through which medicines deliver benefits for patients and society
- ensure value for money and best use of NHS resources

Chapters four and five of the consultation document then go on to discuss how the system might look and operate. However, a key part of the proposals relates to the setting of a range of thresholds or maximum prices reflecting the different values that medicines offer. The threshold structure would be determined as follows:

1. a basic threshold, reflecting the benefits displaced elsewhere in the NHS when funds are allocated to new medicines
2. higher thresholds for medicines that tackle diseases where there is greater “burden of illness”: the more the medicine is focused on diseases with unmet need or which are particularly severe, the higher the threshold
3. higher thresholds for medicines that can demonstrate greater therapeutic innovation and improvements compared with other products
4. higher thresholds for medicines that can demonstrate wider societal benefits

The document then goes on to describe these in greater detail and seek views on them (see Chapter 4).

The consultation closed on 17 March 2011, and the DoH published a response to the submissions received on 18 July 2011. It found a majority of respondents supported the principles underlying the need to move to a new system of pricing for branded medicines. However, there was a significant amount of debate about what that new system should look like. Overall, the DoH said it would seek to continue to engage with relevant stakeholders to reform the pricing of medicines, but stated its intention of pursuing VBP but through an agreement, with negotiations beginning at some point in 2012.
One of the key issues with the DoH’s proposals is that they would have an effect on the way medicine technology appraisals are undertaken, which as discussed above is a devolved matter. Discussions are still on-going with the purpose of further clarifying how the system would work. On 3 August 2012, the Association of the British Pharmaceutical Industry (APBI) and DoH published a joint statement, which discussed this issue:

“It is important that there is a common branded medicines pricing policy across the UK and we expect the new arrangements to form part of a UK-wide scheme. However, the Devolved Administrations determine many aspects of health policies, including those affecting the use and availability of medicines within their health systems. It will therefore be important to ensure close working with the health departments of the Devolved Administrations and with their HTA bodies to ensure a coordinated and coherent approach.” (ABPI and DoH, 2012, p 4).

The current view of the Scottish Government is outlined in an answer to a Parliamentary Question on 23 April 2012, given by the Cabinet Secretary for Health, Wellbeing & Cities Strategy:

“I have corresponded with the Secretary of State for Health several times concerning both the earlier consultation and on the need for full involvement in the design of the proposed value based pricing initiative. I have received assurances that the UK Government and the devolved administrations will continue to work closely together in developing a value based pricing approach. Officials have also been involved in UK-wide discussions concerning the value based pricing of medicines.” (Scottish Parliament, 2012).

**RISK SHARING SCHEMES**

Some medicines, such as orphan medicines, which are deemed highly specialised may be commissioned nationally through a risk sharing scheme operated by National Services Division (NSD) of NHS National Services Scotland (NSS). NSD (2012) outlines the process for establishing whether a medicine should be included in the scheme. This is summarised below.

In the first instance a NHS Board will make a submission asking for a medicine to be placed in the scheme. NSD then establishes whether the medicine has been considered by the Scottish Medicines Consortium and gathers information on the likely numbers of patients who might be assessed as requiring the therapy, and likely total costs to NHS Scotland. NSD then submits this information to the NHS Board Chief Executives’ Group for consideration and decision on inclusion (or otherwise) of the medicine.

To be included, the medicine in question must have been accepted for use by the SMC. The criteria used by NHS Boards to decide which services or therapies fall within the risk share arrangement are:

- the incidence of the condition to be treated is very rare or is unpredictable and sporadic

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8 NSD commissions and manages national screening programmes and specialist clinical services on behalf of NHSScotland
9 NSS is a Non Departmental Public Body which provides advice and services to the rest of NHSScotland. As well as NSD, its health support divisions include Health Protection Scotland and Information Services Division. Its business support divisions include the Central Legal Office and Practitioner Services.
10 The only exception to this relates to 3 Enzyme Replacement Therapies (ERTs) which have been previously agreed by Board Chief Executives for inclusion in the risk share list. These 3 ERTs are currently eligible for inclusion in the national risk share arrangements only where there has been a local recommendation for their use following an Individual Patient Treatment Request.
• the effect is so financially significant that individual NHS Boards could be at financial risk
• clinical practice across Scotland is based on appropriate clinical evidence and/or national protocols (where available), such that services can demonstrate equity of access to treatment across Scotland (accepting there may be local and individual patient needs)
• that there are no unexplained differences in either clinical practice or costing methodology which unbalance the share of costs in one part of the country against another

Advisory Group for National Specialised Services (AGNSS) in England

It is worth noting that in England, over the past couple of years, AGNSS had the role of considering a small number of highly specialised new drugs and technologies, usually consisting of no more than 500 patients and/or four centres in England. However, it should be noted that, at the time of writing, it has not published any guidance. Its role had been to make recommendations to Ministers about whether the drugs and technologies it considers are appropriate for commissioning at a national level. AGNSS only considered drugs and technologies that NICE decided were not suitable for a NICE appraisal because of the very small patient numbers involved.

In light of the Health and Social Care Act 2012, which established a NHS Commissioning Board in England, AGNSS suspended considering these medicines. On 19 July 2012, the UK Department of Health (2012) announced that NICE was to take over this work from April 2013.
SOURCES


Healthcare Improvement Scotland. [Online]. Available at: http://www.healthcareimprovementscotland.org/about_us.aspx


Scottish Medicines Consortium. [Online]. Available at: http://www.scottishmedicines.org/Home


Scottish Medicines Consortium. (2012a) SMC Modifiers used in Appraising New Medicines. [Online]. Available at: http://www.scottishmedicines.org.uk/About_SMC/Policy_Statements/SMC_Modifiers_used_in_Appraising_New_Medicines

Scottish Medicines Consortium. (2012b) Personal communication.


# APPENDIX 1: SUMMARY OF THE NICE MULTIPLE TECHNOLOGY APPRAISAL PROCESS

<table>
<thead>
<tr>
<th>Provisional appraisal topics chosen</th>
<th>The Department of Health (DH) produces a list of provisional appraisal topics.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consultees and commentators identified</td>
<td>Read more about consultees and commentators.</td>
</tr>
<tr>
<td><strong>Scope prepared</strong></td>
<td>NICE works with the DH to develop a scope. The scope defines the disease, the patients and the technologies covered by the appraisal and the questions it aims to answer. Consultees and commentators are requested to comment on the draft scope.</td>
</tr>
<tr>
<td><strong>Appraisal topics referred</strong></td>
<td>The DH refers technology appraisal topics to NICE.</td>
</tr>
<tr>
<td><strong>Evidence submitted</strong></td>
<td>NICE invites consultees and commentators to provide a submission. A submission is a concise, comprehensive and structured report of all relevant information (published and unpublished) for an appraisal.</td>
</tr>
<tr>
<td><strong>Assessment report prepared</strong></td>
<td>NICE commissions an independent academic centre to review published evidence on the technology and prepare an assessment report. Consultees and commentators are invited to comment on the report.</td>
</tr>
<tr>
<td><strong>Evaluation report prepared</strong></td>
<td>Includes all of the evidence that will be looked at by the Appraisal Committee. This evidence includes:</td>
</tr>
<tr>
<td></td>
<td>- the assessment report</td>
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<td></td>
<td>- written submissions</td>
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<td>- patient expert personal statements</td>
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<td></td>
<td>- clinical specialist personal statements</td>
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<td></td>
<td>- comments received on the assessment report.</td>
</tr>
<tr>
<td><strong>Appraisal Committee</strong></td>
<td>An independent advisory committee considers the evaluation report and hears evidence from nominated clinical experts, patients and carers. The Committee discussions are held in public.</td>
</tr>
<tr>
<td><strong>Appraisal consultation document (ACD) produced</strong></td>
<td>The Appraisal Committee makes its provisional recommendations in the ACD. Consultees and commentators have four weeks to comment on the ACD. The ACD is also made available on the NICE website so health professionals and members of the public can comment on it.</td>
</tr>
<tr>
<td><strong>Final appraisal determination (FAD) produced</strong></td>
<td>The Appraisal Committee considers the comments received on the ACD, then makes its final recommendations in the FAD on how the technology should be used in the NHS in England and Wales. Consultees can appeal against the final recommendations in the FAD.</td>
</tr>
<tr>
<td><strong>Guidance issued</strong></td>
<td>If there are no appeals, or an appeal is not upheld, the final recommendations are issued as NICE guidance.</td>
</tr>
</tbody>
</table>

Source: NICE (online) ‘Developing NICE multiple technology appraisals’
APPENDIX 2: SUMMARY OF THE IPTR PROCESS

Scope of IPTR requests

IPTRs can only be sought:
- for a medicine within its licensed indication (i.e. to treat the condition it was licensed to treat)
- where the patient's clinician fully supports the request

IPTRs can be made when:
- the SMC or Healthcare Improvement Scotland has not recommended the use of a medicine (including where the SMC does not recommend a medicine because the pharmaceutical company has not made a submission)
- the request relates to the use of a medicine outside the restriction in the case of a medicine SMC has recommended restricted use
- before the SMC or Healthcare Improvement Scotland has issued advice on the medicine – only in circumstances where the clinician believes a delay in treatment pending the advice would result in a significant adverse outcome for the patient.

Referral criteria for IPTRs

The responsibility making an IPTR rests with the patient's clinician, who is expected to produce a Case Report demonstrating the clinical case for the patient, using the criteria that the patient’s clinical circumstances (condition and characteristics) are significantly different for either:

I. the general population of patient covered by the medicine’s licence

II. the population of patients included in the clinical trials for the medicine’s licensed indication as appraised

Thus, in being given the medicine the patient would gain significantly more benefit from the medicine that would normally be expected.

Clinicians submitting IPTRs are encouraged to seek peer support for the application from colleagues within and outwith their own NHS Board. This is to provide the clinician the opportunity to have their assessment of the potential benefit that a medicine may bring peer reviewed.

IPTR Case Report

This report should comprise:
- the rationale for the IPTR request including patient treatment history, prognosis and specific clinical characteristics;
- information on expected response and benefit;
- consequences of not using the treatment from both a patient and service perspective;
- consequences of using the treatment; and
- any other relevant information such as case reports, further evidence from literature reviews.

IPTR Panels

Requests should be considered by an IPTR Panel, constituted by the NHS Board. The Panel should include a practising medical consultant with (or with access to) specialist knowledge of the relevant clinical area. In addition other appropriate medical, pharmaceutical and managerial (including finance) expertise should also be represented. Members should declare any potential conflicts of interest.

All Members of the Panel should have the opportunity to undertake adequate training, and all should be well versed in the NHS Board’s policy on the managed entry of newly licensed medicines.
Consideration of the IPTR
IPTRs decisions should be based on a range of evidence including the SMC/Healthcare Improvement Scotland advice where available, the referral criteria and the IPTR Case Report from the requesting clinician.

Timescales for IPTR decisions
IPTRs should be prioritised according to the patient’s clinical needs. NHS Boards are expected to undertake an initial examination of the IPTR to ensure consideration is given to the urgency of the request.

Communicating IPTR decisions
The decision should be provided to the requesting clinician, who should then communicate this to the patient. In addition, an accompanying letter from the Chair of Panel should be provided explaining the rationale for the decision. The clinician should then discuss all options open to the patient, and provide contact details for support services with the NHS Board.

IPTR Appeals
NHS Boards should put in place an appeals process which can accommodate the following grounds:

- The NHS Board did not act fairly i.e. due process was not followed
- The NHS Board reached a decision which cannot be justified in light of the evidence received

An appeal can be referred where the patient’s clinician supports it. A Panel should then be established to facilitate a timeous review in accordance with the patient’s clinical circumstances. It should not include any of the members of the IPTR Panel that made the original decision, but its composition should be on the same terms as any IPTR Panel. The Appeals Panel is expected to consider: the NHS Board’s policy on IPTRs; the written evidence submitted in respect of the IPTR; and, the written account of the rationale for the IPTR decision reached. On reaching a decision this should be given to the clinician who should pass this onto the patient. As with IPTR Panels, the patient should receive a letter from the chair of the Appeals Panel explaining the rationale for the decision. Support services should then be offered to the patient.
RELATED BRIEFINGS

Briefing SB 08-17: ‘Licensing of Medicines in the UK and their Use in the NHS’

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