



National Assembly for Wales
Cynulliad Cenedlaethol Cymru

The Approval of Drugs and Medicines in Wales, England and Scotland

Abstract

This paper provides background briefing on the process by which drugs and medicines are licensed, regulated, and approved for use in the health service in Wales, England and Scotland.

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The Approval of Drugs and Medicines in Wales, England and Scotland

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Approval of drugs and medicines

1 Introduction

Issues around access to, licensing and assessment of drugs and medicines have been highlighted by several cases of patients being denied access to the drug Herceptin, which is currently only licensed in the UK for treatment of secondary stage breast cancer.¹ In light of recent cases the National Assembly for Wales held a debate in plenary on the approval of drugs on 7 February 2006 and the Welsh Assembly Government has established a New Drugs Project Board to examine the issues around licensing and assessment of new drugs and medicines in Wales. This research paper explores the process by which drugs and medicines are licensed, regulated and assessed for use in the health service in Wales, England, and Scotland. A broadly similar process is followed in Wales and England, although there are some differences in the process in Scotland.

2 Licensing and regulation of drugs and medicines in the UK

2.1 *The Medical and Healthcare Products Regulatory Agency (MHRA)*

The MHRA² is responsible for licensing and regulating medicines throughout the UK to ensure that they work properly and are acceptably safe.³ It continues to monitor and act against any risks after the product has been licensed. The MHRA works closely with the European Medicines Agency (EMA), which is responsible for drugs for export from the UK to the EU, and vice versa. EMA also co-ordinates the evaluation and suspension of medicinal products throughout the EU.

Once a product has been licensed, it can be prescribed by doctors, but only to people who meet the conditions for which the product is licensed, for example the specific stage or type of a disease. In practice, some doctors do not prescribe a drug until more information is available, and some Local Health Boards (LHBs), (or Primary Care Trusts in England) do not allow new drugs to be prescribed until guidance has been received from the National Institute for Health and Clinical Excellence (NICE) (see section 2.2 below). Some doctors will prescribe drugs and medicines before they have received their licence, or for people outside the conditions of the licence. This practice is known as off-licence or off-label prescribing.

3 Assessment of drugs and medicines in Wales

An initial assessment of new drugs and medicines in Wales is provided by the All Wales Medicines Strategy Group (AWMSG) pending the provision of more detailed guidance by the National Institute for Health and Clinical Excellence. Further information on the work of NICE and the AWMSG is outlined below.

3.1 *The All Wales Medicines Strategy Group*

The AWMSG provides interim recommendations to the Welsh Minister for Health and Social Services on medical products based on clinical and cost-effectiveness data, prior to the publication of NICE guidance (see 2.2 below). The Group's advice focuses on high cost products, i.e. those products with the potential to cost the NHS in Wales over £2,000 per patient per year, including associated costs and the estimated number of patients who

¹ On 9 June 2006 a NICE press release confirmed that new draft guidance expected to be published in early July will recommend Herceptin for women with early stage breast cancer, except where there are concerns about the woman's cardiac function. The full press release is available at: <http://www.nice.org.uk/page.aspx?o=328789>

² Further information on the work of MHRA is available at:

http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&nodeId=20

³ The MHRA also regulates and licences medical devices, nanotechnology, and blood and tissue products in the UK.



would be treated with the product. The Group also advises the Minister in a strategic and advisory capacity on future developments in healthcare, to inform strategic planning.^{4 5} The AWMSG takes into account the NICE future work programme when considering whether to appraise a product, and will not normally consider a product if NICE intends to publish a final appraisal of that product within 18 months.

3.2 *The National Institute for Health and Clinical Excellence*

NICE is an independent organisation responsible for providing guidance on the promotion of good health, and the prevention and treatment of ill health in England and Wales. A key element of its work is the provision of guidance on the use of new and existing medicines, treatments, and procedures in the NHS in Wales and England, through its Technology Appraisals.⁶

On 6 March 2006 the Department of Health launched a consultation on proposals to give NICE a greater say in the selection of its topics for appraisal, although the final decision will remain with Ministers. The proposals aim to accelerate the referral of topics to NICE, and allow higher priority to be given to topics with the greatest impact on the NHS and patients.⁷

3.2.1 *NICE Technology Appraisals*

NICE Technology Appraisals recommendations are based on a review of clinical and economic evidence, and are prepared by an independent Appraisal Committee, made up of NHS professionals and people familiar with issues facing patients and carers. The committee consults patient organisations, carers, health professionals, manufacturers, and relevant NHS organisations. Consultees can comment on the scope of the appraisal, submit evidence to the committee, recommend other consultees, comment on the committee's provisional recommendations, and appeal against the committee's final decision. Members of the public and health professionals who are not formally consulted can send their own feedback to NICE for a period of three weeks after the appraisal consultation is published. NICE Technology Appraisals usually take 12-18 months to complete. Further detailed information on NICE Technology Appraisals is provided in the NICE document *Guide to the methods of technology appraisal*, a copy of which is available on the NICE internet site.⁸

3.2.2 *Implementation of AWMSG decisions and NICE Technology Appraisals*

Pharmaceutical companies are required to notify the AWMSG of details of all new products and medications before being launched, which allows the Group to make a recommendation soon after the product is launched. If a drug or medicine is supported by the AWMSG and is approved by the Minister, LHBs and NHS Trusts in Wales must make funding available within three months of notification of the ministerial decision. Similarly, LHBs and NHS Trusts in Wales must implement NICE Technology Appraisals within three months of publication, although in exceptional circumstances the Welsh Assembly Government has extended the timescale for implementation.⁹

⁴ Further details of the role of the Group, including the AWMSG's current Appraisal Programme, are available on the AWMSG internet site at: <http://www.wales.nhs.uk/sites3/page.cfm?orgid=371&pid=2036>.

⁵ Further details of the role of the AWMSG are available under the "Drug Appraisals" section of the AWMSG internet site in the "Frequently Asked Questions document" and in the "AWMSG Appraisal Work Programme" document. Available at: <http://www.wales.nhs.uk/sites3/page.cfm?orgid=371&pid=2036>

⁶ NICE's other responsibilities include provision of guidance on public health (England only), and on the treatment and care of specific conditions. Further details are available in the NICE document, *A Guide To NICE*, April 2005: <http://www.nice.org.uk/pdf/NewguidetoNICEApril2005.pdf>

⁷ Further details are provided on the Department of Health internet site at: http://www.dh.gov.uk/PublicationsAndStatistics/PressReleases/PressReleasesNotices/fs/en?CONTENT_ID=4131170&chk=s5kDTT

⁸ NICE, *Guide to the methods of technology appraisal*, April 2004: http://www.nice.org.uk/pdf/TAP_Methods.pdf

⁹ Welsh Assembly Government, *Welsh Health Circular (2003) 109, New directions to Local Health Boards and NHS Trusts in Wales to fund implementation of NICE Technology Appraisal Guidance*, 29 October 2003: <http://assembly.health/Key-Publications/Circulars/2003/whc-2003-109-e.pdf>

3.2.3 *How NICE priorities are set*

The NICE work programme is set by the Department of Health in consultation with the Welsh Assembly Government. Approximately every six months, a "wave" of appraisals and guidelines topics are referred to NICE by the Department of Health. Details of the current 12th wave are outlined in a NICE press release of 24 November 2005, a copy of which is available on the NICE internet site.¹⁰

4 Assessment of drugs and medicines in England

As described in section 2.2, assessments and guidance on the use of drugs and medicines is provided to the health service in England through NICE Technology Appraisals. English health Ministers do not have an equivalent group to the AWMSG, but receive advice from the following MHRA committees and Expert Advisory Groups, each of which has a specific remit:

- The Commission for Human Medicines (CHM) which advises on new drugs and medicines and the balance of risks associated with them;
- Section 4 committees - which advise on herbal medicines, homeopathic products, and the British Pharmacopoeia Commission;
- A range of Expert Advisory Groups (EAGs) focusing on individual specialties such as the psychiatry and old age psychiatry EAG, which undertake detailed examination of issues prior to referral to the CHM.

5 Assessment of drugs and medicines in Scotland

Advice to the NHS in Scotland on drugs and medicines is provided by NHS Quality Improvement Scotland (NHS QIS),¹¹ which is a Special Health Board in Scotland responsible for improving the quality of healthcare and treatment, and the patient experience in Scotland. NHS QIS orders its work on the basis of national clinical priorities set for NHSScotland, and takes into account specific pieces of work identified as a clinical priority by the Minister for Health and Community Care. In addition, the Scottish Medicines Consortium, which is part of NHS QIS, provides initial advice to Scottish Ministers, in a similar role to that provided in Wales by the AWMSG. The main forms of advice provided by NHS QIS, and further information about the SMC, are outlined below.

5.1.1 *Health Technology Assessments (HTAs)*

NHS QIS provides NHSScotland with detailed advice on selected topics through its Health Technology Assessments. These focus on the clinical and cost-effectiveness of drugs and medicines, as well as all forms of diagnosis and treatment of conditions. HTAs also focus on health promotion, rehabilitation, clinical procedures, medical devices and patient / organisational issues, such as the need for training and equipment. Health Boards in Scotland are required to meet standards set out in HTAs. Typically HTAs take 12-15 months to complete.

5.1.2 *Evidence Notes*

These have no formal status, but provide brief information which Health Boards in Scotland have identified as being significant in relation to a particular drug or procedure. Evidence Notes usually take 1-3 months to produce.

¹⁰ NICE, *NICE welcomes referral of new work programme topics*, 24 November 2005:
http://www.nice.org.uk/pdf/2005_029_12th_wave_announcement.pdf

¹¹ Further information on the work of NHS QIS is available on its internet site at:
http://www.nhshealthquality.org/nhsqis/qis_display_wide.jsp?pContentID=1835&p_applic=CCC&pElementID=153&pMenuID=140&p_service=Content.show.

5.1.3 *Applicability of NICE guidance in Scotland*

NICE Technology Appraisals are not applicable in Scotland in their own right, but NHS QIS advises NHSScotland on the relevance to the NHS in Scotland of each new NICE Technology Appraisal when it is published. NICE consults NHS QIS before beginning a Technology Appraisal.

5.2 *The Scottish Medicines Consortium (SMC)*

As noted above, the SMC is part of NHS QIS and carries out its functions independently of Ministers. The SMC provides advice to Scottish Ministers on new drugs in a similar role to that provided by the AWMSG in Wales.

Pharmaceutical companies are required to provide a New Product Submission to the SMC for all newly licensed products, and the SMC advises NHSScotland on the clinical and cost-effectiveness of all newly licensed medicines, new formulations of existing medicines, new conditions which particular medicines can be used for and medical devices licensed by the MHRA.¹²

Decisions about approval of new drugs are taken by the members of the SMC, which is made up of a wide range of health professionals and lay representatives. The SMC also takes advice from its New Drugs Committee, comprising experts in the pharmaceutical field, and also from its Patient and Public Involvement Group. Details of the membership of each of these groups are available on the SMC internet site.¹³ The SMC usually notifies pharmaceutical companies of its decisions within 14 weeks of receiving a New Product Submission, and decisions are usually published four weeks later to allow discussion with the pharmaceutical company.

6 National Assembly for Wales debate in plenary, and establishment of a New Drugs Project Board

6.1 *National Assembly for Wales debate in plenary on Drugs Approval, 7 February 2006*

In early 2006 concerns around the availability of the drug Herceptin for early stage breast cancer highlighted the issue of the approval of new drugs generally. The National Assembly for Wales debated the approval of drugs in a debate sponsored by the Liberal Democrats in plenary on 7 February 2006.¹⁴ At the conclusion of the debate the following motions were unanimously passed by the Assembly:

1. The National Assembly calls for the process for approving new drugs to be speeded up so that they become available more quickly to patients in Wales;
2. The National Assembly requires the Welsh Assembly Government to commission an urgent study to report into methods by which new drugs can be made available more quickly;
3. The study should include the full cost implications in the short, medium and longer term and an examination of the Scottish drugs approval process; and
4. [The National Assembly] welcomes the news that after receiving advice from the south-east Wales and north Wales cancer networks, local health boards in these areas have agreed to prescribe Herceptin to treat early-stage breast cancer but regrets that this is not the case throughout the whole of Wales.

¹² Further details of SMC's work are available at: <http://www.scottishmedicines.org.uk/>

¹³ At: <http://www.scottishmedicines.org.uk/membership.asp>

¹⁴ a transcript of the debate is included in the copy of *Record of Proceedings*, available at: <http://assembly/rop/ROP/Plenary%20Session/2006/February/rop060207fv7.pdf>



6.2 *Establishment of a New Drugs Project Board*

Following the debate, the Welsh Assembly Government established a *New Drugs Project Board* to conduct a scoping exercise of the issues of licensing and assessment of drugs. A copy the group's initial briefing paper is attached at Annex 1, which discusses proposals under consideration such as:¹⁵

- Making better use of the National Horizon Scanning Centre in England, which identifies new and expensive drugs and medicines that may be coming on to the market in the next 3-5 years;
- The All Wales Medicines Strategy Group to collaborate more closely with other UK bodies such as the Scottish Medicines Consortium and the National Horizon Scanning Centre;
- Earlier assessment of the impact of existing licensed drugs and medicines; and
- No drugs to be prescribed without a license, or alternatively, requiring any drugs being prescribed off-licence and post-clinical trial to be licensed under clinical trial conditions where appropriate;
- Increased resources to facilitate the above proposals.

The Group will finalise its recommendations to Ministers by August 2006.

¹⁵ Welsh Assembly Government, *Improving The Management Of The Introduction Of New Drugs And New Indications For Existing Drugs Into The NHS In Wales*.

Annex 1

IMPROVING THE MANAGEMENT OF THE INTRODUCTION OF NEW DRUGS AND NEW INDICATIONS FOR EXISTING DRUGS INTO THE NHS IN WALES

Purpose

1. To review and strengthen the framework for managing the introduction of new drugs and new indications for existing drugs into the NHS in Wales, learning the lessons from the difficulties experienced through the recent availability of Trastuzumab (Herceptin) for early stage breast cancer. This review process will identify 'gaps' in the current process and address the different issues raised when dealing with New Chemical Entities (NCE) and extensions to existing market authorisations. This will include addressing clinical trials and the development of exit strategies for patients involved in these trials, especially when trials close early.

Key Considerations

2. It will be essential to gauge accurately the number of new drugs, and new indications for existing drugs, expected to come into use as early as possible in the process and to make this information available to commissioners. More detailed information regarding service requirements and expected costs must also be made available to commissioners for advance resource planning. Rigorous and transparent processes will be needed both within the Welsh Assembly Government and across the NHS in Wales in order to manage the challenges and pressures presented by an increasing number of new drugs that are actively marketed by the pharmaceuticals industry and members of the public who are increasingly well informed and organised.

Scale and Cost

3. The Welsh Assembly Government, NHS and partner organisations need to make better and more effective use of the National Horizon Scanning Centre set up and funded by the Department of Health in England. That looks ahead 3 to 5 years and is an invaluable source of information via its New and Emerging Technology Briefings for new and expensive drugs and treatments coming on stream. This will be complemented by information gathered through clinical networks and other research-based evidence. The role of clinicians engaged in the Clinical Networks is a vital component in identifying the potential of new and existing drugs as they act as the 'eyes and ears' of developments in their areas of expertise. This clinical knowledge must be central in informing the decisions about the targeting of appraisal resources for those drugs to be appraised in the home countries prior to NICE appraisal. Also, engagement with the Pharmaceutical Industry at an early stage at Welsh Assembly Government level and with the clinical networks will provide additional valuable insight to enhance the accuracy of these predictions. Additionally, opportunities exist to enhance the intelligence gathering capability on the future of new and existing drugs through creative partnership with the Industry.

4. More detailed work needs to be done to assess the full cost impact and cost effectiveness of new drugs and new indications for existing drugs on the NHS services in Wales. Figures produced in the past for new drugs may have been unreliable and based on incomplete information. Existing drugs have a much higher degree of certainty with regard to cost, safety and capacity of the NHS to use them. The impact assessment of potential new indications of existing licensed drugs could be undertaken much earlier as



an extension to the original appraisal process in advance of the granting of a marketing authorisation for those indications. Cost assessments will need to cover all direct costs associated with the implementation of the new drug therapy (testing, staff training etc) and not be confined to the cost of the drug alone. This will need to be balanced against an estimate of the costs saved or deferred as a result of drug induced remission of disease. Resources Directorate will develop a sound and scientific methodology for assessing the full cost impact of new drugs in consultation with the Department's Clinical Advisors and Policy Leads. Consideration will also be given as part of the development of new commissioning arrangements as to how new drugs integrate into the care pathway and other systems of care for disease.

5. The Welsh Assembly Government will need to gain a better understanding of the Pharmaceutical Price Regulating Scheme (PPRS) which is used to monitor and regulate the level of profit made by pharmaceutical companies and which helps to manage the overall cost of pharmaceutical products to the NHS in the UK as a whole. This will help inform the cost impact methodology to be developed by the Resources Directorate.

Processes

6. A number of gaps in process had been identified following the availability of Trastuzumab (Herceptin) for early stage breast cancer. Gaps were evident both in the appraisal and monitoring systems operated by the Welsh Assembly Government and in the drug prescribing approval and accountability systems operated between individual clinicians, NHS Trusts and Local Health Boards across Wales.

7. The priority in dealing with drugs being prescribed off licence, in the post-trial, pre-licensing period, must be patient safety. Requiring clinicians prescribing these high cost drugs off licence to do so under clinical trial conditions where this is feasible, collecting and feeding data into the various licensing/appraisal/audit procedures, is suggested as the primary way forward for the NHS in Wales. Such an approach is likely to have resource implications and may face resistance from clinicians because of the additional burden it places on their day to day work, although in the cancer field information systems already support such collection. The issues of transfer risk and liability must be considered when clinical trials are stopped and a larger cohort of eligible patients appears. However, the number of patients involved will limit the value of data collection for Wales alone. Given the challenges, the Chief Medical Officer will be approaching his opposite numbers in the other UK Health Departments to explore the scope for a unified UK wide approach to off licence prescribing.

8. It is considered essential to put in place a mechanism to prevent the routine prescribing of drugs yet to receive either a licence or a positive appraisal from an UK regulatory authority. In Scotland, no new drugs (licensed or unlicensed) are prescribed without first receiving a positive appraisal from the Scottish Medicines Consortium (SMC) and it is recommended that Wales should adopt similar restrictions. This will involve refocusing the work of the All Wales Medicines Strategy Group more in the direction of the information emerging from Horizon Scanning, Clinical Networks and Clinical Advisors. A collaborate approach should be explored with AWMSG, NICE and the SMC to limit the duplication of effort and share the limited expertise that exists in the UK to deliver a more rapid response.

9. There is also a need to harness the resources for new drug impact assessment other bodies, such as the Wales Centre for Health and National Public Health Service in Wales, can offer to ensure maximum efficiency and minimum duplication of effort. Officials



will bring together all relevant bodies in an effort to concentrate effort on the challenges presented by the introduction of new drugs and new indications for existing drugs.

10. A further key element in the management of new drugs is the procedures used by Local Health Boards and NHS Trusts in Wales for dealing with requests from clinicians to prescribe unlicensed drugs. There is a need for greater consistency of approach in dealing with such requests from clinicians in the interim. It is likely that there will need to be a mechanism for dealing with specific requests for specific patients for drugs which fall outside the definitions of expensive or high cost drugs. There is also a problem with the approval procedures for licensed drugs that had still to receive positive appraisal either from NICE or from the AWMSG. The ideal solution would be to bring the timelines for appraisal and licensing as close together as possible. It may be possible to achieve this through mechanisms for assessing data submitted as part of the licensing process and applying it to the appraisal process – a parallel track approach. For new drugs these problems will be largely resolved through the introduction of the appraisal barrier proposed in this paper. The supply chain for new drugs is easier to contain and control. Drugs already approved for other indications present a greater challenge in containing supply. Officials will consider a sample of the procedures currently being used by Local Health Board and Trusts, and recommend a best practice procedure to be used across the NHS in Wales.

11. It should be noted that that the resources required to deliver the activity described above is likely to be significantly greater than that applied now, despite the economies that collaboration across the UK will bring. In particular, there are like to be significant cost implications arising from the work currently being undertaken by the Welsh Medicines Partnership and AWMSG to improve the reaction time for the appraisal of new drugs and new indications for existing drugs. A detailed business case will need to be presented to the Minister. This additional investment should however be balanced against the benefit of not approving certain drugs, the reduction in crisis management arising from the surprises we get now, and the assurance gained from greater confidence that expenditure on new drugs is targeted appropriately.

1 Outputs

12. A Project Board will be established under the chairmanship of the Head of the Department for Health and Social Services to manage the implementation of the recommendations made in this paper. The recommendations themselves will need to be developed following input from the other organisations mentioned and feedback from discussions with the other home countries. Secretariat will be provided by the Healthcare Standards Branch and will report progress to the Minister as directed by the Board.

13. The principal aim of the Project Board will be remodel the existing drug approval/appraisal processes in Wales and to ensure the publication of comprehensive revised guidance to the NHS and partner organisations by August 2006.