

# ORIGINAL ARTICLES

## Scottish Medicines Consortium: an Overview of Rapid New Drug Assessment in Scotland.

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## Introduction

In the past decade, separate external reviews in Scotland and England & Wales have highlighted the need to ensure best value for money from increasing drugs budgets.<sup>1,2</sup> Based on this principle, and because of valid concerns from the public, press and politicians about regional variations in the availability of new medicines (so-called 'post-code' prescribing), new systems have been established to assess the clinical and cost-effectiveness of new medicines; the Scottish Medicines Consortium (SMC) and the National Institute for Clinical Excellence in England and Wales (NICE).<sup>3,4</sup> When first created there were distinctly different, and complementary, approaches taken by SMC and NICE, whereby NICE focused on multiple technology appraisal (MTA), usually of a range of interventions, including medicines, for a single disease area.<sup>5,6</sup> NICE MTA review for medicines was often fairly late after licensing, whereas SMC focused on rapid individual appraisal of all newly licensed medicines, as well as major new indications and formulations for existing products as soon after launch as possible. Recently, NICE has started to undertake single technology appraisal (STA), a process of assessment for selected new drugs close to launch with a number of similarities to the activity of the SMC. In this review we will reflect on the role of the SMC and its achievements, providing a comparison with the work of NICE and discussing future challenges.

## How does SMC work?

Launched in 2001, SMC is a national collaborative venture among the area drug and therapeutics committees (ADTCs) of the (then) 15 Scottish NHS Boards with the aim of improving consistency in decision-making and avoidance of duplication of effort. SMC has the remit of providing advice to the NHS in Scotland about the comparative clinical and cost-effectiveness of all newly licensed medicines, all new formulations of existing medicines, and all new indications for established products. SMC's remit excludes the assessment of vaccines, branded generic medicines, and blood products, while the review of medicines-containing devices is confined to those licensed as medicines by the Medicines and Healthcare Products Regulatory Agency (MHRA) or European Medicines Evaluation Agency (EMA). It does not cover health interventions other than medicines.

SMC's aim is to make decisions about new medicines within 3-4 months of launch. This approach requires companies to make submissions at, or preferably before, the time of launch. These should contain all of the data considered relevant to making the case for clinical and cost-effectiveness, and might well include important unpublished clinical trials that would not have been available to NHS Boards in the past. To achieve rapid appraisal, the SMC process (Figure 1) involves receipt of a structured submission, from the pharmaceutical company marketing the drug, covering evidence of

efficacy, effectiveness, comparative efficacy/effectiveness and safety, and including an economic case to justify the use of the drug (comprehensive details of the process can be found on the SMC website). The submission, together with any relevant publications identified that were not provided by the company, is critically appraised by a specialist pharmacist team and cost effectiveness reviewed by a health economics team. The submission and associated reviews then go to the New Drugs Committee (NDC), a scientific advisory panel comprising around 20 members, mainly from medical and pharmacy backgrounds, chosen for their skills in critical appraisal. The NDC formulates a recommendation, which is then passed on to SMC, comprising around 35 members. Some members provide similar appraisal skills to those required at NDC, whereas others represent regional interests, specific administrative functions (through the involvement of NHS Board chief executives and finance directors) and lay and patient views. As well as reviewing the recommendation from NDC, and the data supporting this recommendation, SMC also considers special issues related to health care provision in Scotland (such as those related to the highland and island communities), and the broader societal and ethical issues. SMC has also formed a Patient and Public Involvement Group, to help patient interest groups provide input to the SMC process, and SMC also considers any comments from the submitting company about the NDC opinion. Stringent arrangements are in place for all SMC/NDC members to declare interests, so as to exclude from the process those with relevant direct interests or interests in competitor products. At various stages during the process, from submission to SMC recommendation, there are opportunities for independent clinical experts, and patients, to comment on the submission.

The pharmaceutical industry – through its trade organisation, the Association of the British Pharmaceutical Industry (ABPI) – is represented on both NDC and SMC. Their role is not to represent specific company interests, but to assist with the work of SMC and to ensure that ABPI maintains a good understanding of, and essential engagement with, the process. Dialogue with industry is

underpinned by a Users' Group Forum, which meets quarterly, and includes representatives from SMC and a wide range of pharmaceutical companies (including both ABPI and non-ABPI companies). We believe that industry involvement has been highly influential in the creation of an effective SMC process, but that ABPI involvement has not distorted individual SMC decisions. It is important to note that the pharmaceutical industry makes no financial contribution to any aspect of the SMC's work.

There are 3 possible outcomes of SMC review: the product may be accepted for use without restriction; it may be accepted for restricted use, either for use by a limited group of prescribers, or for a more limited indication than given in the licence, or indeed both; or it may not be recommended for use within the NHS in Scotland. Decisions are made available, initially in confidence, to the service, the Scottish Executive and the submitting company in the form of a headline recommendation, together with a structured 4-6 paged summary of the review, incorporating a justification for the decision. The decision is made available in the public domain, on the SMC website, 4 weeks later, allowing NHS Boards time to consider how they will implement the advice.<sup>4</sup> Where a product is not recommended for use, the company can either accept the decision, or make a resubmission, though the latter depends on the availability of new data that can address issues raised by SMC. If the company is still not satisfied with the decision, it can ask SMC to form an Independent Review Panel (IRP) to meet, consider the evidence anew, and report its views to SMC.

Drugs reviewed by SMC may be categorised as 'unique' if the specific condition that the drug treats has no other effective therapy. If approved by SMC, unique drugs will be introduced by an agreed national programme making the drug uniformly available across Scotland, normally within 3 months of publication of SMC advice. If an alternative treatment already exists, local health boards and ADTCs can decide whether to add the new drug to their formulary if the medicine is a new agent or an improvement on an existing agent. ADTCs may choose not to include the medicine on their formulary if it represents a 'me-too' drug that they

deem non-superior to an existing formulary drug. If the SMC verdict is not to recommend, then the drug can only be used under exceptional circumstances. There are no rules governing factors that define exceptional status but the patient should be significantly different to the general population of patients with the condition in question and likely to gain significantly more benefit from the drug than the average patient. It is the clinician or patient who requests access to the 'not SMC recommended' drug via application to the local ADTC or NHS Board.

In 2005, the SMC horizon scanning initiative was established to improve financial planning within the NHS in Scotland by providing health boards with early information on new medicines in development. The horizon scanning reports include medicines in late stage development, orphan drugs and some new indications for established medicines, and provide projections of the potential budget impact in years 1 and 5 after medicine launch. The reports include commercially sensitive information and are only available to Health Board Chief Executive Officers, Directors of Finance, Directors of Pharmacy and Medical Directors/Directors of Public Health and are accompanied by a confidentiality agreement.

### **What has SMC achieved so far?**

Since its creation, from the delivery of the first recommendation in February 2002 up to the end of 2006, SMC has issued 360 recommendations. Of these, 236 were based on full submissions (30 in 2002, 45 in 2003, 52 in 2004, 55 in 2005 and 54 in 2006), 75 were based on abbreviated submissions (restricted to modest changes in formulation with minimal budget impact: 6 in 2003, 16 in 2004, 16 in 2005 and 37 in 2006); and 49 on resubmissions (1 in 2002, 8 in 2003, 7 in 2004, 7 in 2005 and 18 in 2006). Of the full submissions, 58 were recommended without restriction, 92 with restriction, and 86 were not recommended for use in NHS Scotland, giving an acceptance rate of 64%. Of the 49 submissions that were revised after rejection and resubmitted to SMC, 10 were subsequently accepted without restriction, 15 with restriction, and 24 were still not approved.

Importantly, it would appear that budget impact has not been an important driver for decisions at SMC, with medicines that were accepted without restriction having an anticipated spread of budget impact at 5 years after launch (mean £387,684; 95%CI £206,847-£568,521; based on company figures) broadly similar to those for medicines accepted for restricted use (£548,955; £323,835-£774,073) and those rejected (£460,323; £228,624-£692,023).

It should be recognised that the health economics team does not always accept the cost per QALY (quality adjusted life year) submitted by the company, or indeed the models from which they have been derived. In some cases the assumptions do not seem to reflect Scottish, or even UK, clinical practice, and in others the values have very wide confidence limits and substantial sensitivity to minor changes in assumptions. Nevertheless, there appears to be evidence that SMC has a 'willingness to pay' that diminishes with increasing cost per QALY. Of 54 products that were submitted with a cost per QALY or cost per life year gained of ≤£20,000, only 18% were rejected by SMC, whereas for those of £20,000-30,000, 64% were rejected. Therefore, although SMC has not defined a specific threshold for an acceptable cost per QALY it does appear that higher values increase the chance of rejection.

So far the SMC has completed only qualitative work on the impact of SMC on ADTCs and prescribers. An independent review of SMC led by Aberdeen University concluded *"the SMC presents a substantial change in medicines management in Scotland... It has shown an ability to produce recommendations (for) new medicines close to the time of launch. There have also been substantial changes at ADTC level, with increased consistency (with) which new drugs are considered, and the evidence base used for local implementation."* The evaluation also showed that SMC had freed up time for local medicines management groups to focus on other important local work on safe and effective use of medicines.

Sampling of some of the agents reviewed by SMC,

choosing those for which no other indication exists to complicate interpretation (Figure 2), suggests that SMC can influence prescribing of medicines that it did not consider good value for money. A more formal review of impact has recently been funded and is now underway.

### Comparison with NICE MTA

SMC's work programme is independent of the Scottish Executive Health Department and covers all new drugs, indications and formulations in a simple all-encompassing approach. By contrast NICE MTA has a wider remit, which extends beyond medicines, in a work programme directed by the Department of Health. Whereas SMC aims to provide its recommendations relatively close to launch, this is not possible within the NICE MTA assessment framework, which involves substantial periods of external and independent academic appraisal, including data modelling, as well as of consultation. In the 35 cases where SMC and NICE MTA have looked at essentially the same medicines and indications (Table I) the decision from SMC has been generated on average 12 months earlier, and the recommendation from NICE has been the same as that at SMC in all but six cases. Interestingly, the decisions from SMC have also been highly consistent (>80% concordant) with the decisions from technology appraisal of new medicines undertaken in Australia, by the Pharmaceutical Benefits Advisory Committee, where drug costs may be different (data not shown).<sup>7</sup>

It is important to recognise that there are at least 2 reasons why SMC and NICE MTA decisions may differ, tending to make these processes complementary in function, especially as the work programme at NICE tends to focus on high cost and sometimes more controversial areas. Firstly, given the different time scales, coming up to a year or more after SMC decisions, NICE has the benefit of considering any new trial data that may have emerged since product launch. Second, SMC assesses only the submission provided by the company and, if the case made does not suggest good value for money, it is forced to reject the submission. Here, the approach taken by NICE of

doing its own modelling, though time-consuming and costly, may identify a sub-group of patients for whom the drug appears cost-effective. For these reasons, determinations from NICE MTAs on new medicines are implemented in Scotland, through the actions of NHS Quality Improvement Scotland, and supersede any previous recommendation from SMC.

### Comparison with NICE STA

SMC has been a national experiment in the assessment of cost-effectiveness close to product launch. SMC is now one of the earliest independent bodies to review the cost effectiveness of new medicines worldwide, seeking to do so in as transparent a way as possible while working with commercially sensitive information.<sup>8</sup> The SMC makes 40% of its decisions within 90 days and 90% within 120 days. These decisions have been reached so early after launch, in an efficient way that seems fit-for-purpose, by a partnership arrangement whereby manufacturing companies make the submissions to SMC, and these subsequently receive independent critical pharmacy and health economic appraisal. A key assumption in this work is that companies present all the relevant data, and do not divulge information selectively. It is unlikely that divulging information selectively would be in the interest of a company in the long term. In this way SMC has been able to use its relatively limited resources (annual budget of < £1 million compared with NICE's budget of around £30 million) to undertake a large number of thorough reviews, and, importantly, has had the ability to say 'no' to medicines that do not appear to offer value for money to the NHS in Scotland. SMC has also maintained dialogue with its users, the pharmaceutical industry, and accepts resubmissions where new data have emerged to better support a case for use. Also, although involving national clinical experts and patient advocacy groups, SMC has minimised the time to a decision by not using other means of external consultation.

The delay between a medicine being licensed and the publication of a NICE MTA created a vacuum

with prescribing of new drugs being patchy or often withheld until a decision was released by NICE, so called NICE 'blight'. To address this problem NICE introduced STA in November 2005. This process of rapid assessment of single new drugs or existing drugs with new indications using a single submission of evidence from the manufacturer is similar to the established work of the SMC. However, as opposed to SMC, who look at all new drugs, NICE is selective in its approach to STA and inclusion is finally decided by the Secretary of State for Health.

By the end of 2006 there were 4 medications that had been reviewed by both NICE STA and SMC. The decisions were the same (to accept for use) for all four – trastuzumab (early stage breast cancer), docetaxel (breast cancer), gemcitabine (metastatic breast cancer) and rituximab (non-Hodgkin's lymphoma). If future decisions differ, as they may do in situations where fine judgements are involved, and where service priorities may differ, there is a risk of confusion in the service, and pressure when only one of the bodies reaches a decision that a medicine is not cost-effective. For that reason, and given the reliability of SMC decisions, the Scottish Executive Health Department has made it clear through HDL (2007) 26 that they expect 'NHS Boards to continue to comply with the SMC advice because of the robustness of the SMC process and its wide recognition and acceptability within NHS Scotland'.<sup>9</sup>

### **The future - SMC and changes to the drug pricing system**

In a potentially very significant report, the Office of Fair Trading (OFT) recently recommended reform of the Pharmaceutical Price Regulation Scheme to provide more patient- and value-focused drug pricing that the OFT suggest would produce considerable savings to the NHS and reward pharmaceutical companies that produce innovative, valuable new drugs.<sup>10</sup> The role of NICE and SMC is reviewed in this report and a number of significant reforms are proposed. SMC and NICE do not have the authority to negotiate the price of a new drug

with a manufacturer, their remit being to give an opinion on the cost-effectiveness at the price proposed. The OFT report proposes a new system with the SMC and NICE cost-effectiveness analysis leading to Department of Health negotiation over a drug's price if the drug is deemed not to be cost-effective. As already mentioned, SMC advises on the clinical and cost-effectiveness of all new medications but NICE restricts its advice to only those drugs referred. The OFT report highlights the potential problems this may cause with a two tier system of NICE assessed and non-assessed new drugs. This may then result in a new form of NICE 'blight', whereby funding of NICE STA decisions by primary care trusts is achieved at the expense of other important developments. Alternatively, drugs deemed non cost-effective by the SMC may continue to be used in England and Wales because NICE has not issued guidance.

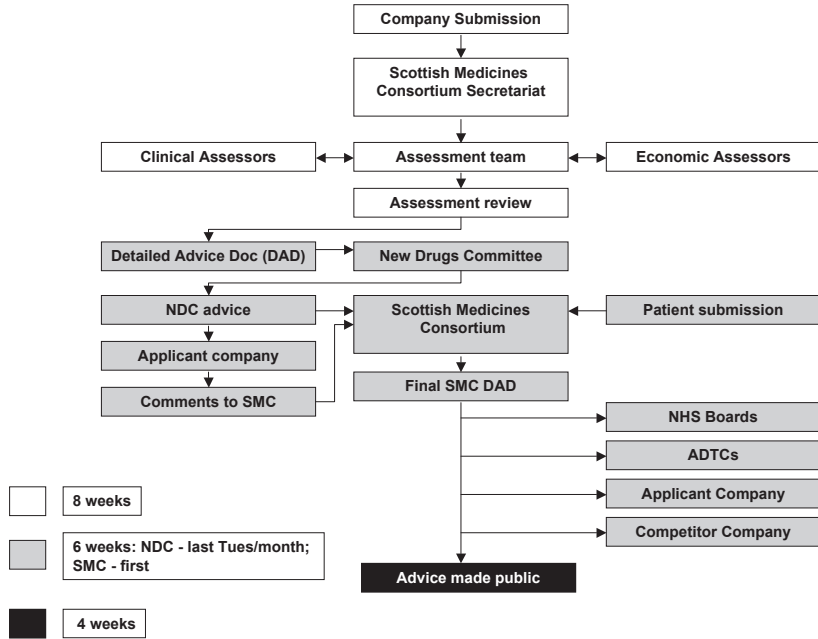
### **Conclusion**

The SMC has succeeded in providing the NHS in Scotland with rapid assessments of the clinical and cost-effectiveness of new medicines. This assessment has been achieved, on average, one year earlier than NICE MTA. The value of early assessment has recently been recognised by NICE in the creation of their STA process that has close similarities to the existing work of SMC.

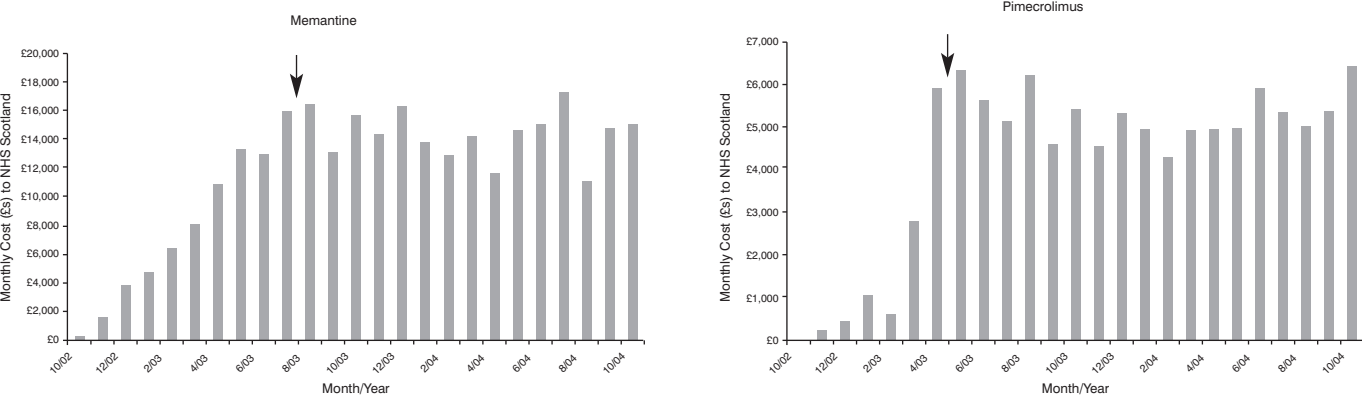
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**Figure 1:** The assessment process at SMC is initiated by a pharmaceutical company submission for a new medicine. This undergoes independent evaluation before the development of a draft recommendation at the New Drug Committee (NDC), which is subsequently considered, and if necessary revised, by SMC, where there is an opportunity for input from patient interest groups and lay members. The whole process takes between 3 and 4 months. SMC advice is available in confidence for 4 weeks so that relevant groups can prepare a plan of response.



**Figure 2:** Uptake in Scotland within primary care of 2 drugs that were rejected by SMC. Memantine and pimecrolimus were launched in October and November 2002, and rejected by SMC in August and May 2003, respectively (date shown by arrow). The Information and Statistics Division of National Services Scotland provided data for medicines prescribed mainly in primary care for the SMC indication. The figure shows monthly gross ingredient costs over time. In both cases, use never exceeded 200 prescriptions per month. These data appear to show that there is some use of medicines in advance of SMC advice, though these examples are from early in our activity, and we anticipate our planned audit will show that this has diminished. They also show that there is a change in uptake after a negative decision from SMC. Patterns for prescribing of memantine and pimecrolimus are consistent with a halt in new prescribing, but not of that which has already been initiated. Studies over a longer period will resolve if there is a true reversal of prescribing trends with time.



SMC and NICE MTA guidance issued			Guidance available		
	Medicine / Indication	Verdict	SMC	NICE	Time Difference in months (SMC before NICE)
1	Imatinib for chronic myeloid leukaemia (CML), 2nd line	Both accept	Mar-02	Oct-02	7
2	Insulin glargine for diabetes	Both accept	Oct-02	Dec-02	2
3	Capecitabine for advanced breast cancer	Both accept	Mar-03	May-03	2
4	Olanzapine for bipolar disorder	Both accept	Jun-03	Sep-03	3
5	Rituximab for non-Hodgkins lymphoma	Both accept	Mar-03	Sep-03	6
6	Imatinib for gastrointestinal stromal tumours	Both accept	Aug-03	Oct-03	2
7	Anakinra for rheumatoid arthritis	Both not recommended	Nov-02	Nov-03	12
8	Pegylated interferon for hepatitis C	Both accept	May-02	Jan-04	20
9	Topiramate for epilepsy	Both accept for second line use	Jan-04	Mar-04	2
10	Imatinib for chronic myeloid leukaemia, first line	Both accept	Jan-03	May-04	16
11	Clopidogrel for acute coronary syndrome	Both accept	Feb-04	Jul-04	5
12	Drotrecogin alfa for septic shock	Both accept	Oct-02	Aug-04	22
13	Pimecrolimus for atopic dermatitis	SMC not recommended, NICE restricted accept	May-03	Aug-04	15
14	Tacrolimus for atopic dermatitis	Both restricted accept	Oct-02	Aug-04	22
15	Mycophenolate mofetil after kidney transplant	Both accept	Dec-04	Sep-04	-2
16	Risedronate for osteoporosis	Both accept	May-03	Jan-05	20
17	Teriparatide for osteoporosis	Both accept	Dec-03	Jan-05	13
18	Rosuvastatin for raised cholesterol	Both accept	May-03	Nov-05	31
19	Adefovir for hepatitis B	Both accept for restricted use	Mar-05	Feb-06	11
20	Pegylated interferon alpha-2a for hepatitis B	Both accept	Jun-05	Feb-06	9
21	Atomoxetine for attention-deficit hyperactivity disorder	Both accept for restricted use	Jun-05	Mar-06	9
22	Capecitabine for stage C colon cancer	Both accept	Jul-05	Apr-06	9
23	Oxaliplatin for stage C colon cancer	Both accept	Oct-05	Apr-06	6
24	Docetaxel for advanced prostate cancer	SMC not recommended, NICE accept	Nov-05	Jul-06	8
25	Efalizumab for psoriasis	SMC not recommended, NICE restricted accept	Dec-04	Jul-06	19
26	Etanercept for ankylosing spondylitis	Both accept	Oct-05	Jul-06	9
27	Infliximab for ankylosing spondylitis	Both restricted accept	Oct-05	Jul-06	9
28	Bevacizumab for advanced colon cancer	Both not recommended	Jan-06	Aug-06	7
29	Cetuximab for colon cancer	Both not recommended	Feb-05	Aug-06	18
30	Memantine for severe Alzheimer's disease	Both not recommended	Aug-03	Jul-06	36
31	Anastrozole for early breast cancer	Both accept	Aug-05	Nov-06	15
32	Exemestane for early breast cancer	SMC restricted accept, NICE accept	Nov-05	Nov-06	12
33	Letrozole for early breast cancer	Both accept	Feb-05	Nov-06	21
34	Cinacalcet for hyperparathyroidism	SMC not recommended, NICE restricted accept	Apr-05	Dec-06	20
35	Inhaled insulin in diabetes	SMC not recommended, NICE restricted accept	Jun-06	Oct-06	4
				<b>average</b>	<b>12</b>

**Table I.** Medicines that have been reviewed by both SMC and NICE MTA. The medicines, recommendations and timings are shown. The average time difference between a recommendation by SMC and NICE is 1 year.