Access to newly licensed medicines
Roche Products Ltd

Key Points

• Scotland has a high incidence of cancer

• Scotland has a poor uptake of cancer medicines, with the lowest spend per head of population of the UK nations. This is most noticeable with medicines less than 5 years old

• The reason for poor uptake is due to the system of establishing cost-effectiveness through the cost per QALY, and compounded by inherent problems when applying this method for medicines for rare diseases and in the End of Life setting

• The IPTR Process does nothing to improve access to medicines declined by the SMC and has reduced the ability of patients to access these medicines in comparison with the situation in 2008 when Petition PE1108 was submitted

• An assessment system should be considered by the SMC that transparently raises the threshold of acceptability for patients who need medicines that fall within specific criteria, such as End of Life, rare diseases and unmet clinical need

• The IPTR process should be overhauled to ensure it benefits patients

• There are sufficient issues to suggest that the committee should consider further more detailed evidence on the availability of cancer medicines

1. Background

Roche Products Ltd values the opportunity to give evidence to the Health Committee of the Scottish Parliament. Roche has significant experience in the supply of specialist medicines to the NHS, and is the single largest supplier of cancer medicines to NHS Scotland. Roche continues to invest in research and development of medicines to ensure these are translated into patient benefits. This paper seeks to explore and identify key issues in the processes used in NHS Scotland in making these medicines available, with specific reference to cancer medicines.

The Department of Health paper *Extent and causes of international variations in drug usage* gave a definitive view of uptake of many medicines across Europe. This highlighted some clear areas where
medicines were not made available in the UK, most notably in cancer where uptake for medicines less than 5 years old was amongst the lowest in the examined countries. Given that the UK Government sought to resolve this for England through the introduction of the Cancer Drugs Fund, it can be assumed that due to the continued lack of action on access in Scotland, it now ranks amongst the lowest for provision of cancer medicines less than 5 years old in the western world.

This view has been ratified by the Rarer Cancer Foundation in its report *Nations Divided* ii. It found that people in Scotland are three times less likely to get access to a newer cancer drug than their neighbours in England, and that if levels of access were the same, then 248 patients would benefit each year in Scotland, instead of 74. Although the methodology has been disputed by Scottish Government, the data is based upon what is recorded by NHS Boards and available through Freedom of Information requests.

Further analysis of medicines in Scotland shows that despite having the second highest incidence of cancer of all UK countries (422 cases per 100 000), Scotland spends the smallest amount on cancer medicines per head of population (Scotland £13.33 per head, Northern Ireland £13.78 per head, Wales £16.96 per head and England £17.27 per head. This is based on 2011 figures and is prior to the impact made by the Cancer Drugs Fund). iii The level of Scottish expenditure was corroborated by the answer to a Parliamentary Question showing an overall spend on cancer medicines of around £65 million pounds. iv

The discrepancy in access to medicines between Scotland and England is increasing. This is most marked in the field of cancer, as stated above, but the causal issues of this disparity are not exclusive to cancer treatments. Cancer medicines have been hit the hardest due to the number of ground-breaking treatments discovered and brought to licence, but medicines in other areas are also affected. It is therefore important for the Committee to consider and understand why so many of these medicines are deemed “not cost-effective” by the current Scottish Medicines Consortium (SMC) processes.

2. Does the Individual Patient Treatment Request process not fill the gap?

No. Not in the field of cancer. Despite the statement by the Minister that the vast majority of IPTRs are accepted v, if only those refused by the SMC are considered (as evidenced in *Nations Divided*) it becomes clear that patients in Scotland do not have access to these medicines. Figure 1 below shows the value of medicines procured in Scotland by head of
population versus England for 9 of the most commonly used medicines available through the Cancer Drugs Fund. It becomes absolutely clear that patients in Scotland do not have access to the benefits of these medicines vi. Interestingly cetuximab has some usage in Scotland through a very specific Patient Access Scheme that was approved by the SMC, but uptake still lags behind the total figure for the whole of the UK.

Figure 1. Sales in Scotland of nine of the most commonly prescribed medicines made available through the Cancer Drugs Fund, compared with the UK average

![Graph showing sales comparison between Scotland and UK for selected medicines.]

3. Have Petitions Committee recommendations resulting from Petition PE 1108 (2008) not improved access to cancer medicines? vii

The Petitioner of 2008 highlighted serious discrepancies in NHS Boards’ approaches in accessing non-SMC approved medicines. His case was not unique and was put forward eloquently to the Committee. Subsequent evidence demonstrated the lack of transparency in the systems that allow patients access to medicines both at a national and local level. It was also highlighted that the complexity of the system made it difficult for patients to understand. It was therefore important that NHS Boards put in place named individuals responsible for guiding patients and carers through these processes. Government therefore directed the boards to undertake these changes. These recommendations do not appear to have been completed as per the Committee’s request.
There are now 3 separate documents giving guidance to NHS Boards. Chief Executive Letter CEL 17 (2010) was the first piece of guidance which described how SMC approved and declined medicines should be made available for patients across NHS Scotland and introduced the concept of Individual Patient Treatment Requests (IPTRs). Chief Medical Officer Letter CMO 3 (2011) sought to offer “clarity” on these processes. This document highlights that IPTRs can only be used for licensed medicines in areas with an SMC restriction, but with significant evidence showing clinical benefit. This set of rules essentially rules out any medicine available in the UK that has been declined by the SMC cost-effectiveness process since manufacturers apply for a licence based on all available evidence, then have this reviewed by the SMC. Hence if the medicine or indication is declined by the SMC, there is no other mechanism available for a patient to access the medicine. It also rules out the clinician using this process for any patient with a rare condition who is reliant on the off-label use of a medicine for the treatment of their disease. The Exceptional Case process was commonly used for this patient group to great effect, and the guidance given by Government has largely closed this route enabling very vulnerable patients to access medicines that could be of benefit to them. If strictly adhered to, this could prevent many paediatric patients accessing medicines as few are licensed for use in this patient group. Lastly, a letter from the Chief Medical Officer Letter (CMO 1[2012]) added the caveat of “unmet clinical need” but left all the other criteria in place. The confusion, ambiguity and contradictions in guidance now means that no patient in Scotland gets access to the medicine for the condition or set of circumstances that the Petitioner of PE1108 had. When he brought his Petition to the Parliament we do not believe his intent was to close access to every patient across the whole of Scotland for SMC declined medicines like the one from which he benefitted. This may be seen as equitable but the outcome seems perverse given the intent of the Parliamentary Inquiry of 2008. This disconnect between recommendations by the Committee and current Government policy is stark especially when the Petitions Committee was of the understanding that all requirements laid down by the Committee had been met and so the Petition closed.

4. Why do so many cancer medicines get declined?

The Scottish Medicines Consortium can rightly be proud of conducting a comprehensive and rapid programme of health technology appraisals for new medicines.

There are some key reasons why the current system does not make certain medicines available:
a. The value of new medicines to both the patient and society is not currently reflected in the cost-effectiveness assessment performed by the SMC.

The SMC and National Institute of Clinical Effectiveness and Health (NICE) use an assessment that encompasses both NHS costs and health benefit, expressed through a measure known as the Quality Adjusted Life Year (QALY). This is the benefit seen by an individual within the context of an average life span of 70 years. By employing these 2 measures in the calculation of value for money, we often get results that are hard to reconcile with how we view and value healthcare. For example, a cancer medicine that can add a significant amount of time (e.g. 3 months) to the end of a patient’s life, increasing their life expectancy by 20 or 30%, can have the same QALY figure as a lifestyle intervention for a non-life threatening condition. The public does not see these as interchangeable and would be more likely to pay more for the treatment of cancer than they would for the non-life threatening condition.

b. Adjustments to reflect greater value in cancer, terminal illness and rare illness

NICE carried out research with the public that confirmed that some QALYs, particularly those bought near the end of life, should have a higher value than others.\(^{xi}\) This led to the development and use of the NICE “End of Life” criteria which raises the threshold of acceptable cost effectiveness from £20 to £30k per QALY to £50k per QALY. These criteria are explicit and transparent.

The SMC produced a set of modifiers which attempt to offer a similar degree of flexibility. We believe that these modifiers are inconsistently interpreted and applied. Similarly we are concerned that the modifiers are insufficient to reflect the current status of cancer medicines and medicines to treat rare diseases for which medicines discovery, mode of action, and the number of treatable diseases has changed markedly over recent years. This perspective is difficult to corroborate as there is no SMC documentation available as to how often and when these modifiers are used in the appraisal of medicines.

c. Cost effectiveness levels may vary by indication but the price of the medicine is fixed.
A more complex issue is now being seen. If we use a Roche medicine as an example of a multiple indication medicine, this can easily be demonstrated. Herceptin has a licence which allows its use in multiple indications. The pricing mechanism for medicines in the UK, the Pharmaceutical Price Regulation Scheme (PPRS) does not allow for the unit cost of a medicine to be increased or decreased when it receives a licence for a new indication. This means that the price paid per unit of the medicine remains constant, whilst the cost-effectiveness calculated by the SMC for that medicine will vary from one disease to another due to the benefits varying from one disease to another. The SMC processes do not take this anomaly into account and can therefore produce guidance where one patient can access the medicine for one condition, but not for another. This can be compounded by the lack of transparency in the use of modifiers to produce outcomes that could be seen as odd. The SMC has made Herceptin available for patients with HER2 positive breast cancer, but not for patients with HER2 positive gastric cancer. By contrast NICE recommended Herceptin in both tumour types through the utilisation of the End of Life criteria when it considered gastric cancer. This inequity must be avoided wherever possible.

5. Medicines Pricing

In February 2007 the Office of Fair Trading (OFT) reviewed the pricing of medicines in the UK and recognised that the current system is not fit for purpose. The Department of Health response was an overhaul of the current system to ensure that the true value of medicines is recognised and the amount charged by the manufacturer reflected that value. They suggested a “Value Based Pricing” mechanism which is under construction at the moment and due for implementation in 2014. It is hoped that the unmet clinical need, innovation, and treatment towards the end of life are all valid measures of value which will ensure access for patients. It is important to note that the latest reports on this mechanism highlight the need for the devolved nations to explain how this will be implemented in their own areas. It is important to note that this will only be prospective, and those medicines currently unavailable to patients in Scotland will remain unavailable. England identified this issue and put in place the Cancer Drugs Fund (CDF) to solve this conundrum for cancer. As can be seen, there is an urgent need for Scotland to deal with this important issue.

6. Is it affordable to fund cancer medicines?
The entire medicines budget in NHS Scotland equates to approximately £1.14 billion, or approximately 10% of the entire NHS budget of £10.8 billion in 2009/2010\textsuperscript{xv \textsuperscript{xvi}}. Figures for 2010/2011 have not been made available. The total cost of cancer medicines for all patients across NHS Scotland is approximately £65 million per annum\textsuperscript{xvii}. This equates to around 5.7% of the total medicines budget. Current prescribing for statins, one medicine used to lower cholesterol costs NHS Scotland almost exactly the same amount (£59 Million per annum)\textsuperscript{xviii}. Cancer is not an expensive disease to treat when considering medicines spend. Given that many of these high volume low cost medicines are becoming generic during the course of 2012, we would argue that these savings should be re-invested in ensuring innovative lifesaving or life extending medicines are made available to patients who need them, when they need them, across the whole of Scotland, thus giving an equitable footing with England and our near European neighbours.

7. **What about other diseases?**

The value of medicines in other diseases should be evaluated under similar criteria to ensure equity and transparency. The criteria of unmet clinical need, innovation and issues of evidence in the end of life setting are parameters that could be applied to any disease. It must be remembered that there is already inequity where patients with end stage cancer are essentially discriminated against by the current cost-effectiveness evaluation system.

8. **Recommendations**

a. The SMC process has not been revisited since the inception of the Health Technology Board for Scotland and should be reviewed to ensure its mechanisms of evaluation are current and fit for current purpose.

b. The value of medicines is reflected in evaluation undertaken by the SMC and includes:

i. End of Life

ii. Unmet clinical need

iii. Orphan or Ultra Orphan diseases

c. The SMC health technology appraisal process should accept a greater range of cost-effectiveness (cost per QALY) according to set criteria which reflect the value that these medicines bring. These should be explicit in number and transparent in applicability.
i. Treatment towards the end of life where survival gain in severe or terminal illness is distinguished from subtle quality of life improvement over several decades.

ii. The use of medicines towards the end of life reflects the clinical value which clinicians see in them. Current SMC modifiers and NICE “End of Life” criteria are however insufficient to reflect the value which both doctors and patients place in end-of-life treatments. Most medicines made available through the CDF exceed not only the commonly accepted thresholds of SMC and NICE (£30,000/QALY), but also the higher threshold frequently adapted as an upper limit for “End of Life” medicines within NICE appraisals (£50,000/QALY). Please see Appendix A for a list of Cost per QALY levels for the most widely prescribed medicines from the Cancer Drugs Fund.

iii. Evaluation of medicines with multiple indications should include flexibility when cost effectiveness thresholds are being calculated. This would ensure that there is equitable access to all patients across all indications for a given medicine and would avoid discrimination on the basis that calculations have only accounted for one tumour type, as was the case with Herceptin (Section 4.c.)

iv. Orphan and Ultra-orphan diseases where the evidence base may mean proving cost-effectiveness is difficult.

d. Within a licensed indication for a medicine, if the manufacturer can produce evidence that a lower dose of the medicine is both clinically and cost-effective, then a clear and robust system should be in place to ensure that the SMC can review that information via a submission or re-submission by the manufacturer.

e. The current system of IPTR review does not work in improving access to medicines. An alternative mechanism or better processes are required to enable access to medicines, in which the clinician should be the one to judge if the patient could benefit from any given medicine. The process should also be open for that clinician to submit to, and this “open submission” process should be subject to scrutiny via a publicly available audit which tracks applications by medicine through to a positive or negative outcome and any resultant appeal.
f. The Committee seeks to understand the detail around the issues of access to medicines, especially those in cancer, through a further specific Inquiry or set of evidence sessions.

Appendix A - Cost per QALY levels for the most widely prescribed medicines from the Cancer Drugs Fund

<table>
<thead>
<tr>
<th>Drug name</th>
<th>Indication</th>
<th>Most plausible cost per QALY (determined by NICE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avastin (bevacizumab)</td>
<td>In combination with capecitabine is not recommended within its marketing authorisation for the first-line treatment of metastatic breast cancer, that is, when treatment with other chemotherapy options including taxanes or anthracyclines is not considered appropriate, or when taxanes or anthracyclines have been used as part of adjuvant treatment within the past 12 months</td>
<td>&gt; £82,000(^{xix})</td>
</tr>
<tr>
<td>Avastin (bevacizumab)</td>
<td>In combination with non-oxaliplatin (fluoropyrimidine-based) chemotherapy is not recommended for the treatment of people with metastatic colorectal cancer that has progressed after first-line chemotherapy</td>
<td>No economic model submitted</td>
</tr>
<tr>
<td>Avastin (bevacizumab)</td>
<td>In combination with a taxane for the first-line treatment of metastatic breast cancer</td>
<td>• £110,000 to £259,000 (vs paclitaxel) (^{xx})</td>
</tr>
<tr>
<td>Avastin (bevacizumab)</td>
<td>In combination with a taxane for patients who were triple negative or had previously received treatment with a taxane for the treatment of metastatic breast cancer (2 sub-group analyses)</td>
<td>Estimates not able to be carried forward due to uncertainties</td>
</tr>
<tr>
<td>Avastin (bevacizumab)</td>
<td>In combination with oxaliplatin and either fluorouracil plus folinic acid or capecitabine for the treatment of</td>
<td>£68,100 - £70,500 (with Patient Access Scheme) (^{xxi})</td>
</tr>
<tr>
<td>Drug</td>
<td>Description</td>
<td>Cost Range</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>-----------------------------------------------------------------------------</td>
<td>---------------------</td>
</tr>
<tr>
<td><strong>Avastin</strong> (bevacizumab)</td>
<td>First-line treatment for people with advanced and/or metastatic renal cell carcinoma</td>
<td>£53,820 to £171,301</td>
</tr>
<tr>
<td><strong>Avastin</strong> (bevacizumab)</td>
<td>In combination with 5-fluorouracil plus folinic acid, with or without irinotecan, is not recommended for the first-line treatment of metastatic colorectal cancer</td>
<td>£62,857 - £88,436 (External Reference Group calculation)</td>
</tr>
<tr>
<td><strong>Erbitux</strong> (cetuximab)</td>
<td>Recurrent and/or metastatic squamous cell cancer of the head and neck</td>
<td>&gt;£121,367</td>
</tr>
<tr>
<td><strong>Erbitux</strong> (cetuximab)</td>
<td>The treatment of metastatic colorectal cancer after first-line chemotherapy</td>
<td>£90,000, £88,000</td>
</tr>
<tr>
<td><strong>Erbitux</strong> (cetuximab)</td>
<td>The treatment of metastatic colorectal cancer</td>
<td>&gt;£30,000</td>
</tr>
<tr>
<td><strong>Afinitor</strong> (everolimus)</td>
<td>Second-line treatment of advanced renal cell carcinoma</td>
<td>£51,661</td>
</tr>
<tr>
<td><strong>Tyverb</strong> (lapatinib)</td>
<td>In combination with an aromatase inhibitor for the first-line treatment of metastatic hormone-receptor-positive breast cancer that overexpresses HER2</td>
<td>Closer to £74,000</td>
</tr>
<tr>
<td><strong>Levact</strong> (bendamustine)</td>
<td>First-line follicular lymphoma for patients who are refractory to rituximab</td>
<td>n/a</td>
</tr>
<tr>
<td><strong>Levact</strong> (bendamustine)</td>
<td>First-line follicular lymphoma in combination with rituximab</td>
<td>n/a</td>
</tr>
<tr>
<td><strong>Nexavar</strong> (sorafenib)</td>
<td>Treatment of advanced hepatocellular carcinoma</td>
<td>£76,000 (without Patient Access Scheme)</td>
</tr>
<tr>
<td><strong>Nexavar</strong> (sorafenib)</td>
<td>First and second line treatment of advanced and/or metastatic renal cell carcinoma</td>
<td>£65,900 &amp; &gt;£72,500 or £74,900</td>
</tr>
<tr>
<td><strong>Faslodex</strong> (fulvestrant)</td>
<td>Locally advanced or metastatic breast cancer in postmenopausal women whose cancer has relapsed on or after</td>
<td>&gt;£35000</td>
</tr>
<tr>
<td>AMN011</td>
<td>adjuvant anti-oestrogen therapy, or who have disease progression on anti-oestrogen therapy</td>
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<tr>
<td>Halaven (eribulin)</td>
<td>The treatment of locally advanced or metastatic breast cancer that has progressed after at least two chemotherapy regimens for advanced disease</td>
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<tr>
<td></td>
<td>&gt;=£68,000xxiii</td>
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xxiv Roche data on file, Devolved Nation Cancer Spend Analysis, July 2012


xxvii Roche data on file, IMS sales for 9 of the top 10 molecules by CDF approvals to date, September 2012


xxxviii Scottish Parliament, Parliamentary Question S4W-06394, 29 March 2012

xxxix Scottish Parliament, Parliamentary Question S4W-06394, 29 March 2012


Roche Products Ltd
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