



**SMC ‘accepted for use’ and
‘accepted for restricted use’ advice:**
an investigation of medicines use across NHSScotland



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Scottish Medicines Consortium Evaluation Programme

SMC 'accepted for use' and 'accepted for restricted use' advice - an investigation of medicines use across NHSScotland

Executive Summary and Full Report

Prepared by the SMC Evaluation Project Team

This work was undertaken by the National Medicines Utilisation Unit,
Information Services Division, NHS National Services Scotland in
collaboration with the Scottish Medicines Consortium

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Executive summary

Introduction

The remit of the Scottish Medicines Consortium (SMC) is to advise NHS boards and their Area Drug and Therapeutics Committees (ADTCs) across Scotland about the status of all newly licensed medicines, all new formulations of existing medicines and new indications for established products (licensed from January 2002). Advice is made available as soon as practical after the launch of the medicine. NHS board ADTCs advise clinicians not to prescribe a new medicine prior to the publication of SMC advice. The SMC issues three categories of advice: 'accepted for use', 'accepted for restricted use', and 'not recommended'. 'Accepted for use' advice is given when the SMC decides that a medicine should be prescribed according to the licensed indication specified in the submission. If the SMC advises that a medicine should be prescribed only in a specific situation or by a particular prescribing group, then it is 'accepted for restricted use'.

Where alternative drug treatment(s) already exists for a condition, implementation of advice for medicines that are 'accepted for use' or 'accepted for restricted use' is subject to local NHS board decision-making. This means that although treatment for a clinical condition is available uniformly across Scotland, there may be variation in the individual medicines chosen locally to treat that clinical condition.

This study investigates the use of medicines in primary care and hospitals across NHSScotland for which the SMC issued 'accepted for use' or 'accepted for restricted use' advice over the period January 2002 to December 2005.

Methods

Medicine definition

Between January 2002 and December 2005, 150 medicines were 'accepted for use' or 'accepted for restricted use' by the SMC. Medicines with multiple indications were excluded from the study. Specialists were consulted to identify which medicines from the remaining cohort were most suitable for investigation in hospital. This resulted in a cohort of 41 medicines that were mainly used in primary care and 13 used mainly in hospitals.

Medicine utilisation

Usage data for primary care medicines (n=41) were obtained through the PRescribing Information System for Scotland (PRISMS). For hospital medicines (n=13), usage data were obtained from hospital pharmacies and manufacturers. A 'medicine profile' was developed for each of the 54 medicines. The profile included: the SMC advice; a description of the epidemiology of the indication for the medicine; NHSScotland medicines use over time, annotated with key milestones; a comparison of the actual versus estimated manufacturer's budget impact; and potential factors that may be influencing medicines use within

NHSScotland. From these data, actual expenditure and an estimate of the number of patients treated were calculated at defined time periods. In addition, a qualitative review of the medicine profiles was undertaken to identify potential factors that may limit the interpretation or explain the patterns of medicines use.

Key findings

Figure 1 (page 9) presents the 41 primary care and 13 hospital medicines included in the study.

Use before SMC ‘accepted for use’ or ‘accepted for restricted use’ advice

In the majority of cases (81%), SMC ‘accepted for use’ or ‘accepted for restricted use’ advice was issued within 6 months of launch of the medicine, and within 3 months for 41% of medicines. Approximately £1 million was spent in NHSScotland on the 41 primary care medicines before SMC advice was issued. This is in the context of a cumulative spend in the primary care drugs bill over the study period (2002–2003 to 2005–2006) of £3.7 billion.

There were insufficient expenditure data for four hospital medicines: imatinib tablets; Tachosil® (human fibrinogen/human thrombin medicated sponge); miglustat capsules; and vinorelbine capsules. Approximately £1 million was spent on the remaining nine hospital medicines before SMC advice was issued.

Use after SMC ‘accepted for use’ or ‘accepted for restricted use’ advice

The qualitative review identified three key factors that may limit interpretation or explain some of the patterns in medicines use observed after SMC advice. These factors are useful in understanding the challenges in the assessment, uptake and monitoring of new medicines in NHSScotland:

- **Limitations of data obtained from NHS boards and manufacturers**

There were marked differences in the ability to obtain national data on prescribing in primary care and hospitals. Extracting data from hospital and industry systems is challenging, and the data provided by NHS boards and manufacturers proved to be incomplete for a number of medicines used in hospital. Unlike primary care, there is no national database of medicines prescribed in hospitals, and several NHS boards experienced difficulties in providing data. In some cases, this was because the medicine may be supplied through different hospital systems. For example, Tachosil® for improvement of haemostasis in liver surgery, may be supplied through General Stores in some hospitals. In other cases, some patients may receive active treatment with a new medicine within clinical trials, such as imatinib tablets for chronic myeloid leukaemia. Licensed medicines that are used in clinical trials may or may not be part of the hospital pharmacy stock control system.

There were also differences in how NHS boards reported costs for hospital medicines, including whether or not VAT was included, and lack of clarity with respect to which formulations or doses were dispensed. Sufficient data were provided by manufacturers for six of the 12 medicines that were requested: fosamprenavir tablets and oral suspension; bortezomib injection; pegylated interferon alfa 2a (Pegasys[®]) injection; pemetrexed injection; Tachosil[®]; and pegylated interferon alfa-2b (ViraferonPeg[®]) injection. Comparison of industry and hospital data for these showed similar trends and, for Pegasys[®] and pemetrexed injections, suggested that industry supply data are reportable 3–6 months prior to hospital utilisation data.

- **Challenges in interpreting data for ‘restricted use’ medicines**

For medicines that were ‘accepted for restricted use’ by the SMC (19 primary care and 6 hospital medicines), it was not possible to identify whether the data reflected the SMC restriction alone, due to absence of patient level data. For example, SMC advised that methylphenidate sustained release OROS formulation tablets (Concerta XL[®]) should be restricted to second line therapy and used only in exceptional circumstances where the supervising clinician has clear evidence of compliance problems. Approximately £1 million was spent on Concerta XL[®] between January and December 2006 but it is unknown whether this expenditure reflects the SMC restriction.

- **Availability of alternative treatment(s) for a clinical condition**

The new medicines investigated in this study were used to treat clinical conditions for which other treatment already existed. However, in some cases, the new medicine offered advantages over previously available therapy. For example, in primary care, the greatest expenditure was for the long-acting antimuscarinic bronchodilator, tiotropium inhaler, which was launched in September 2002 and ‘accepted for use’ by the SMC in December 2002. Tiotropium represented an advance over the available short-acting antimuscarinic bronchodilator, which has been available for many years, for the treatment of chronic obstructive pulmonary disease. Analysis shows increasing use of tiotropium inhaler, with tiotropium accounting for 67% of prescriptions for antimuscarinic bronchodilators between January and December 2006.

In other cases, the advantage of the new medicine over existing products may be less clear. For example, expenditure in primary care was low for MicardisPlus[®] tablets, which contain an angiotensin-II receptor antagonist (telmisartan) with a diuretic (hydrochlorothiazide). MicardisPlus[®] was recommended for restricted use in the treatment of essential hypertension. However, seven angiotensin-II receptor antagonists existed before MicardisPlus[®], of which four were already available in combination with a diuretic, and these may, therefore, compete for market share. Table 1 (page 7) lists other examples of medicines and their market share from January–December 2006.

Table 1: NHSScotland market share of some new medicines in the study

Name of new medicine	Indication	Total number of medicines in therapeutic class	Market share of new medicine* (Jan–Dec 2006)
Aripiprazole tablets	Schizophrenia	7 atypical antipsychotics	3% of prescriptions
Carbomer 0.25% gel	Dry eye syndrome	4 carbomer products	6% of prescriptions
Olmesartan tablets	Hypertension	7 angiotensin-II receptor antagonists	2% of prescriptions
Rosuvastatin tablets	Hyperlipidaemia	5 statins	4% of prescriptions
Tadalafil tablets	Erectile dysfunction	3 phosphodiesterase type-5 inhibitors	24% of expenditure
Vardenafil tablets	Erectile dysfunction	3 phosphodiesterase type-5 inhibitors	7% of expenditure

*market share of new medicine represented as a percentage of the total expenditure or number of prescriptions for all medicines in the therapeutic class for NHSScotland. Data source: PRISMS, ISD, Scotland from dispensed items. Excludes private prescriptions.

Conclusions

NHS board ADTCs advise clinicians not to prescribe a new medicine prior to SMC 'accepted for use' or 'accepted for restricted use' advice. In the context of the overall primary care drugs bill, expenditure on the study primary care medicines before SMC advice was small.

The SMC aims to issue advice as soon as practical after the launch of the new medicine. This was supported by the findings of this study, which showed that for the majority (81%) of the investigated medicines, advice was issued within 6 months of launch.

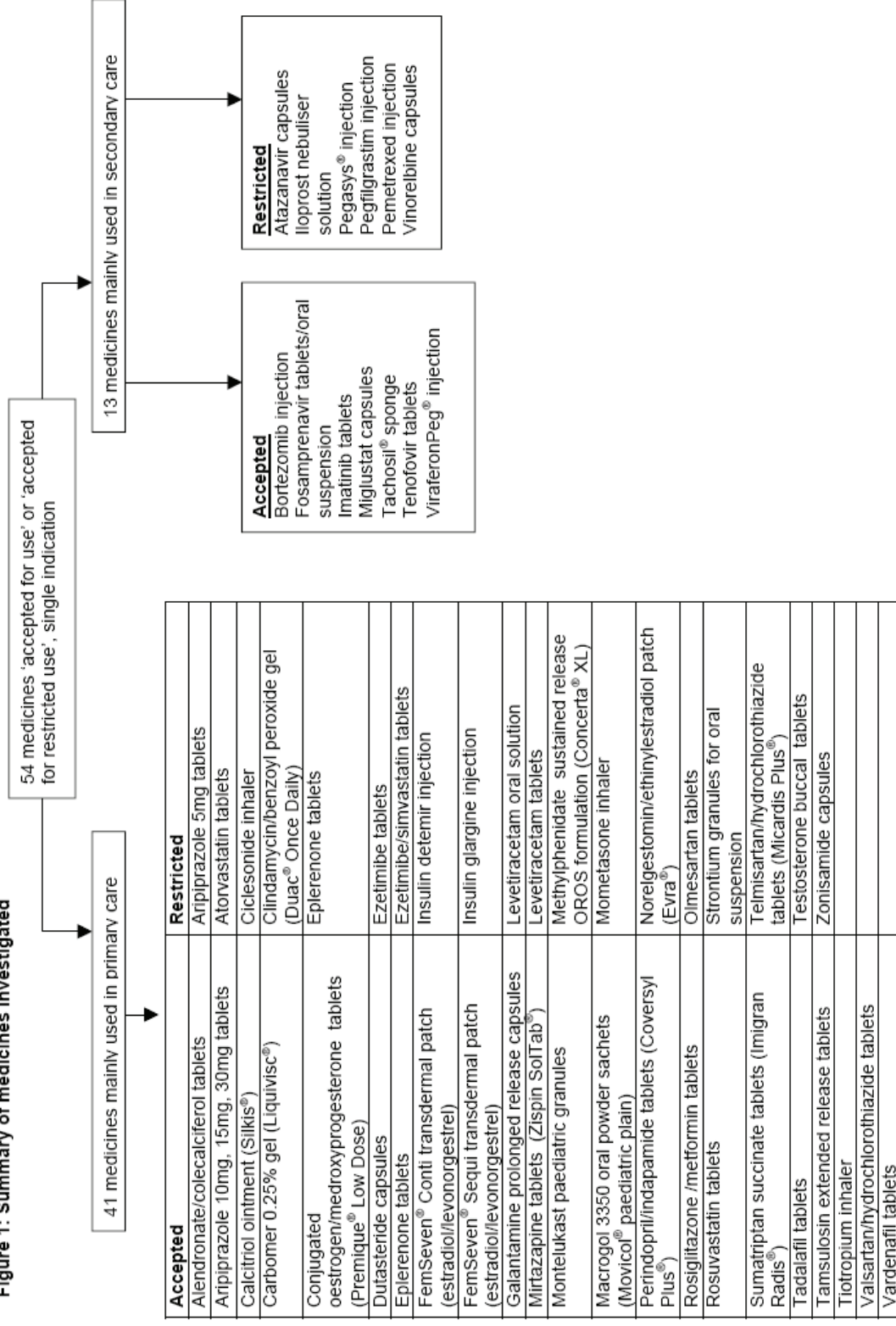
The study confirms the challenges that exist around hospital medicines utilisation data. National data at a medicine level are available in primary care through PRISMS. However, this is not the case for secondary (hospital) care data and both NHS boards and manufacturers had challenges in providing the data requested for hospital medicines. This included issues with quantifying medicine use through clinical trial and non-pharmacy supply, and differences in reporting formulations, leading to inconsistencies and gaps in the reporting of data. However, where sufficiently robust data were available from both sources, industry and hospital data showed similar trends.

There is no robust methodology to determine market share of a medicine for specific indications and this, together with the absence of national patient level medicines utilisation data, makes it challenging to determine whether prescribing is appropriate

- For medicines that are 'accepted for restricted use', it is not possible to identify whether the data reflect the SMC restriction. Expenditure on medicines that are 'accepted for restricted use' may, therefore, reflect use for patient groups that have not been assessed or accepted by SMC.

- For a clinical condition, where several medicines are available of similar efficacy, variation in prescribing of a new medicine between NHS boards may be clinically appropriate. NHS boards and local clinicians use their knowledge and expertise to decide whether a new medicine should replace existing treatment in local Formulary Management Systems.

Figure 1: Summary of medicines investigated



Full report

Background

The remit of the Scottish Medicines Consortium (SMC) is to provide advice to NHS boards and their Area Drug and Therapeutics Committees (ADTCs) across Scotland about the status of all newly licensed medicines, all new formulations of existing medicines and new indications for established products (licensed from January 2002). Advice is made available as soon as practical after the launch of the medicine. NHS board ADTCs advise clinicians not to prescribe a new medicine prior to the publication of SMC advice. The SMC issues three categories of advice: 'accepted for use', 'accepted for restricted use', and 'not recommended'. 'Accepted for use' advice is given when the SMC decides that a medicine should be prescribed according to the licensed indication specified in the submission. If the SMC advises that a medicine should be prescribed only in a specific situation or by a particular prescribing group, then it is 'accepted for restricted use'.

Where alternative drug treatment(s) already exists for a condition, implementation of advice for medicines that are 'accepted for use' or 'accepted for restricted use' is subject to local NHS board decision-making. This means that although treatment for a clinical condition is available uniformly across Scotland, there may be variation in the individual medicines chosen locally to treat that clinical condition.

To understand the effect of SMC 'accepted for use' or 'accepted for restricted use' advice on medicine use, it is necessary to examine individual medicines and also to explore if there are any patterns in medicines use. A literature review identified no standard method to measure 'successful' implementation of health technology assessment (HTA) guidance, rather several approaches identifying variable factors that should be considered. This study investigates the use of medicines in primary care and hospitals across NHSScotland for which the SMC issued 'accepted for use' or 'accepted for restricted use' advice over the period January 2002 to December 2005.

Chapter 1: An investigation of medicines used in primary care for which SMC issued 'accepted for use' or 'accepted for restricted use' advice

Method of study

Medicine definition

Between January 2002 and December 2005, the SMC issued 'accepted for use' or 'accepted for restricted use' advice for 87 medicines that were mainly used in primary care.

Medicines were excluded from the study if they had multiple indications that limited interpretation of medicines utilisation for the SMC advice issued. This resulted in a cohort of 22 medicines that were 'accepted for use' and 19 that were 'accepted for restricted use'. Data were sourced through the national primary care prescribing database, PRISMS.

Medicine utilisation

A 'medicine profile' was developed for each of the 41 medicines. The profile included: the SMC advice; a description of the epidemiology of the indication for the medicine; NHSScotland medicines use over time; a comparison of the actual versus estimated manufacturer's budget impact; and potential factors that may be influencing medicines use within NHSScotland. A more limited profile was created for 14 of these medicines, where an abbreviated submission was completed by the manufacturer for the SMC.

Medicines use was defined as Gross Ingredient Cost (GIC) over the time period July 2001 to December 2006. This was presented graphically at national level, annotated with key milestones including medicine launch and SMC advice. From these data, actual expenditure and an estimate of the number of patients treated were calculated at defined time periods for the medicines in the study.

A qualitative review of the medicine profiles was then undertaken to identify potential factors that may limit the interpretation or explain the patterns of medicines use. This process initially focused on the five medicines that accounted for the greatest and least expenditure. The remaining medicine profiles were then examined in the context of these factors.

Key findings

Table 3 (page 15) summarises the 41 medicines included in the investigation (22 'accepted for use' and 19 'accepted for restricted use'). These cover a broad range of therapeutic areas and clinical conditions. Appendix 1 (page 25) presents the NHSScotland utilisation over time for each medicine. A full medicine profile for each medicine is available at <http://www.scottishmedicines.org.uk/>. Table 4 (page 17) quantifies the individual medicine and total expenditure in primary care before and after SMC advice was issued. An estimate of the number of patients treated after SMC advice was issued and the number of medicines in each therapeutic class are also included.

Use before SMC 'accepted for use' or 'accepted for restricted use' advice

NHS board ADTCs advise clinicians not to prescribe a new medicine prior to SMC advice. A total of £1,066,627 was spent in NHSScotland on the 41 medicines before SMC advice was issued. This is in the context of a cumulative spend in the primary care drugs bill over the study period (2002–2003 to 2005–2006) of £3.7 billion. The top five medicines by expenditure were: insulin glargine injection (10%); atorvastatin tablets (10%); tiotropium inhaler (10%); mometasone inhaler (9%); and methylphenidate sustained release OROS tablets (Concerta[®] XL) (9%). Of these, four medicines were subsequently 'accepted for restricted use': insulin glargine injection; atorvastatin tablets; mometasone inhaler; and methylphenidate sustained release OROS tablets.

For 19 medicines (45%), advice was issued within 3 months of launch. In the majority of cases (36 medicines, 88%), advice was issued within 6 months.

Use after SMC 'accepted for use' or 'accepted for restricted use' advice

The top five medicines by expenditure were: tiotropium inhaler (28%); insulin glargine injection (11%); rosuvastatin tablets (11%); ezetimibe tablets (10%); and mirtazapine orodispersible tablets (7%). Two of these were 'accepted for restricted use': ezetimibe tablets and insulin glargine injection. The five medicines that accounted for the least expenditure were: carbomer 0.25% gel (0.02%); testosterone mucoadhesive buccal tablets (0.03%); FemSeven[®] Sequi transdermal patch (0.07%); Premique Low Dose[®] tablets (0.08%); and telmisartan/hydrochlorothiazide tablets (Micardis[®] Plus) (0.09%). Of these, two were 'accepted for restricted use': testosterone mucoadhesive buccal tablets and telmisartan/hydrochlorothiazide tablets.

Review of the medicine profiles identified two key factors that may limit the interpretation or explain some of the patterns of medicines use after SMC advice.

Factor: Availability of alternative treatment(s) for a clinical condition

The new medicines investigated in this study were used to treat clinical conditions for which other treatment already existed. This is illustrated in Table 2 by the number of medicines in each therapeutic class, recognising that, in some cases, medicines in a different therapeutic class may be used to treat a clinical condition. In some cases, the new medicine offered advantages over previously available therapy. For example, the greatest expenditure was for the long-acting antimuscarinic bronchodilator, tiotropium inhaler, which was launched in September 2002 and ‘accepted for use’ by the SMC in December 2002. Tiotropium represented an advance over the available short-acting antimuscarinic bronchodilator, which has been available for many years, for the treatment of chronic obstructive pulmonary disease. Analysis shows increasing use of tiotropium inhaler, with tiotropium accounting for 67% of prescriptions for antimuscarinic bronchodilators between January and December 2006.

In other cases, the advantage of the new medicine over existing products may be less clear. For example, the least expenditure in primary care was for carbomer 0.25% gel (Liquivisc[®]), which was ‘accepted for use’ by the SMC for the symptomatic treatment of dry eye syndrome where a carbomer product is the treatment of choice. It differs in minor respects from other carbomer products, and analysis shows that between January and December 2006, it accounted for 6% of prescriptions for all four available carbomer products. Expenditure in primary care was also low for MicardisPlus[®] tablets, which contain an angiotensin-II receptor antagonist (telmisartan) with a diuretic (hydrochlorothiazide). MicardisPlus[®] was recommended for restricted use in the treatment of essential hypertension. However, seven angiotensin-II receptor antagonists existed before MicardisPlus[®], of which four were already available in combination with a diuretic, and these may, therefore, compete for market share. Table 2 lists other examples of medicines and their market share from January–December 2006.

Table 2: NHSScotland market share of some new medicines in the study

Name of new medicine	Indication	Total number of medicines in therapeutic class	Market share of new medicine* (Jan–Dec 2006)
Aripiprazole tablets	Schizophrenia	7 atypical antipsychotics	3% of prescriptions
Olmesartan tablets	Hypertension	7 angiotensin-II receptor antagonists	2% of prescriptions
Rosuvastatin tablets	Hyperlipidaemia	5 statins	4% of prescriptions
Tadalafil tablets	Erectile dysfunction	3 phosphodiesterase type-5 inhibitors	24% of expenditure
Vardenafil tablets	Erectile dysfunction	3 phosphodiesterase type-5 inhibitors	7% of expenditure

*market share of new medicine represented as a percentage of the total expenditure or number of prescriptions for all medicines in the therapeutic class for NHSScotland. Data source: PRISMS, ISD, Scotland from dispensed items. Excludes private prescriptions.

Factor: Challenges in interpreting data for 'restricted use' medicines

For 19 medicines that were 'accepted for restricted use' by the SMC, it was not possible to identify whether the data reflected the SMC restriction alone, due to absence of patient level data. For example, SMC advised that methylphenidate sustained release OROS formulation tablets (Concerta XL[®]) should be restricted to second line therapy and used only in exceptional circumstances where the supervising clinician has clear evidence of compliance problems. Approximately £1 million was spent on Concerta XL[®] between January and December 2006 but it is unknown whether this expenditure reflects SMC advice.

Conclusion

NHS board ADTCs advise clinicians not to prescribe a new medicine prior to SMC 'accepted for use' or 'accepted for restricted use' advice. In the context of the overall primary care drugs bill, expenditure on the study primary care medicines before SMC advice was small.

The SMC aims to issue advice as soon as practical after the launch of the new medicine. This was supported by the findings of this study, which showed that for 19 medicines (45%), advice was issued within three months of launch. In the majority of cases (36 medicines, 88%), advice was issued within 6 months.

Review of the medicine profiles identified two key factors that may limit the interpretation or explain some of the patterns of medicines use after SMC 'accepted for use' or 'accepted for restricted use' advice

- Availability of alternative treatment(s) for a clinical condition: there is no robust methodology to determine market share of a medicine and this, together with the absence of national patient level medicines utilisation data, makes it challenging to determine whether prescribing is clinically appropriate. Where several medicines of similar efficacy are available for a clinical condition, NHS boards and local clinicians may use their knowledge and expertise to decide whether the new medicine should replace existing treatment in local Formulary Management Systems.
- Challenges in interpreting data for 'restricted use' medicines: this study showed that for medicines that are 'accepted for restricted use', it is not possible to identify whether the data reflect the SMC restriction due to lack of national data on individual patient use of medicines. Expenditure on medicines that are 'accepted for restricted use' may, therefore, reflect use for patient groups that have not been assessed or accepted by SMC.

Table 3: Summary of medicines**(a) Medicines that were 'accepted for use' by the SMC (n=22)**

Name of medicine	Clinical condition	BNF Section
alendronate 70mg, colecalciferol 2800IU tablets (Fosavance [®])	Postmenopausal osteoporosis	Endocrine
aripiprazole tablets(Abilify [®])	Schizophrenia	Mental health / central nervous system
calcitriol 3µg/g ointment (Silkis [®])	Psoriasis	Skin
carbomer 0.25% gel (Liquivisc [®])	Dry eye syndrome	Eye
conjugated oestrogen, medroxyprogesterone tablets (Premique Low Dose [®])	Oestrogen deficiency	Obstetrics, gynaecology, and urinary-tract disorders
dutasteride capsules (Avodart [®])	Benign prostatic hyperplasia	Endocrine
epirenone tablets	Myocardial infarction	Cardiovascular
estradiol and levonorgestrel transdermal patch (FemSeven [®] Conti)	Oestrogen deficiency	Obstetrics, gynaecology, and urinary-tract disorders
estradiol and levonorgestrel transdermal patch (FemSeven [®] Sequi)	Oestrogen deficiency	Obstetrics, gynaecology, and urinary-tract disorders
galantamine prolonged-release capsules (Reminyl [®] XL)	Mild-to-moderately severe dementia	Central nervous system
mirtazapine orodispersible tablets (Zispin SolTab [®])	Major depression	Mental health / central nervous system
montelukast paediatric 4mg granules(Singulair [®])	Asthma	Respiratory
Movicol [®] Paediatric Plain oral powder	Paediatric faecal impaction	Gastro-intestinal
perindopril/indapamide tablets (Coversyl Plus [®])	Hypertension	Cardiovascular
rosiglitazone maleate/metformin hydrochloride tablets (Avandamet [®])	Type 2 diabetes	Endocrine
rosuvastatin tablets (Crestor [®])	Coronary heart disease (CHD)	Cardiovascular
sumatriptan tablets (Imigran Radis [®])	Migraine	Central nervous system
tadalafil tablets (Cialis [®])	Erectile dysfunction	Obstetrics, gynaecology, and urinary-tract disorders
tamsulosin hydrochloride extended release tablets (Flomaxtra [®] XL)	Benign prostatic hypertrophy	Obstetrics, gynaecology, and urinary-tract disorders
tiotropium bromide inhaler (Spiriva [®] inhaler)	Chronic obstructive pulmonary disease (COPD)	Respiratory
valsartan/hydrochlorothiazide tablets (Co-Diovan [®])	Hypertension	Cardiovascular
vardeafil tablets (Levitra [®])	Erectile dysfunction	Obstetrics, gynaecology, and urinary-tract disorders

(b) Medicines that were 'accepted for restricted use' by the SMC (n=19)

Name of medicine	Clinical condition	BNF Section
aripiprazole 5mg tablets(Abilify [®])	Schizophrenia	Mental health / Central nervous system
atorvastatin tablets (Lipitor [®])	Reduction of elevated total cholesterol in children aged 10 years and older	Cardiovascular
ciclesonide 80, 160µg inhaler (Alvesco [®])	Asthma	Respiratory
clindamycin/benzoyl peroxide gel (Duac [®] Once Daily gel)	Acne	Skin
eplerenone tablets	Myocardial infarction	Cardiovascular
ezetimibe tablets (Ezetrol [®])	Hypercholesterolaemia	Cardiovascular
ezetimibe/simvastatin tablets (Inegy [®])	Hypercholesterolaemia	Cardiovascular
insulin detemir injection	Diabetes mellitus	Endocrine
insulin glargine injection (Lantus [®])	Diabetes mellitus	Endocrine
levetiracetam (Keppra [®]) 100mg oral solution	Seizures	Central nervous system
levetiracetam (Keppra [®]) 750mg tablets	Seizures	Central nervous system
methylphenidate sustained release OROS tablets (Concerta [®] XL)	Attention-deficit hyperactivity disorder (ADHD)	Mental health / central nervous system
mometasone furoate inhaler (Asmanex Twisthaler [®])	Asthma	Respiratory
norelgestomin/ethinylestradiol patch (Evra [®])	Contraception	Obstetrics, gynaecology, and urinary-tract disorders
olmesartan medoxomil tablets (Olmotec [®])	Hypertension	Cardiovascular
strontium ranelate 2g granules for oral suspension (Protelos [®])	Postmenopausal osteoporosis	Endocrine
telmisartan, hydrochlorothiazide tablets (MicardisPlus [®])	Hypertension	Cardiovascular
testosterone 30 mg mucoadhesive buccal (prolonged release) tablets (Striant [™] SR)	Hypogonadism	Endocrine
zonisamide hard capsules 25 mg, 50 mg, 100 mg (Zonegran [®])	Epilepsy	Central nervous system

Table 4: Medicine Utilisation before and after SMC advice
(a) Medicines that were 'accepted for use' by the SMC (n=22)

Medicine Name	Time between launch of medicine and SMC advice (months)	Total GIC before SMC advice (from launch to advice)* (£)	Total GIC after SMC advice (Jan-Dec 2006)* (£)	Estimated number of patients after SMC advice (Jan-Dec 06)**	Number of medicines in therapeutic class (BNF March 2006)
alendronate 70mg/colecalciferol tablets (Fosavance®)	2	7,433	84,269	100-1,000	4 bisphosphonates
aripiprazole (Abilify®) 10,15 and 30mg tablets	2	24,144	1,478,048***	>1,000***	7 atypical antipsychotics
calcitriol 3µg/g ointment (Silkis®)	12	53,599	153,037	>1,000	3 vitamin D and analogues
carbomer 0.25% gel (Liquivisc®)	19	2,612	8,651	100-1,000	4 carbomers
conjugated oestrogen, medroxyprogesterone tablets (Premique Low Dose®)	6	29,574	35,219	100-1,000	Many oral HRT formulations
dutasteride capsules (Avodart®)	3	10,113	597,024	>1,000	2 specific inhibitors of 5α reductase
FemSeven® Conti transdermal patch (estradiol/levonorgestrel)	2	4,533	41,747	100-1,000	5 HRT patches containing estradiol/progestogen
FemSeven® Sequi transdermal patch (estradiol/levonorgestrel)	3	1,052	29,278	100-1,000	5 HRT patches containing estradiol/progestogen
galantamine prolonged release capsules (Reminyl® XL)	0	0	835,132	100-1,000	3 acetylcholinesterase inhibitors
macrogol 3350 oral powder sachets (Movicol® Paediatric Plain)	4	3,172	97,468	>1,000	1 macrogol licensed for child under 8 years old. Many other laxatives.
mirtazapine orodispersible tablets (Zispin SolTab®)	1	1,430	2,772,066	>1,000	Many medicines for major depression
montelukast paediatric granules (Singulair®)	5	3,310	57,963	100-1,000	2 leukotriene receptor antagonists
perindopril/indapamide (Coversyl Plus®)	16	30,639	206,512	>1,000	5 ACE inhibitors with diuretic
rosiglitazone/metformin tablets (Avandamet®) (2mg/1g and 4mg/1g)	0	3994.53	1,195,610	>1,000	2 glitazones
rosiglitazone/metformin tablets (Avandamet)	4	14557	414,375	100-1,000	2 glitazones
rosuvastatin tablets (Crestor®)	2	41,042	4,378,937	>1,000	5 statins
sumatriptan succinate tablets (Imigran Radis®)	4	6,412	51,813	>1,000	7 5HT ₁ agonists
tadalafil tablets (Cialis®)	3	77,675	1,486,952	>1,000	3 phosphodiesterase type-5 inhibitors
tamsulosin extended release tablets (Flomaxtra® XL)	-1	19,278	1,800,219	>1,000	6 alpha-blockers for urinary retention
telmisartan/hydrochlorothiazide tablets (Micardis® Plus)	4	227	37,551	100-1,000	4 angiotensin-II receptor antagonists with diuretic
tiotropium inhaler	3	104,133	11,746,289	>1,000	2 antimuscarinic bronchodilators
valsartan/hydrochlorothiazide tablets (Co-Diovan®)	2	195	67,805	100-1,000	4 compound angiotensin-II receptor antagonists/diuretic
varденаfil tablets (Levitra®)	3	6,440	440,837	>1,000	3 phosphodiesterase type-5 inhibitors

*Data source: PRISMS, ISD, Scotland from dispensed items. Excludes private prescriptions.

**Figures relating to patient numbers are estimates based on the Gross Ingredient Cost (GIC). The actual patient base is not known.

***includes aripiprazole 5mg tablets.

(b) Medicines that were 'accepted for restricted use' by the SMC (n=19)

Medicine Name	Time between launch of medicine and SMC advice (months)	Total GIC before SMC advice (from launch to advice)* (£)	Total GIC after SMC advice (Jan–Dec 2006)* (£)	Estimated number of patients after SMC advice (Jan–Dec 06)**	Number of medicines in therapeutic class (BNF March 2006)
aripiprazole (Abilify [®]) 5mg tablets	5	13,578	Included in total in Table 2(a)	Included in total in Table 2(a)	7 atypical antipsychotics
atorvastatin tablets (Lipitor [®])	6	111,595	205,849	100-1,000	5 statins
ciclesonide 80, 160µg inhaler (Alvesco [®])	6	13,588	66,063	100-1,000	5 inhaled corticosteroids
clindamycin/benzoyl peroxide gel (Duac [®])	6	14,179	277,665	>1,000	3 topical benzoyl peroxide with antimicrobials
epplerenone tablets (Inspra [®])	2	2,093	221,070	100-1,000	2 aldosterone antagonists
ezetimibe tablets (Ezetrol [®])	5	45,844	4,113,450	>1,000	1 (5 statins)
ezetimibe/simvastatin tablets (Inegy [®])	4	1,469	316,785	100-1,000	1 (5 statins)
insulin detemir injection (Levemir [®])	2	18,736	1,279,972	>1,000	2 long acting human insulin analogue (many insulins)
insulin glargine injection (Lantus [®])	2	111,819	4,746,116	>1,000	2 long acting human insulin analogue (many insulins)
levetiracetam (Keppra [®]) 100mg oral solution	3	2,840	101,601	10-100	1 (many medicines for epilepsy)
levetiracetam (Keppra [®]) 750mg tabs	3	2,334	95,979	10-100	1 (many medicines for epilepsy)
methylphenidate sustained release OROS formulation (Concerta [®] XL)	5	96,169	1,124,043	>1,000	3 medicines for ADHD. 3 formulations of methylphenidate.
mometasone inhaler (Asmanex Twisthaler [®])	10	96,254	144,483	100-1,000	5 inhaled corticosteroids
norelgestomin/ ethinylestradiol patch (Evra [®])	4	26,631	100,666	>1,000	1 low strength combined contraceptive patch. 3 low strength combined oral contraceptives.
olmesartan tablets (Olmotec [®])	4	5,257	269,689	>1,000	7 angiotensin-II receptor antagonists
strontium granules for oral suspension (Protelos [®])	9	40,991	162,756	100-1,000	4 bisphosphonates
testosterone mucoadhesive buccal tablets (Striant [®] SR)	5	2,907	12,792	10-100	1 oral, 1 buccal, 3 patches, 5 injections, 1 implant
zonisamide capsules (Zonegran [®])	6	14,778	118,259	100-1,000	1 (many medicines for epilepsy)

*Data source: PRISMS, ISD, Scotland from dispensed items. Excludes private prescriptions.

**Figures relating to patient numbers are estimates based on the Gross Ingredient Cost (GIC). The actual patient base is not known.

Chapter 2: An investigation of medicines used in secondary (hospital) care for which SMC issued 'accepted for use' or 'accepted for restricted use' advice

Method of study

Medicine definition

Between January 2002 and December 2005, the SMC issued 'accepted for use' or 'accepted for restricted use' advice for 63 medicines that were mainly used in secondary (hospital) care. Three categories of medicines were identified for investigation in secondary (hospital) care, reflecting national clinical priorities: medicines used in cancer; antimicrobial medicines; and other specified medicines that were 'accepted for use' or 'accepted for restricted use' by the SMC.

Due to the challenges of extracting data from hospital systems, the number of medicines investigated was limited and specialists were consulted to identify which should be selected for evaluation. Medicines that were 'accepted for use' or 'accepted for restricted use' were considered for selection if they were mainly used in hospital for a single clinical indication and, in general, had a high cost or high volume of use. This resulted in a cohort of 13 medicines of which seven were 'accepted for use' and six were 'accepted for restricted use' (Figure 2, page 20). Data on medicines use were obtained from hospital pharmacies. To support validation of hospital data, a data collection form was produced for manufacturers, in collaboration with the ABPI; This requested information on sales of the individual medicines, before and after SMC advice.

Medicine utilisation

A 'medicine profile' was developed for each of the 13 medicines. The profile included: the SMC advice; a description of the epidemiology of the indication for the medicine; NHSScotland medicines use over time; a comparison of the actual versus estimated manufacturer's budget impact; and potential factors that may be influencing medicines use within NHSScotland.

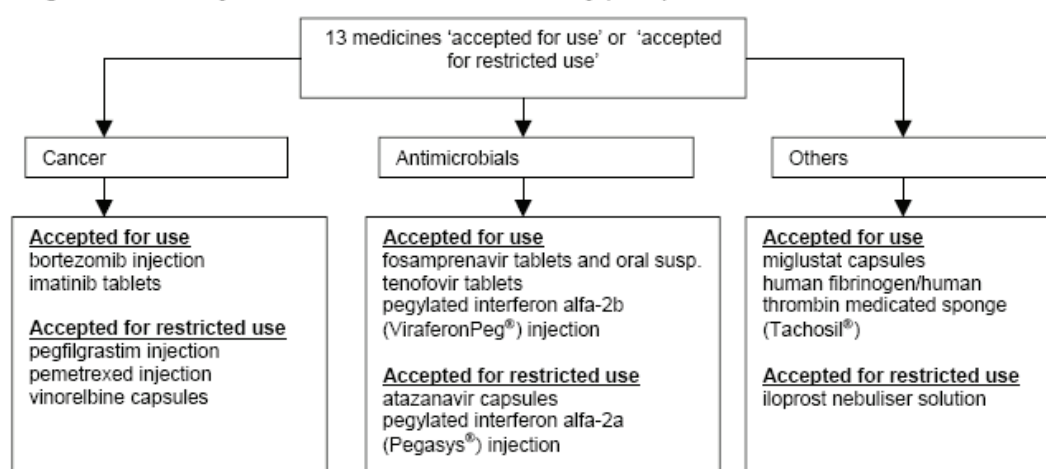
Medicines use was defined as hospital expenditure over the time period July 2001 to March or December 2006. This was presented graphically at national level, annotated with key milestones including medicine launch and SMC advice, and compared with industry data where available. From these data, actual expenditure and an estimate of the number of patients treated were calculated at defined time periods for the medicines in the study.

A qualitative review of the medicine profiles was then undertaken to identify potential factors that may limit the interpretation or explain the patterns of medicines use. This process initially focused on the five medicines that accounted for the greatest and least expenditure. The remaining medicine profiles were then examined in the context of these factors.

Key findings

Figure 2 and Table 5 (page 26) summarise the 13 medicines included in the study. Appendix 2 (page 36) presents the NHSScotland utilisation over time for each medicine. A full medicine profile for each medicine is available at <http://www.scottishmedicines.org.uk/>. Table 6 (page 27) quantifies the individual medicine and total expenditure in secondary (hospital) care, before and after SMC advice was issued. An estimate of the number of patients treated after SMC advice was issued and the number of medicines in each therapeutic class are also included.

Figure 2: Summary of medicines included in the study (n=13)



Use before SMC 'accepted for use' or 'accepted for restricted use' advice

For three medicines (23%), advice was issued within 3 months of launch. For eight medicines (62%), advice was issued within 6 months of launch.

A total of £987,884 was spent on nine hospital medicines before SMC advice was issued. There were insufficient data for four medicines: imatinib tablets; human fibrinogen/human thrombin medicated sponge (Tachosil®); miglustat capsules; and vinorelbine capsules. The top five medicines by expenditure were: iloprost nebuliser solution (41%); atazanavir capsules (18%); fosamprenavir tablets and oral suspension (16%); pemetrexed injection (8%); and tenofovir tablets (7%). Of these, three were 'accepted for restricted use': iloprost nebuliser solution; atazanavir capsules; and pemetrexed injection.

Use after SMC 'accepted for use' or 'accepted for restricted use' advice

The top five medicines by expenditure were: imatinib tablets (38%); tenofovir tablets (18%); pegylated interferon alfa 2a (Pegasys®) injection (15%); bortezomib injection (9%); and atazanavir capsules (6%). Two of these were 'accepted for restricted use': pegylated interferon alfa 2a injection; and atazanavir capsules.

The five medicines that accounted for the least expenditure were: iloprost nebuliser solution (0.2%); Tachosil® (0.3%); vinorelbine capsules (0.9%); fosamprenavir tablets and oral suspension (1%); and pegfilgrastim injection (3%). Of these, three were 'accepted for restricted use': iloprost nebuliser solution; vinorelbine capsules; and pegfilgrastim injection.

Review of the medicine profiles identified three key factors that may limit the interpretation or explain some of the patterns of medicines use after SMC advice.

Factor: Limitations of data obtained from NHS boards and manufacturers

The interpretation of medicines use after SMC advice was limited by the variation in reporting and completeness of data. Extracting data from hospital and industry systems was challenging, and the data provided by NHS boards and manufacturers proved to be incomplete for a number of medicines used in hospital. Unlike primary care, there is no national database of medicines prescribed in hospital, and several NHS boards experienced difficulties in providing hospital data. In some cases, this was because the medicine may be supplied through different hospital systems. For example, Tachosil® for improvement of haemostasis in liver surgery may be supplied through General Stores in some hospitals. In other cases, some patients may receive active treatment with a new medicine within clinical trials, such as imatinib tablets for chronic myeloid leukaemia. Licensed medicines that are used in clinical trials may or may not be part of the hospital pharmacy stock control system.

There were also differences in how NHS boards reported costs for hospital medicines, including whether or not VAT was included, and lack of clarity with respect to which formulations or doses were dispensed. Sufficient data were provided by manufacturers for six of the 12 medicines that were requested: fosamprenavir tablets and oral suspension; bortezomib injection; pegylated interferon alfa 2a (Pegasys®) injection; pemetrexed injection; Tachosil®; and pegylated interferon alfa-2b (ViraferonPeg®) injection. Comparison of industry and hospital data for these showed similar trends (Figure 3, page 24) and, for Pegasys® and pemetrexed injections, suggested that industry supply data is reportable 3–6 months prior to hospital utilisation data.

Factor: Availability of alternative treatment(s) for a clinical condition

The new medicines investigated in this study were used to treat clinical conditions for which other treatment often already existed. This is illustrated in Table 6 (page 27) by the number of medicines in each therapeutic class, recognising that, in some cases, medicines in a different therapeutic class may be used to treat a clinical condition. For example, three peginterferons are available in the UK: Pegasys® injection; PegIntron® injection; and ViraferonPeg® injection. Due to the challenges in obtaining data from hospital systems, it was not possible to obtain data for all medicines within a therapeutic class. However, in this study, data were obtained

from hospitals for two peginterferons (ViraferonPeg[®] and Pegasys[®] injections) that were 'accepted for use' or 'accepted for restricted use' by SMC for chronic hepatitis C. These may compete for market share and analysis showed that use of both medicines increased after SMC advice was issued. However, while use of ViraferonPeg[®] injection stabilised, use of Pegasys[®] injection continued to increase, reaching an expenditure (Jan–Dec 2006) of £1,185,355 for Pegasys[®] injection and £386,606 for ViraferonPeg[®] injection. A similar case is observed with the protease inhibitors. Ten protease inhibitors are currently available, and data were obtained for two of these (fosamprenavir tablets and oral suspension, atazanavir capsules) that were 'accepted for use' or 'accepted for restricted use' by SMC for the treatment of human immunodeficiency virus (HIV). Expenditure for atazanavir capsules (Apr 2005–March 2006) was £453,386 compared with £108,687 for fosamprenavir tablets and oral suspension.

Factor: Challenges in interpreting data for 'restricted use' medicines

For six medicines that were 'accepted for restricted use' by the SMC, it was not possible to identify whether the data reflected the SMC restriction alone, due to absence of patient level data. For example, imatinib tablets were recommended for restricted use by the SMC for the treatment of chronic myeloid leukaemia. It should be used only by or under the direction of haematologists/oncologists experienced in this field. Approximately £3 million was spent on imatinib tablets between April 2005 and March 2006 but it is unknown whether this expenditure reflects the SMC restriction.

Conclusion

The SMC aims to issue advice as soon as practical after the launch of the new medicine. This study demonstrated that for eight medicines (62%), advice was issued within 6 months of launch. For three medicines (23%), advice was issued within 3 months of launch. This is reflected in a low expenditure for the medicines before SMC advice was issued. However, this low expenditure may also be due in part to the number of patients with clinical conditions that could be treated with the selected medicines.

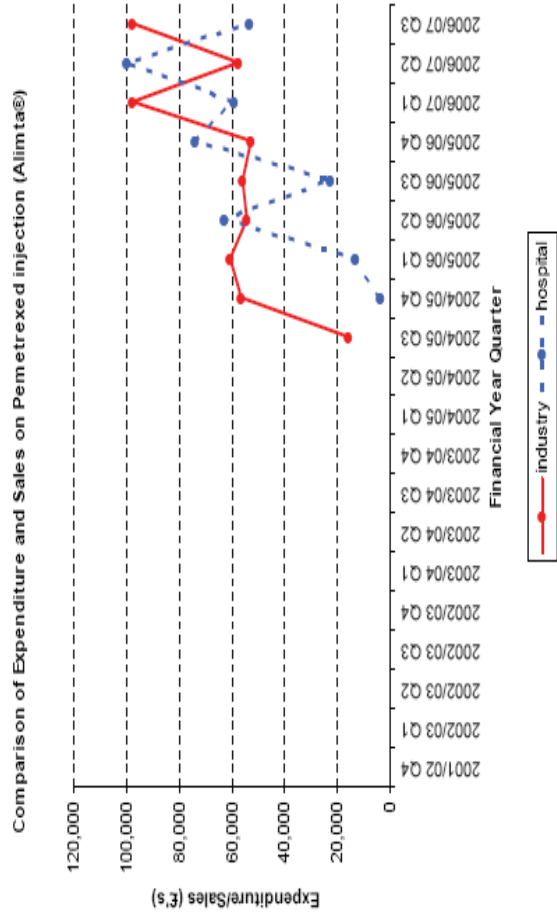
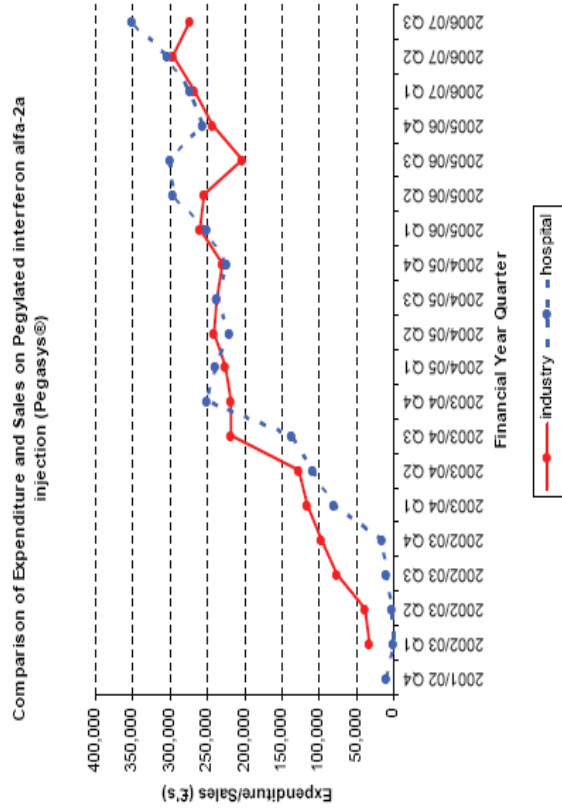
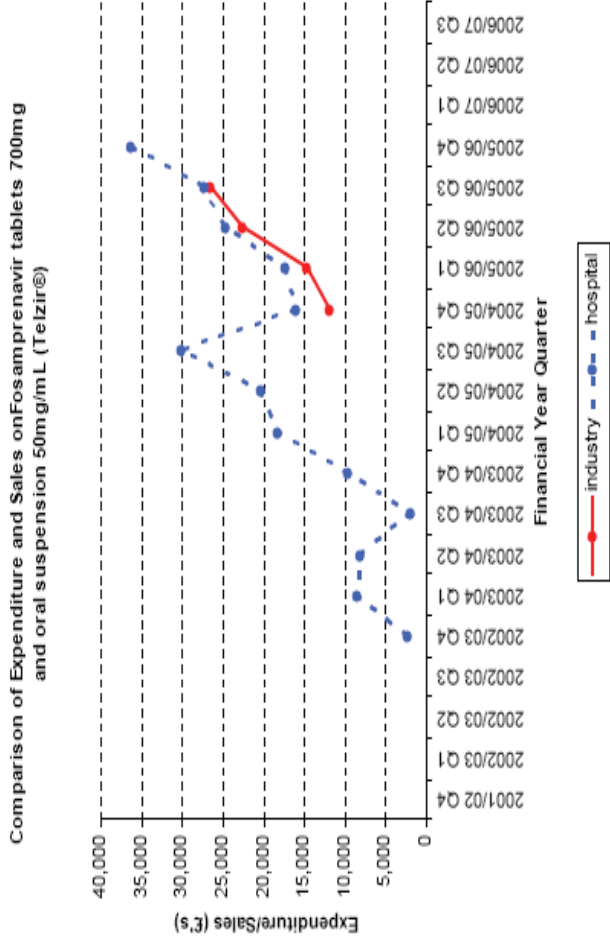
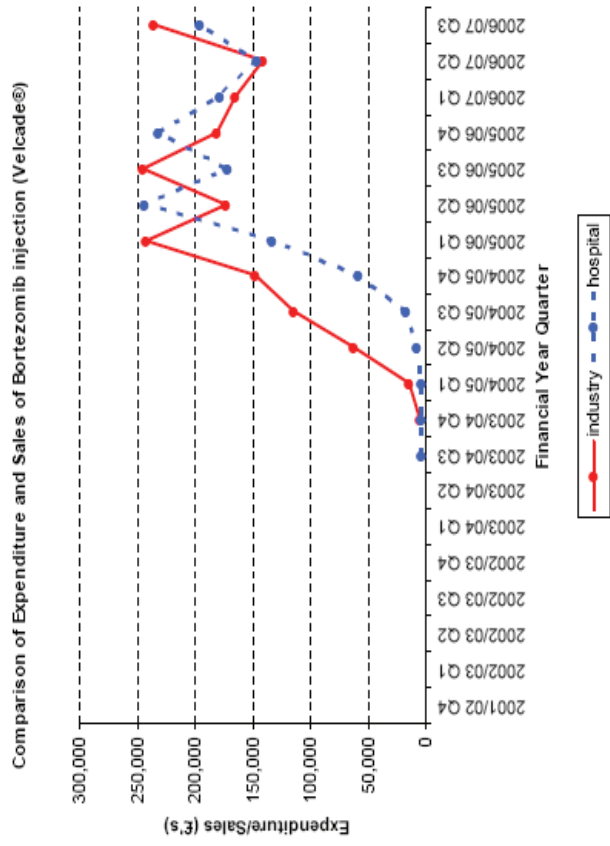
Review of the medicine profiles identified three key factors that may limit the interpretation or explain some of the patterns of medicines use after SMC 'accepted for use' or 'accepted for restricted use' advice.

- Limitations of data obtained from NHS boards and manufacturers: the study confirms the challenges that exist around hospital medicine utilisation data. National data at a medicine level is available in primary care through PRISMS. However, this is not the case for secondary (hospital) care data and both NHS boards and manufacturers faced challenges in providing the data requested for hospital medicines. This included issues with quantifying medicine use through clinical trial and non-pharmacy supply, and

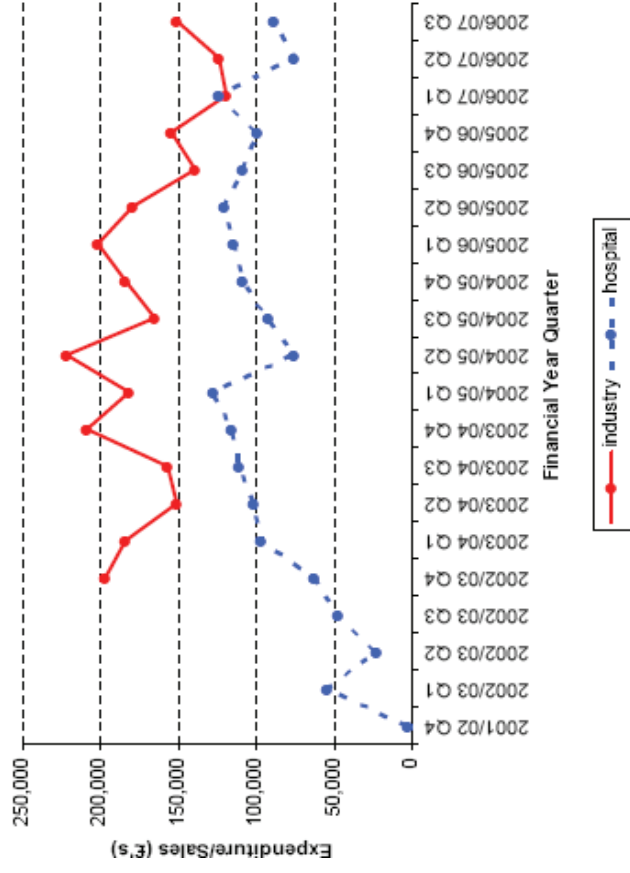
differences in reporting formulations, leading to inconsistencies and gaps in the reporting of data. However, where sufficiently robust data were available from both sources, industry and hospital data showed similar trends.

- Availability of alternative treatment(s) for a clinical condition: there is no robust methodology to determine market share of a medicine and this, together with the absence of national patient level medicines utilisation data, makes it challenging to determine whether prescribing is clinically appropriate. Where several medicines of similar efficacy are available for a clinical condition, NHS boards and local clinicians may use their knowledge and expertise to decide whether the new medicine should replace existing treatment in local Formulary Management Systems.
- Challenges in interpreting data for 'restricted use' medicines: this study showed that for medicines that are 'accepted for restricted use', it is not possible to identify whether the data reflect the SMC restriction due to lack of national data on individual patient use of medicines. Expenditure on medicines that are 'accepted for restricted use' may, therefore, reflect use for patient groups that have not been assessed or accepted by SMC.

Figure 3: Comparison of industry and secondary (hospital) care data (n=6)



Comparison of Expenditure and Sales on Pegylated interferon alfa-2b (VirafeonPeg®) injection



Comparison of Expenditure and Sales on Human Fibrinogen 5.5mg and Human Thrombin 2.0 IU per cm² medicated sponge (TachoSil®)

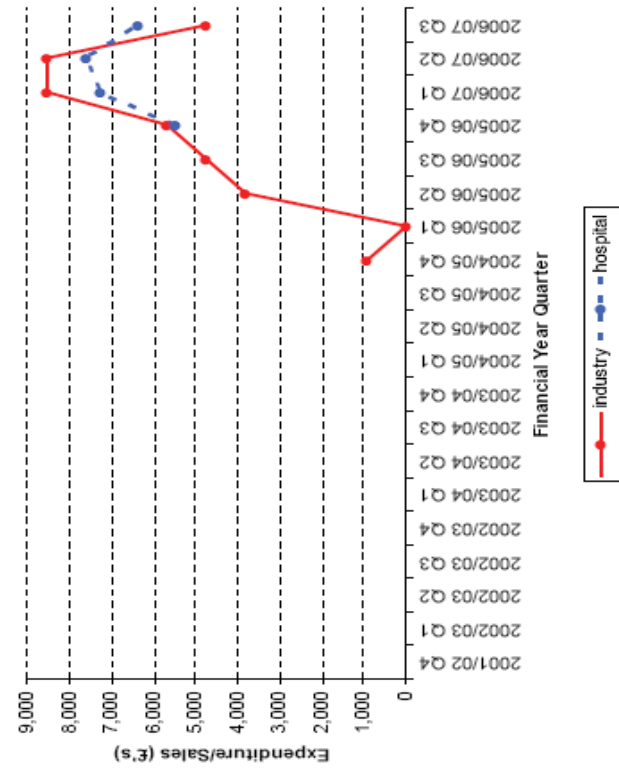


Table 5: Summary of medicines

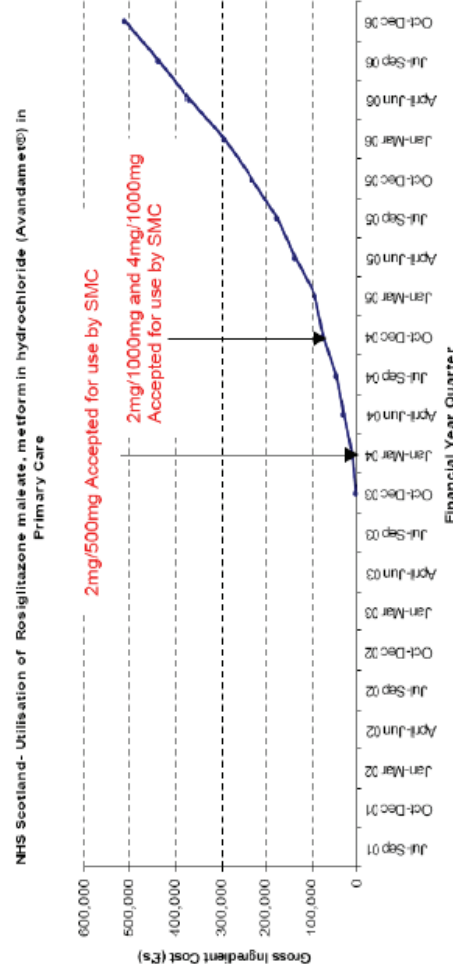
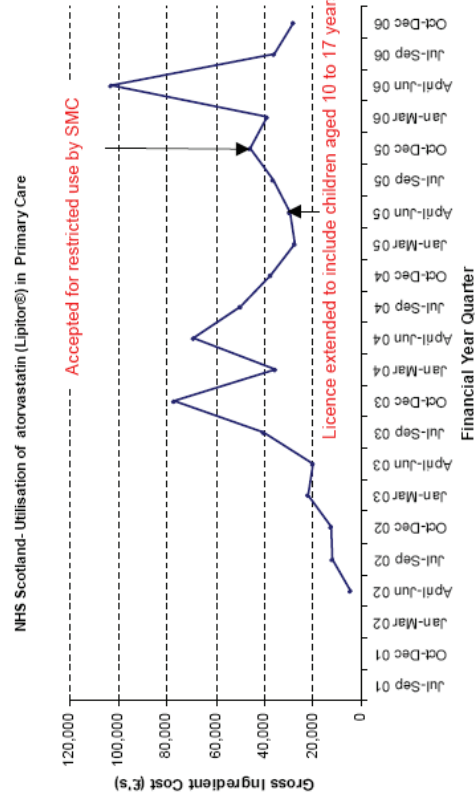
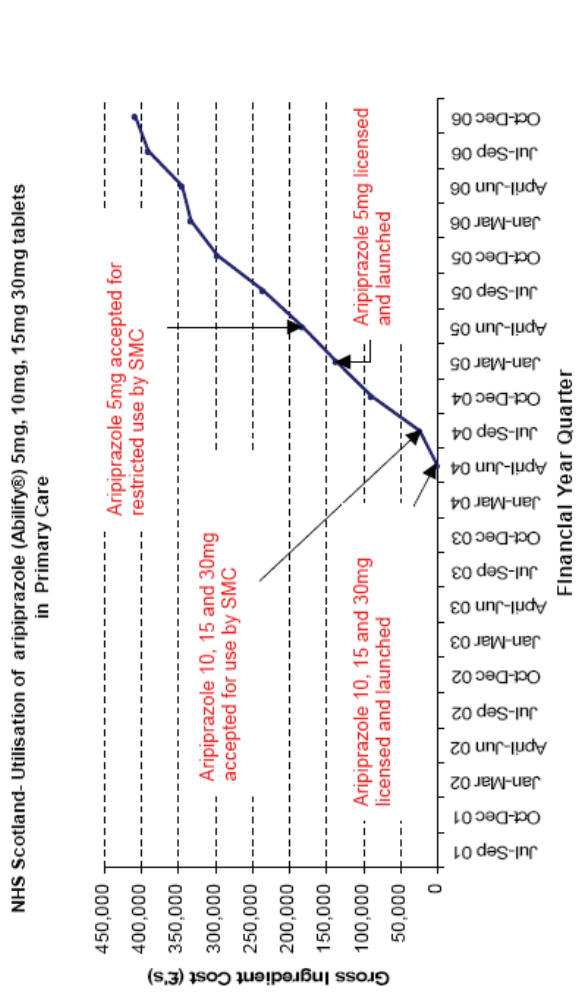
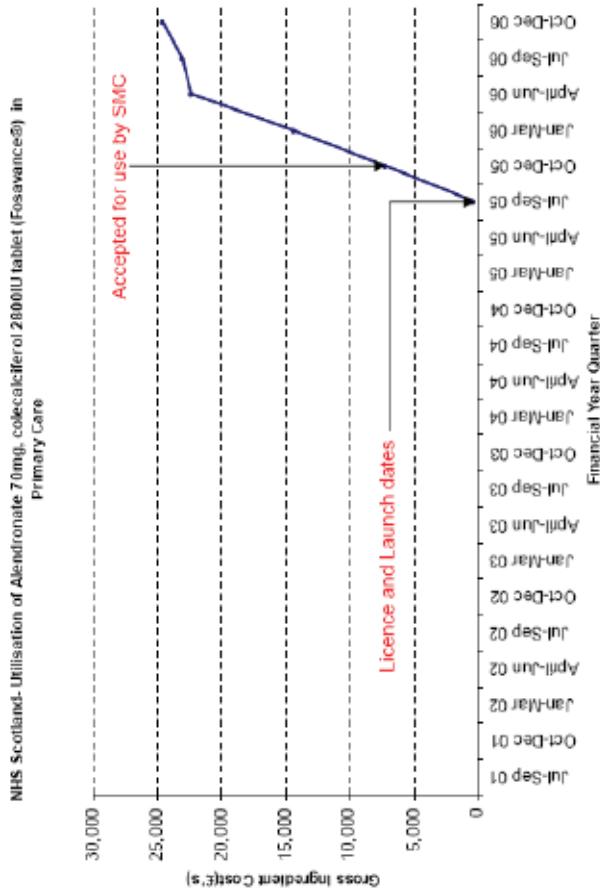
Name of medicine	Clinical condition	British National Formulary (BNF) section
Atazanavir capsules	HIV infection	Infections
Bortezomib injection	Multiple myeloma	Malignant disease and immunosuppression
Fosamprenavir tablets and oral suspension	HIV infection	Infections
Human fibrinogen 5.5mg and human thrombin 2.0 IU per cm ² medicated sponge (Tachosil®)	Improvement of haemostasis in liver surgery	Not included
Iloprost trometamol nebuliser solution	Pulmonary hypertension	Cardiovascular system
Imatinib tablets	Chronic myeloid leukaemia	Malignant disease and immunosuppression
Miglustat capsules	Gaucher's disease	Nutrition and blood
Pegfilgrastim injection	Neutropenia	Nutrition and blood
Pegylated interferon alfa 2a (Pegasys®) injection	Chronic hepatitis C	Infections
Pegylated interferon alfa-2b (ViraferonPeg®) injection	Chronic hepatitis C	Infections
Pemetrexed injection	Malignant pleural mesothelioma	Malignant disease and immunosuppression
Tenofovir tablets	HIV infection	Infections
Vinorelbine capsules	Lung cancer	Malignant disease and immunosuppression

Table 6: Medicine use in secondary (hospital) care before and after SMC advice

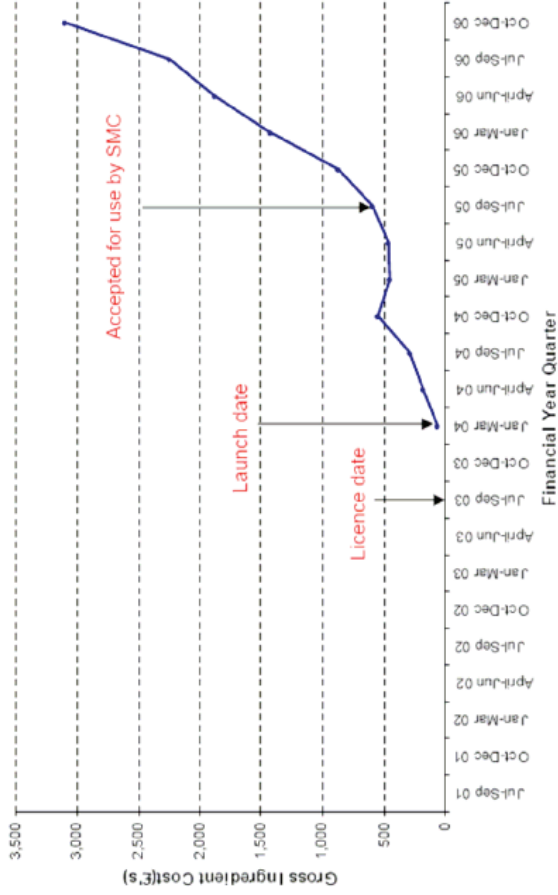
Medicine name	Time between launch of medicine and SMC advice (months)	Total expenditure before SMC advice (including pre-launch) (£)	Expenditure after SMC advice (Jan–Dec 2006)* (£)	Estimated number of patients after SMC advice (Jan–Dec 2006)*	Number of medicines in therapeutic class (BNF March 2006)
Atazanavir capsules	6	174,421	452,298	100-1,000	9 protease inhibitors
Bortezomib injection	6	36,232	753,609	10-100	1 proteasome inhibitor
Fosamprenavir tablets and oral suspension	11	156,785	105,391	10-100	9 protease inhibitors
Human fibrinogen 5.5mg and human thrombin 2.0 IU per cm ² medicated sponge (Tachosil [®])	8	No data	26,681	10-100	Not included in BNF
Iloprost trometamol nebuliser solution	23	402,135	16,537	<10	3 drugs licensed for primary pulmonary hypertension
Imatinib tablets	5	No data	3,065,457	100-1,000	1 protein-tyrosine kinase inhibitor
Miglustat capsules	21	No data	No data	No data	2 drugs for Gaucher's disease
Pegfilgrastim injection	6	5,414	225,082	10-100	3 drugs used in neutropenia
Pegylated interferon alfa 2a (Pegasys [®]) injection	2	11,167	1,185,355	100-1,000	3 peginterferon alfa
Pegylated interferon alfa-2b (ViraferonPeg [®]) injection	0	56,027	386,606	10-100	3 peginterferon alfa
Pemetrexed injection	9	79,908	286,848	10-100	12 antimetabolites
Tenofovir tablets	4	65,795	1,412,002	100-1,000	8 nucleoside reverse transcriptase inhibitors
Vinorelbine capsules	1	No data	74,061	10-100	4 vinca alkaloids

*for atazanavir capsules, tenofovir tablets, fosamprenavir tablets and oral suspension, and imatinib tablets the time period was April 2005 to March 2006. For fosamprenavir, SMC advice was issued in July 2005 and the expenditure (April 2005–March 2006), therefore, includes some use before SMC advice was issued.

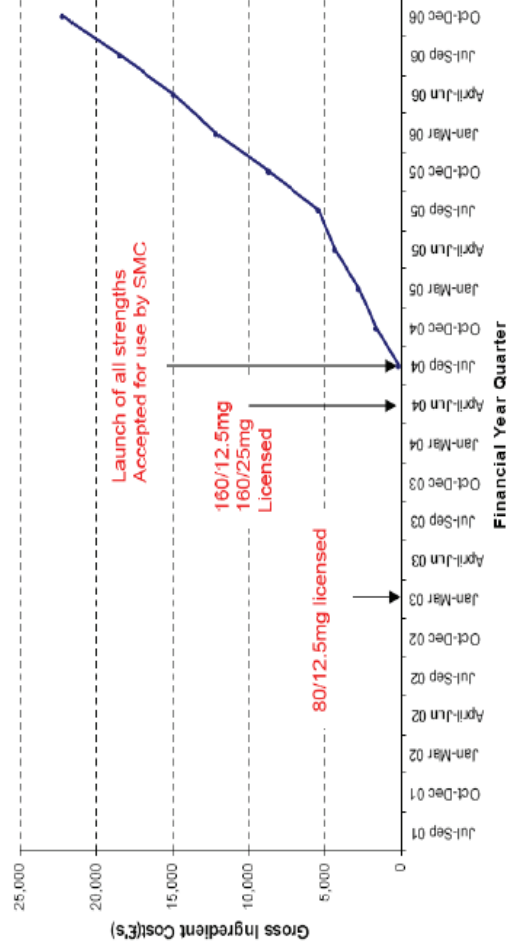
Appendix 1: Primary care utilisation



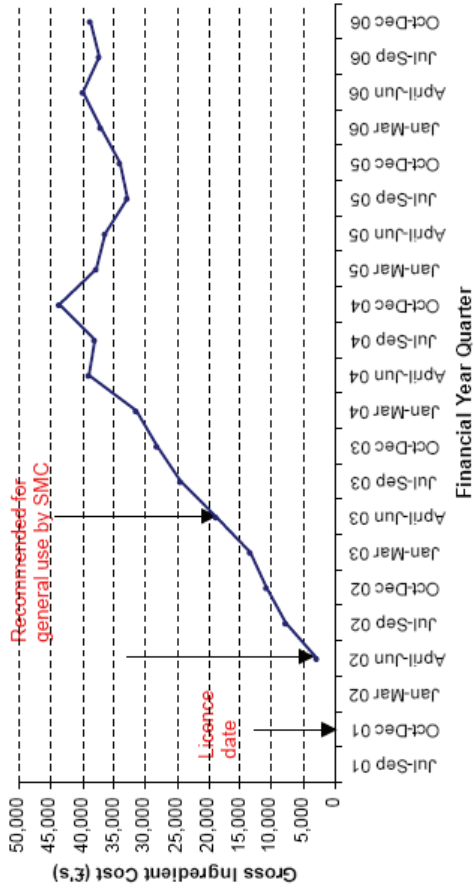
NHS Scotland- Utilisation of Carbomer 0.25% gel (Liquivisc®) in Primary Care



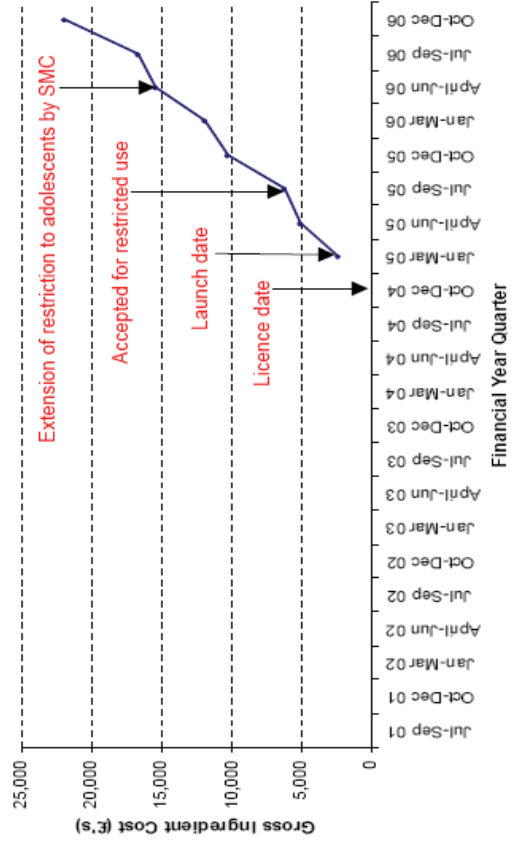
NHS Scotland- Utilisation of Valsartan/hydrochlorothiazide (Co-Diovan®) in Primary Care



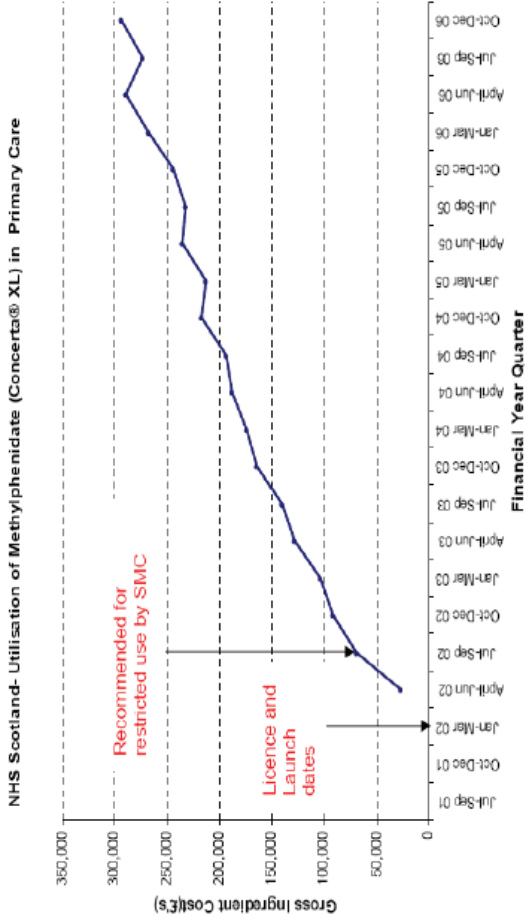
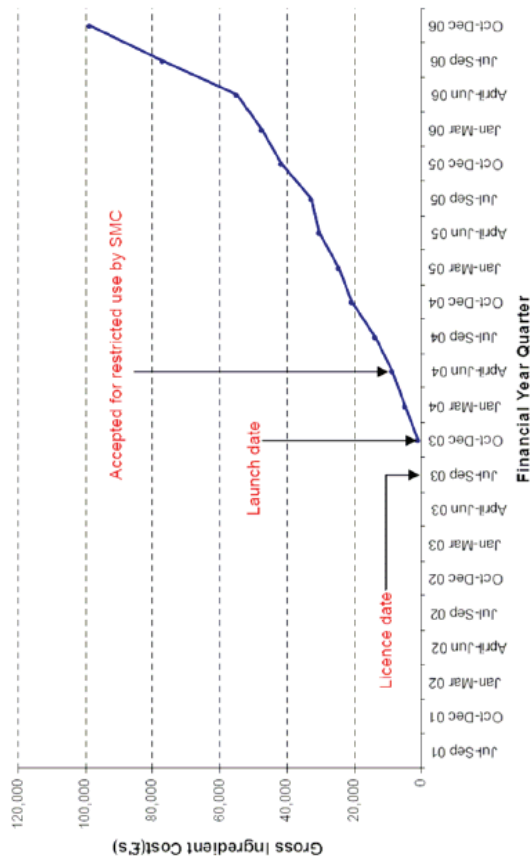
NHS Scotland- Utilisation of Calcitriol 3 micrograms/g ointment (Silkis®) in Primary Care



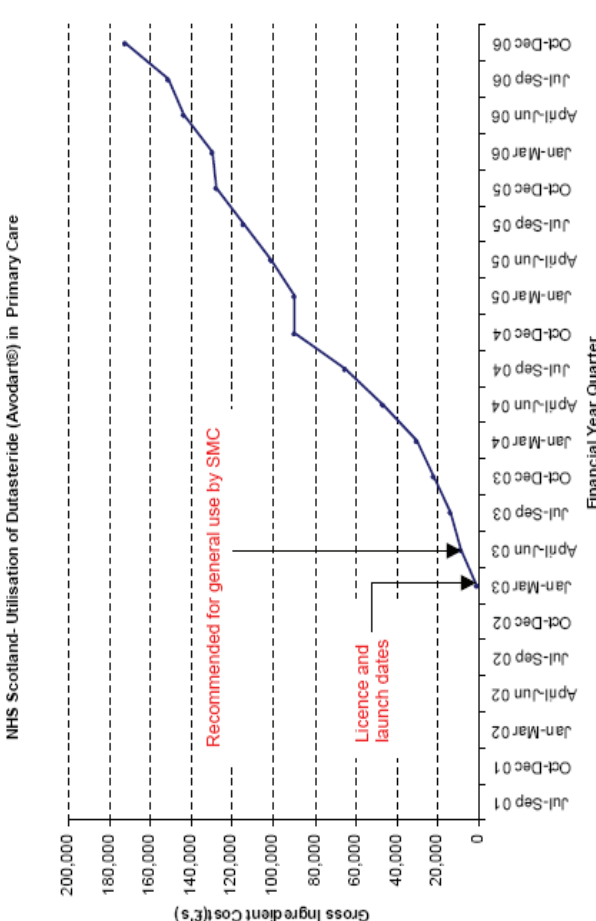
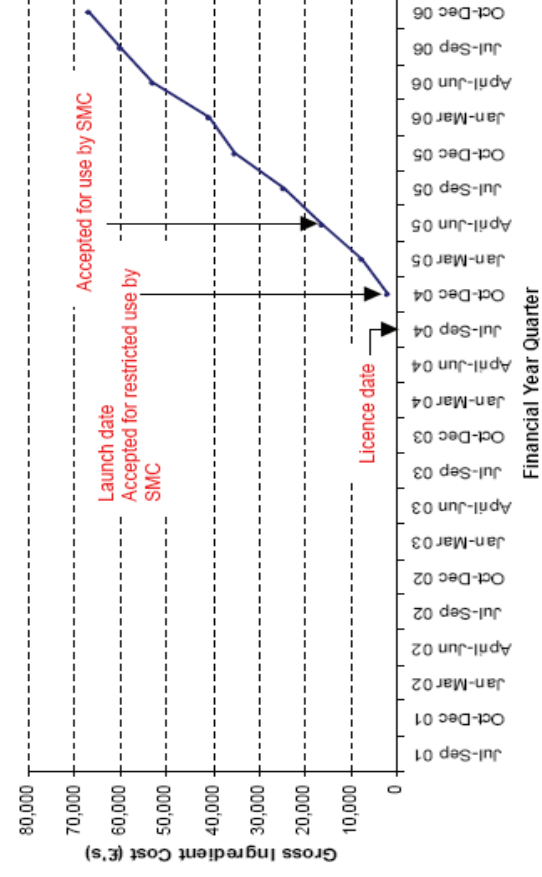
NHS Scotland- Utilisation of Ciclesonide 80, 160µg inhaler (Alvesco®) in Primary Care



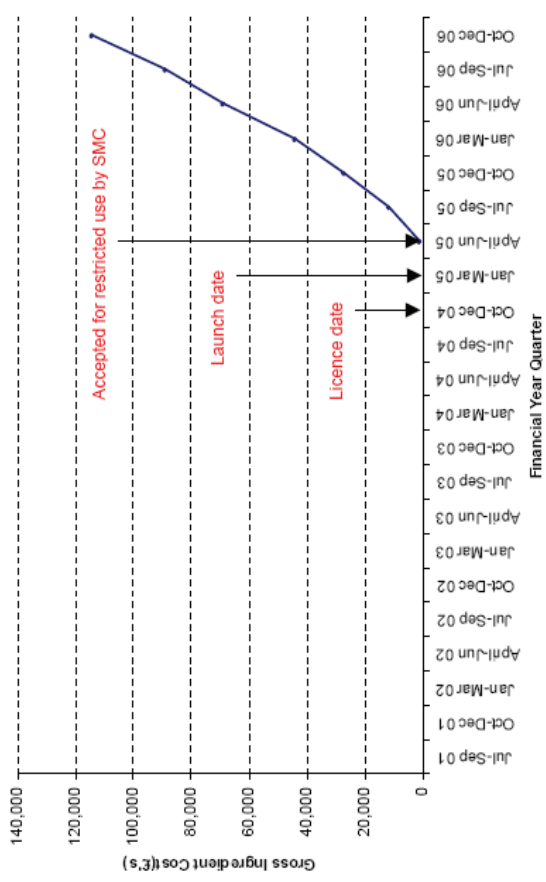
NHS Scotland- Utilisation of Clindamycin 1% and benzoyl peroxide 5% gel (Duac® once daily gel) in Primary Care



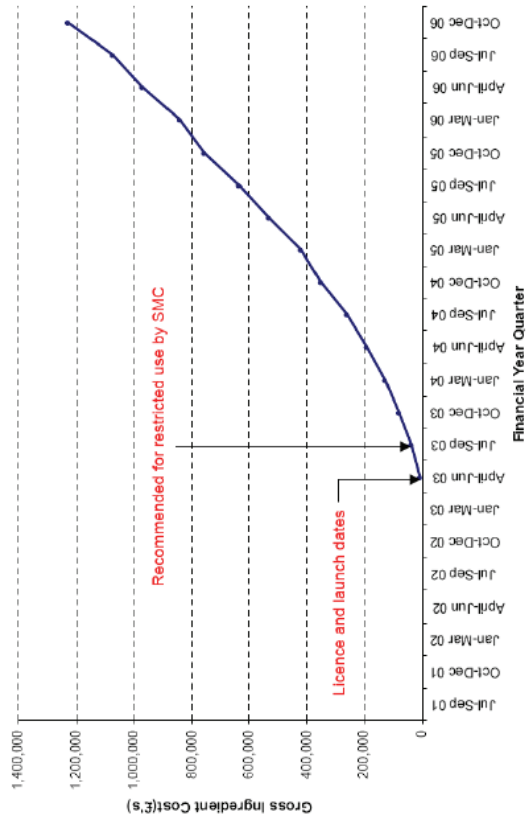
NHS Scotland- Utilisation of Eplerenone 25mg and 50mg tablets (Inspra®) in Primary Care



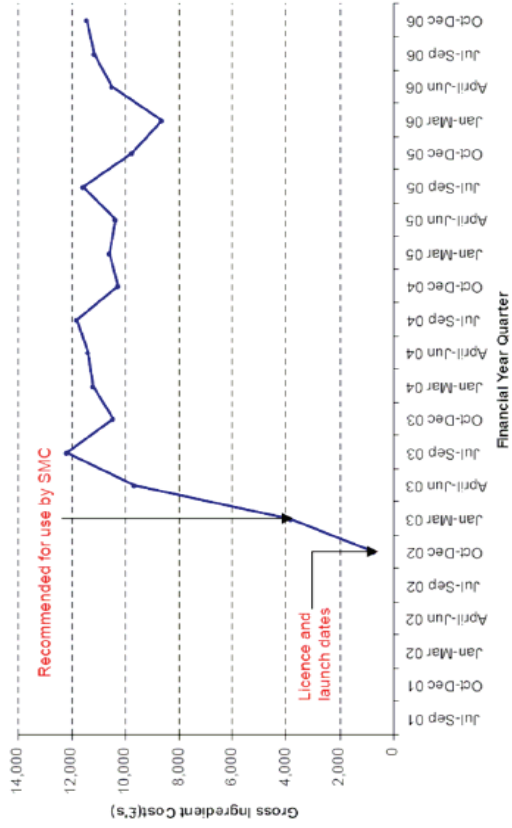
NHS Scotland- Utilisation of Ezetimibe/simvastatin (Inegy®) in Primary Care



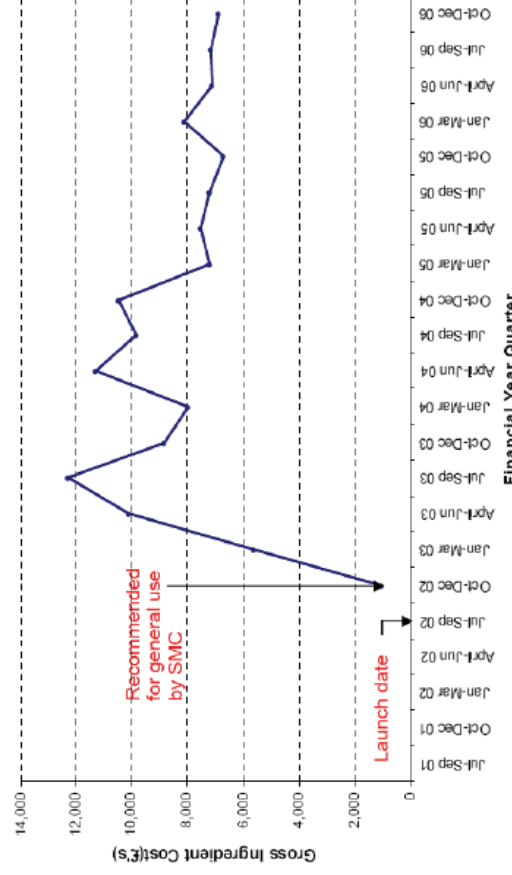
NHS Scotland- Utilisation of Ezetimibe (Ezetrol®) in Primary Care



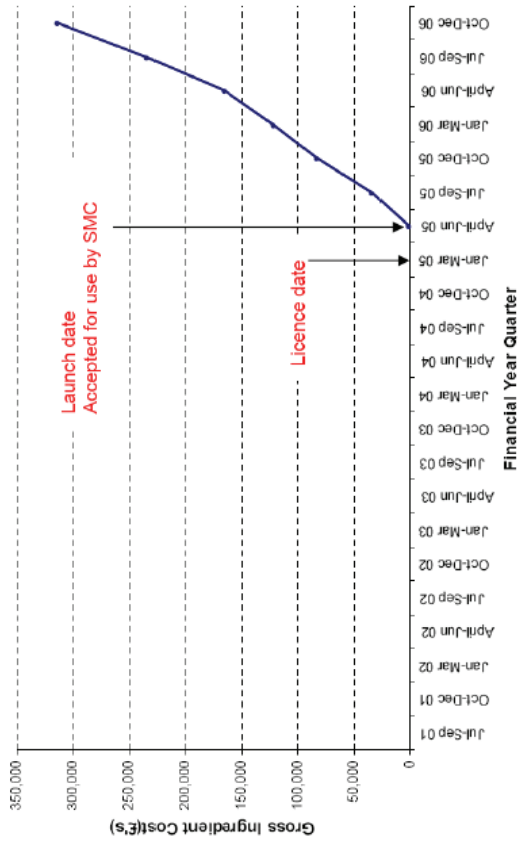
NHS Scotland- Utilisation of estradiol and levonorgestrel transdermal patch (FemSeven®) in Primary Care



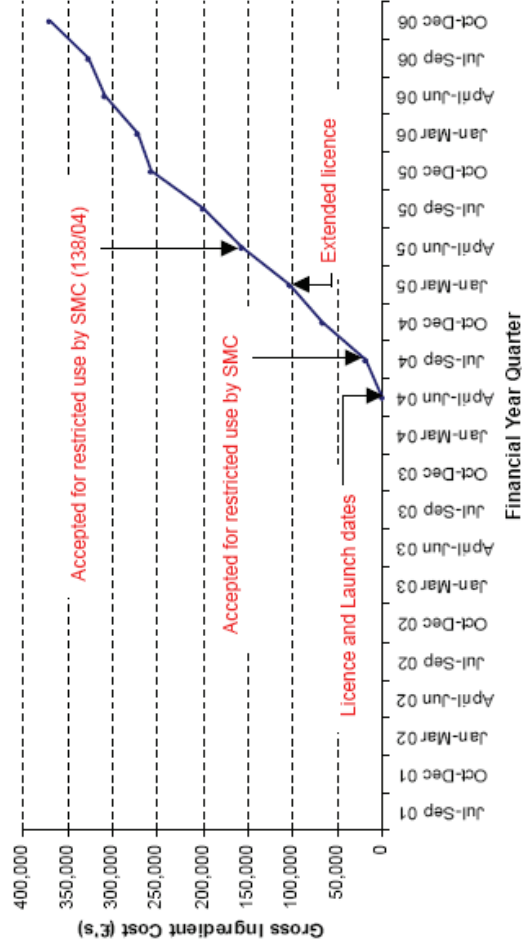
NHS Scotland- Utilisation of estradiol and levonorgestrel transdermal patch (FemSeven®) Sequi in Primary Care



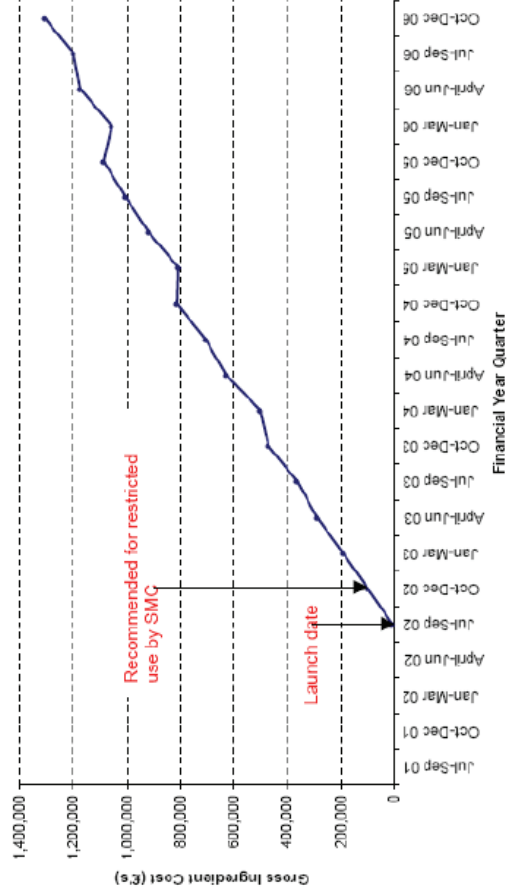
NHS Scotland- Utilisation of galantamine modified release 8mg, 16mg, 24mg (Reminyl® XL) in Primary Care



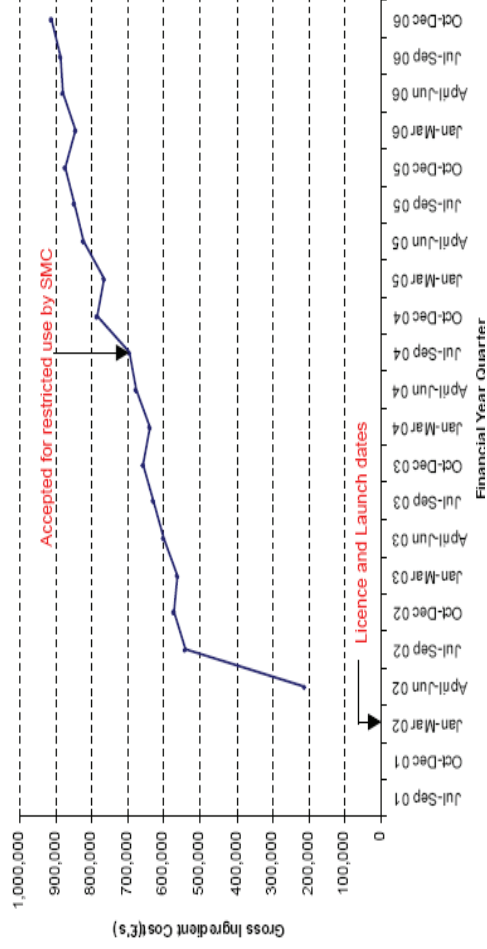
NHS Scotland- Utilisation of insulin detemir (Levemir®) in Primary Care



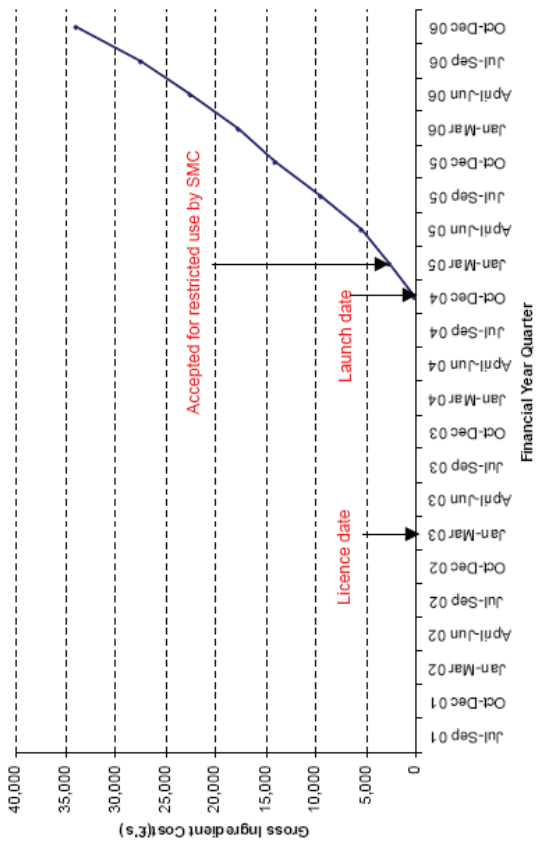
NHS Scotland- Utilisation of Insulin glargine (Lantus®) in Primary Care



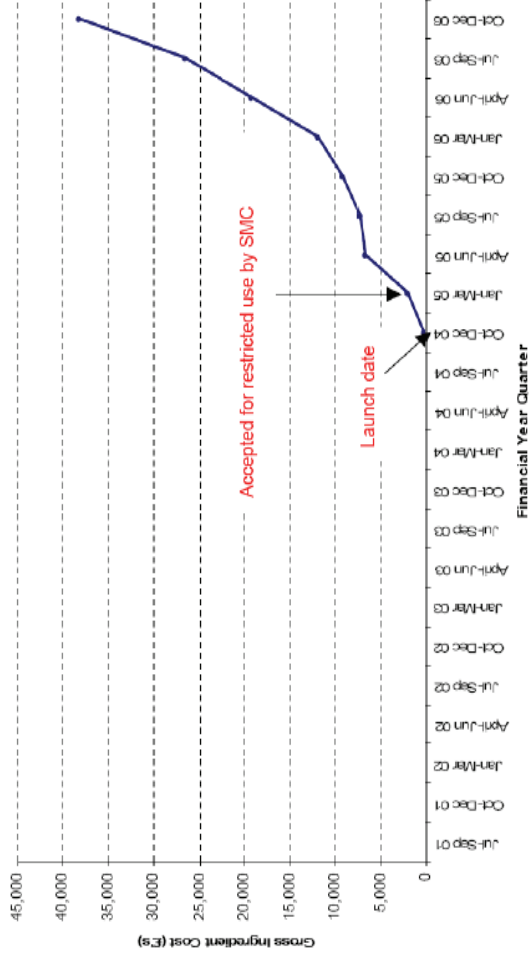
NHS Scotland- Utilisation of latanoprost (Xalatan®) in Primary Care



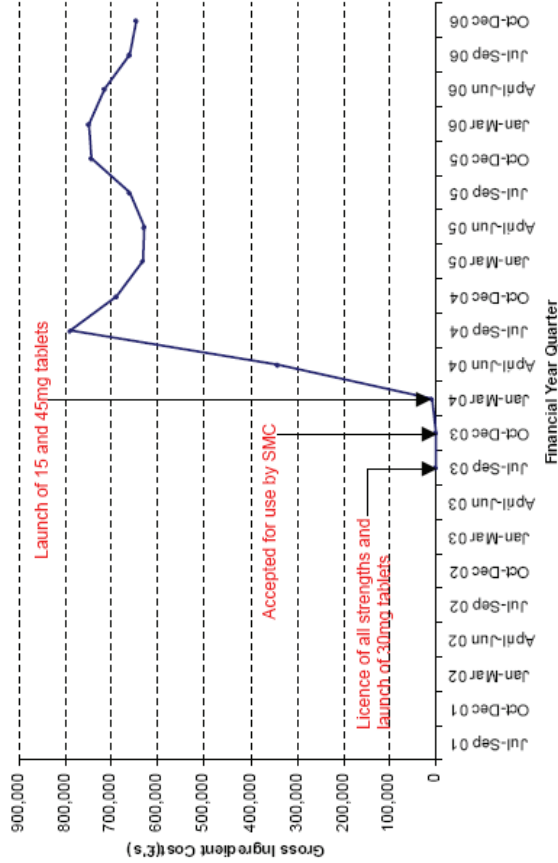
NHS Scotland- Utilisation of levetiracetam (Keppra®) 100mg/ml oral solution in Primary Care



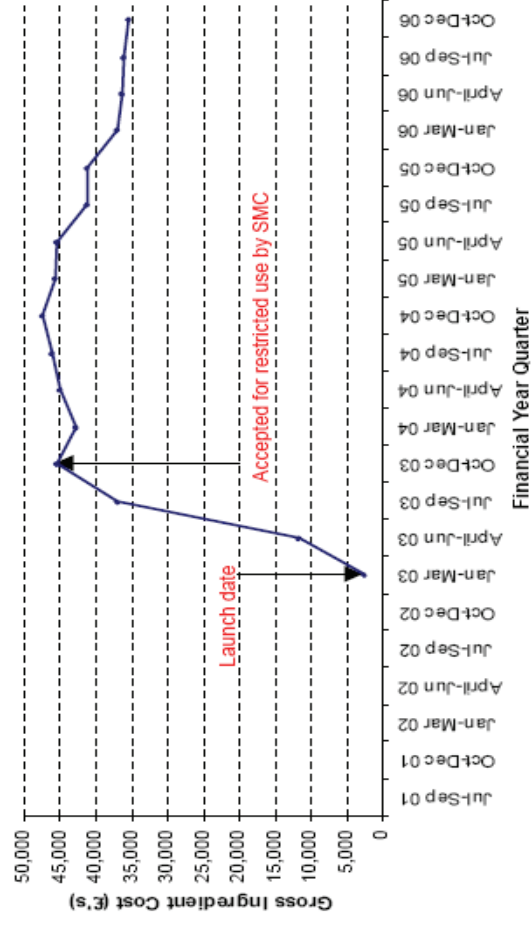
NHS Scotland- Utilisation of levetiracetam (Keppra®) 750mg tabs in Primary Care



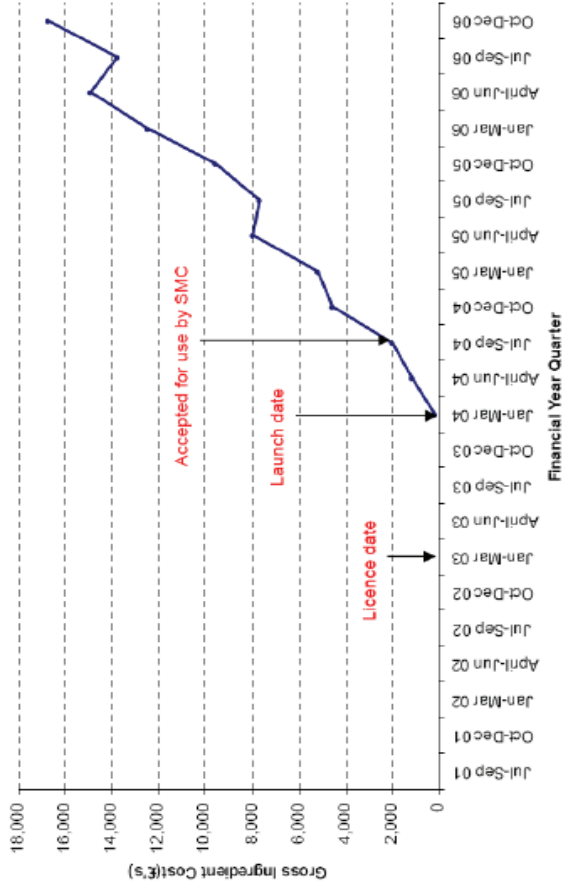
NHS Scotland- Utilisation of Mirtazapine (Zispin SolTab®) in Primary Care



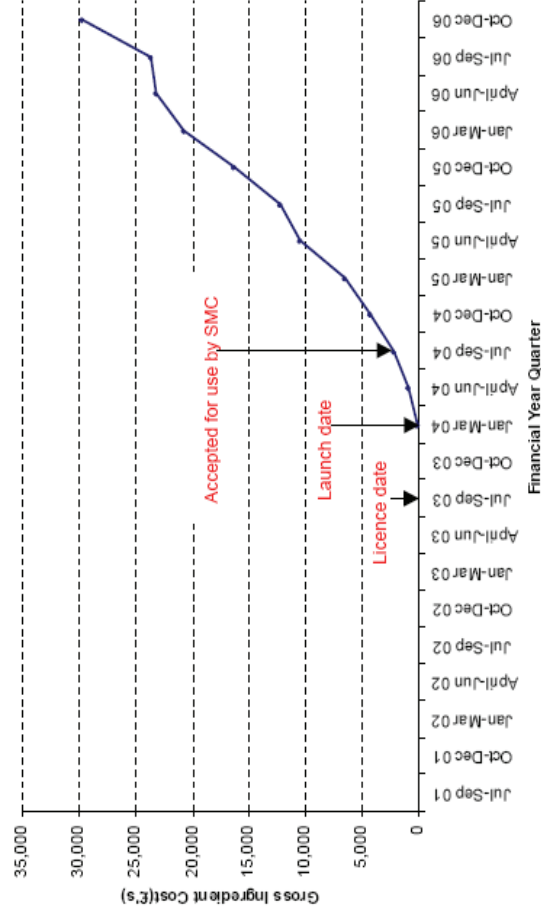
NHS Scotland- Utilisation of Mometasone furoate dry powder inhaler (Asmanex Twisthaler®) 200 micrograms, 400 micrograms in Primary Care



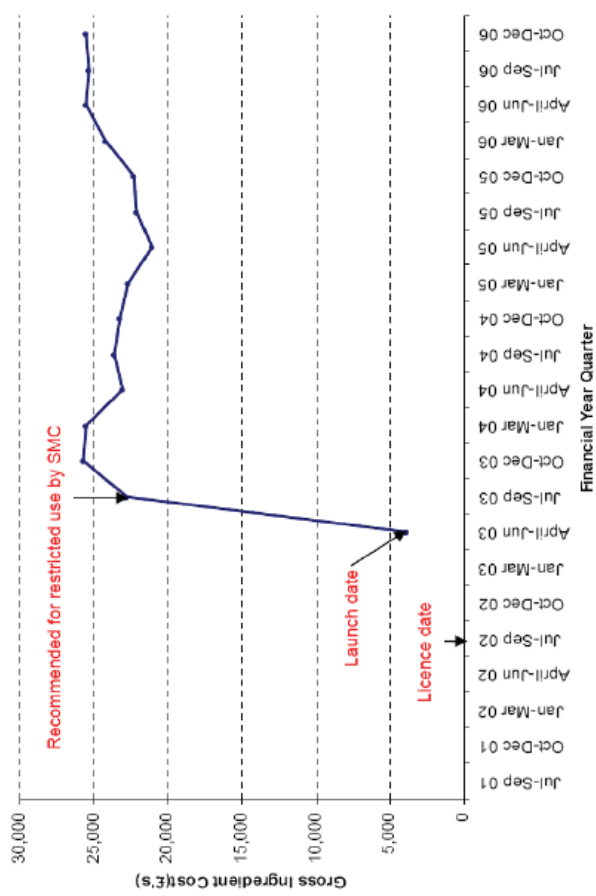
NHS Scotland- Utilisation of montelukast paediatric 4mg granules (Singulair®) in Primary Care



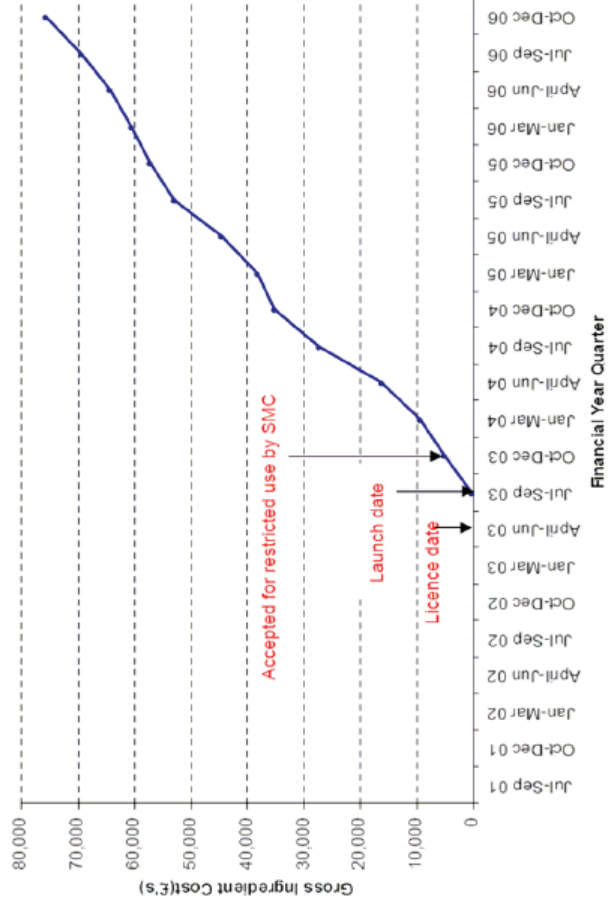
NHS Scotland- Utilisation of Macrogol 3350 oral powder 6.9g sachet (Movicol Paediatric Plain) in Primary Care



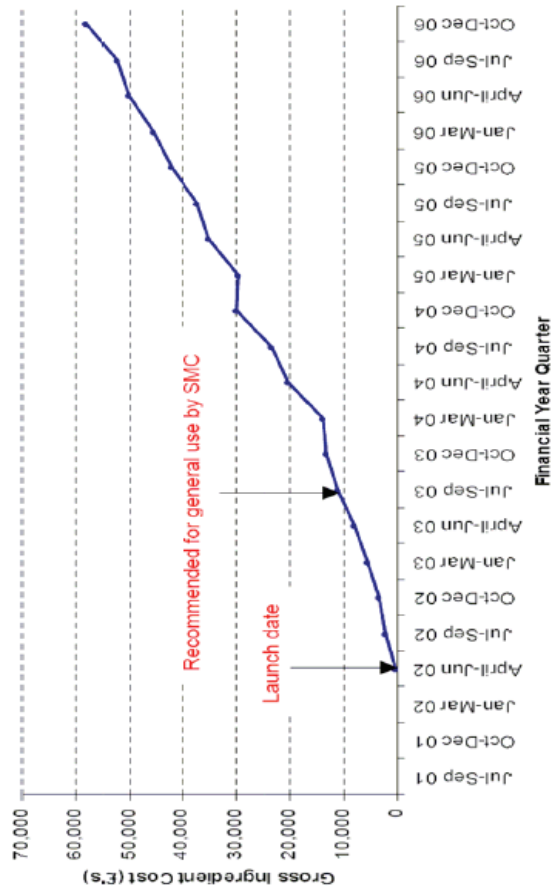
NHS Scotland- Utilisation of Norelgestromin/ethinyloestradiol (Evra®) in Primary Care



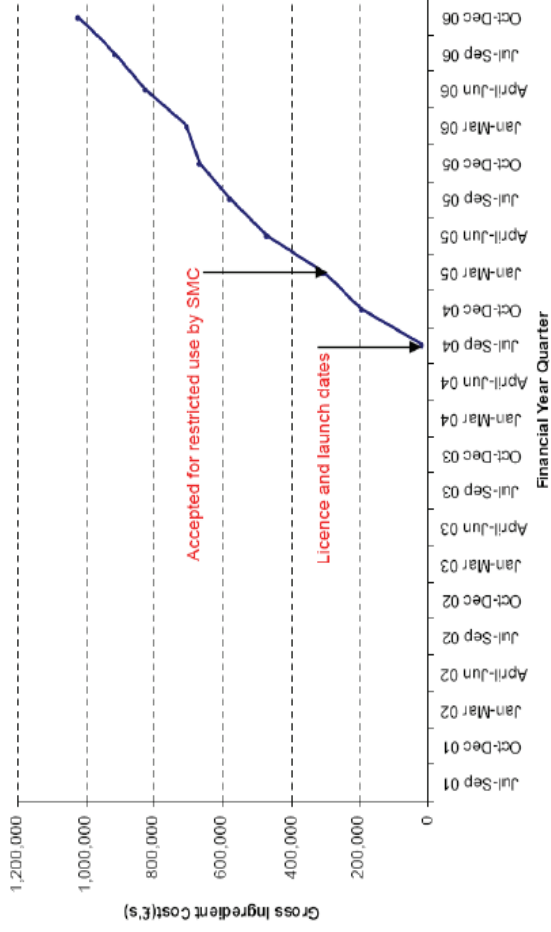
NHS Scotland- Utilisation of Olmesartan medoxomil (Olmotec®) in Primary Care



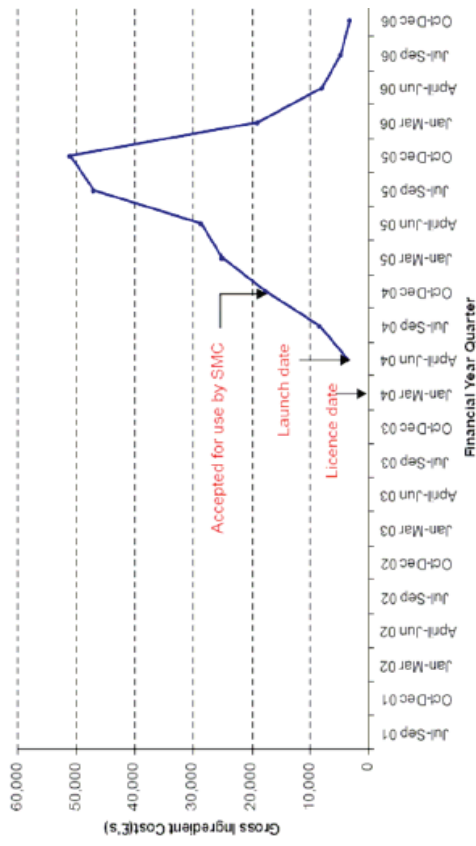
NHS Scotland- Utilisation of perindopril/indapamide (Coversyl Plus®) in Primary Care



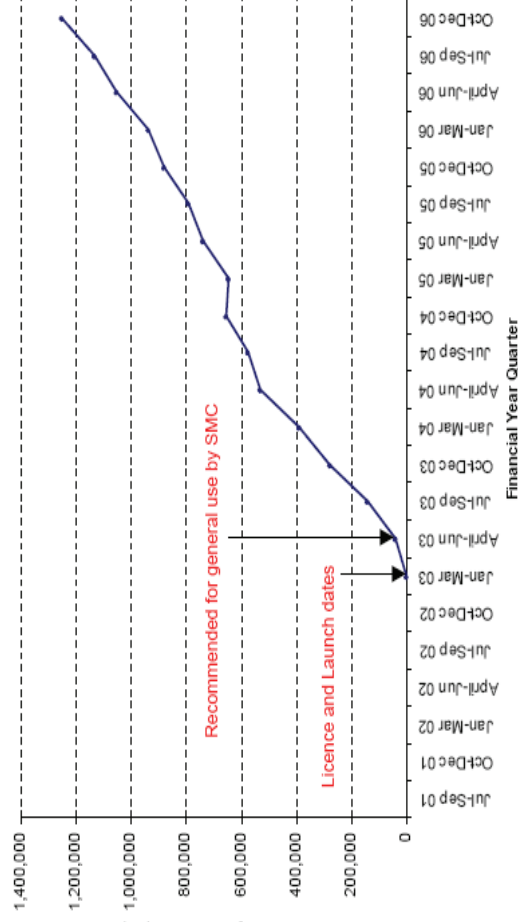
NHS Scotland- Utilisation of pregabalin (Lyrica®) capsules in Primary Care



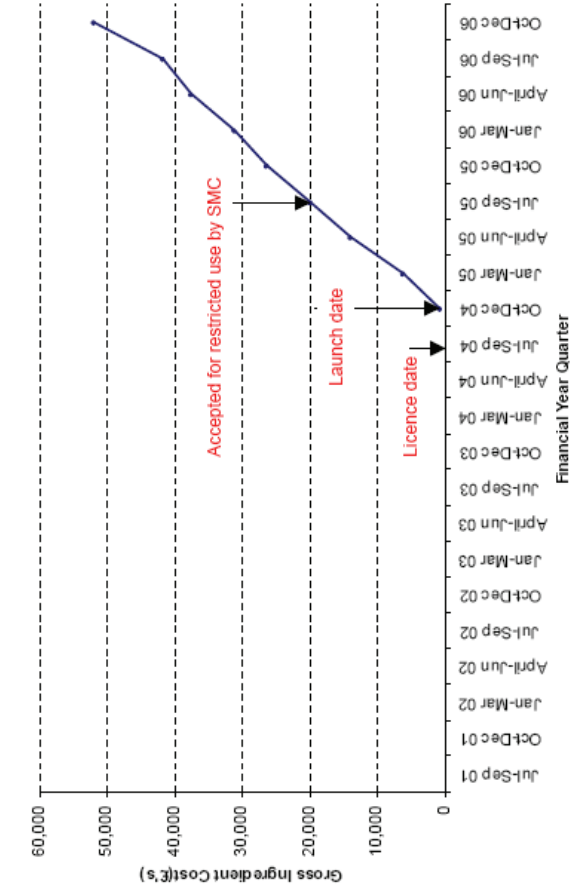
NHS Scotland- Utilisation of Conjugated oestrogen, medroxyprogesterone (Premique Low Dose®) in Primary Care



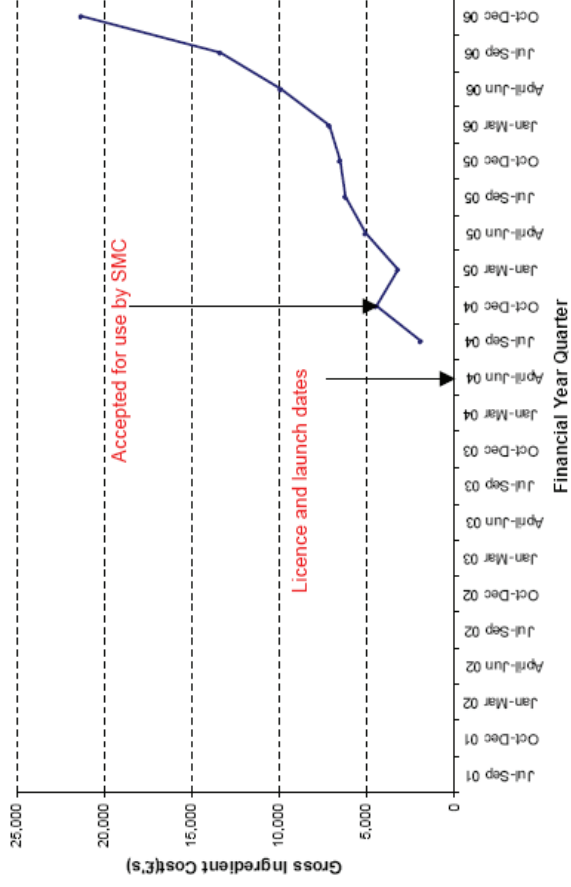
NHS Scotland- Utilisation of Rosuvastatin (Crestor®) in Primary Care



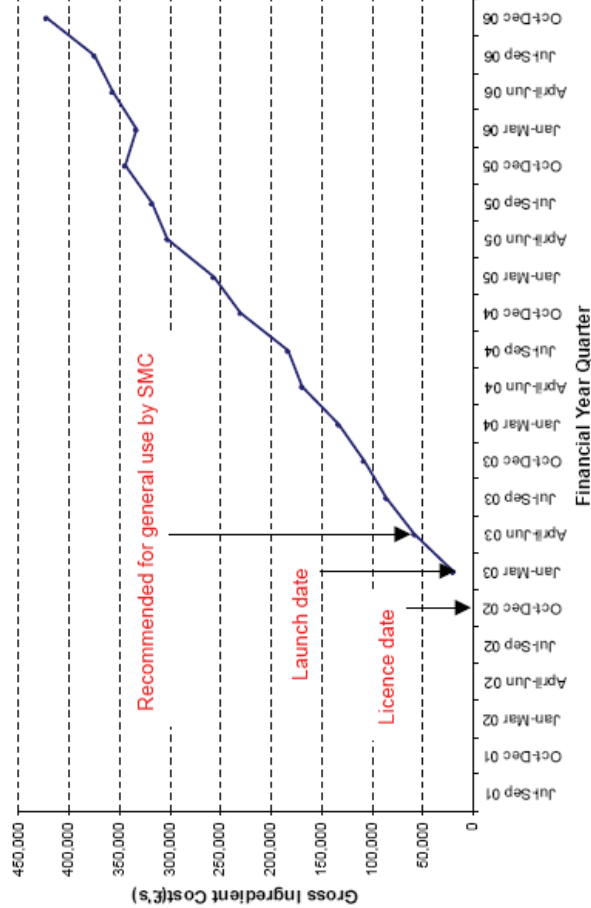
NHS Scotland- Utilisation of strontium ranelate 2g granules for oral suspension (Protelos®) in Primary Care



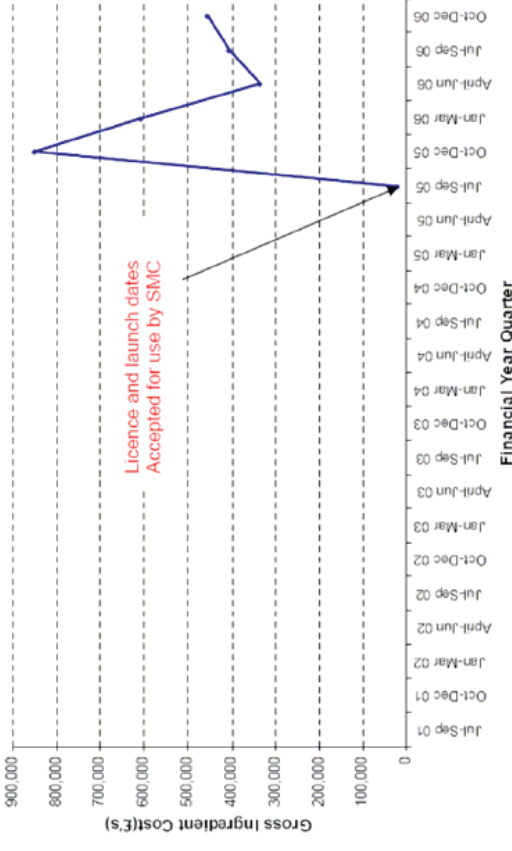
NHS Scotland- Utilisation of Sumatriptan succinate (Imigran Radis®) in Primary Care



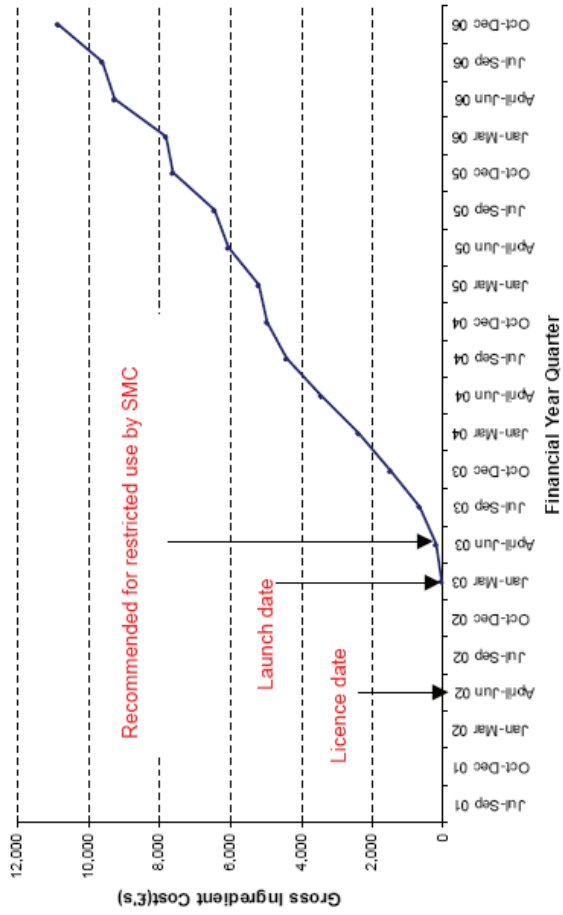
NHS Scotland- Utilisation of tadalafil (Cialis®) in Primary Care



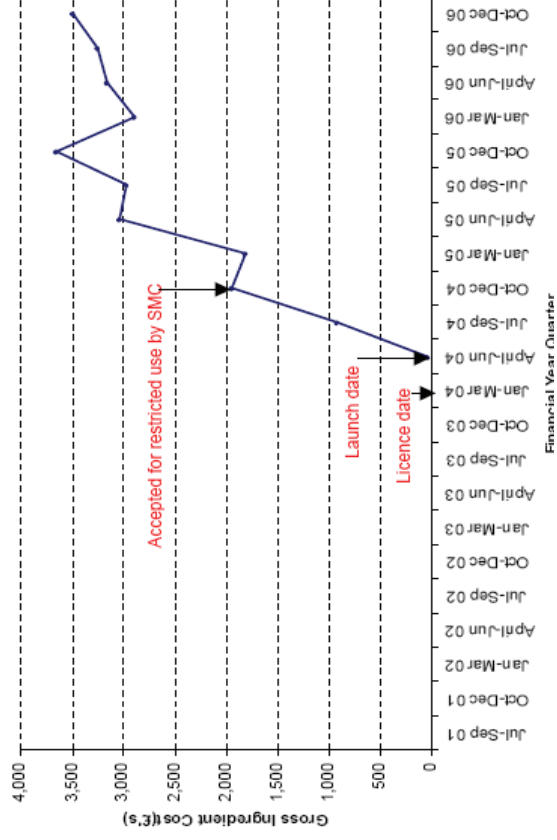
NHS Scotland- Utilisation of Tamsulosin hydrochloride (Flomaxtra® XL) in Primary Care



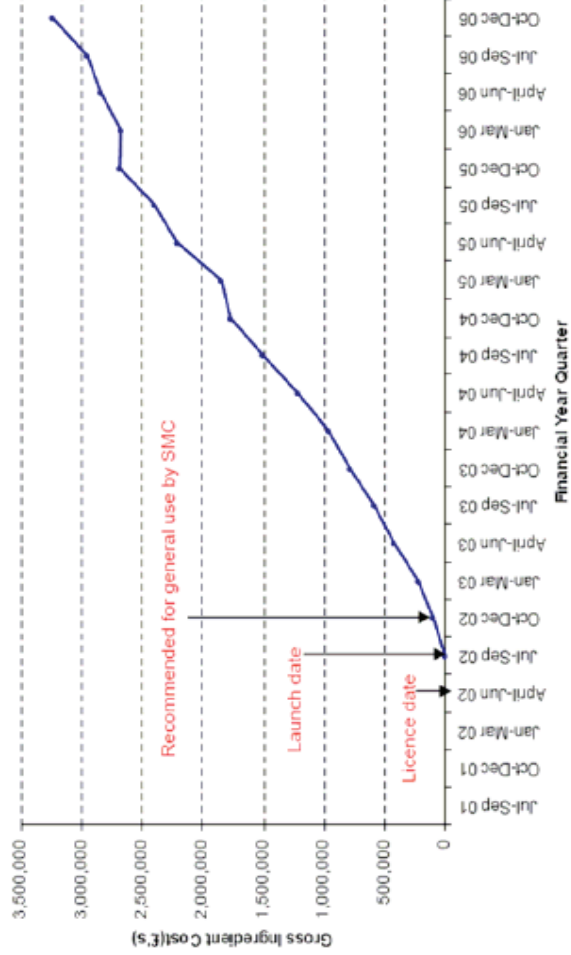
NHS Scotland- Utilisation of Telmisartan, hydrochlorothiazide (MicardisPlus®) in Primary Care



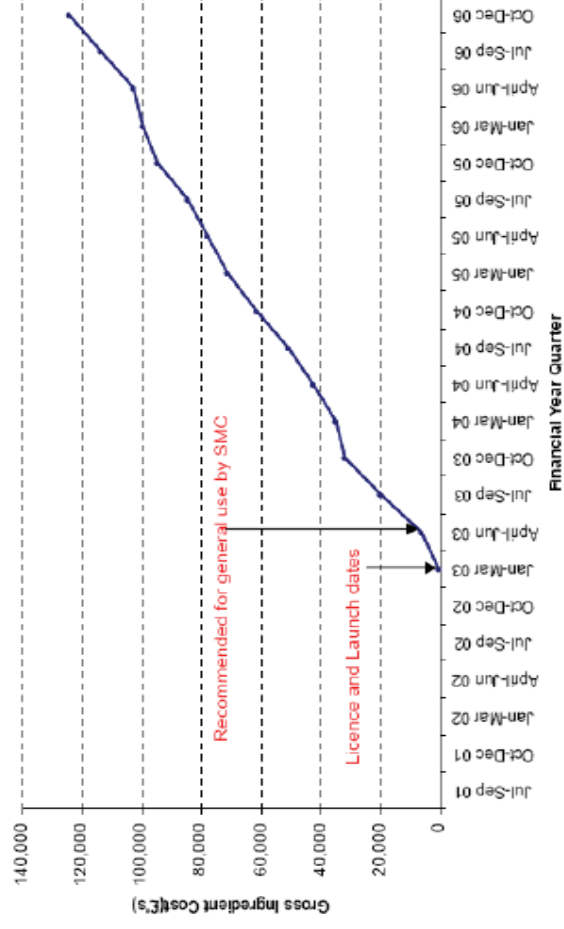
NHS Scotland- Utilisation of Testosterone mucoadhesive buccal tablets (Striant®) in Primary Care



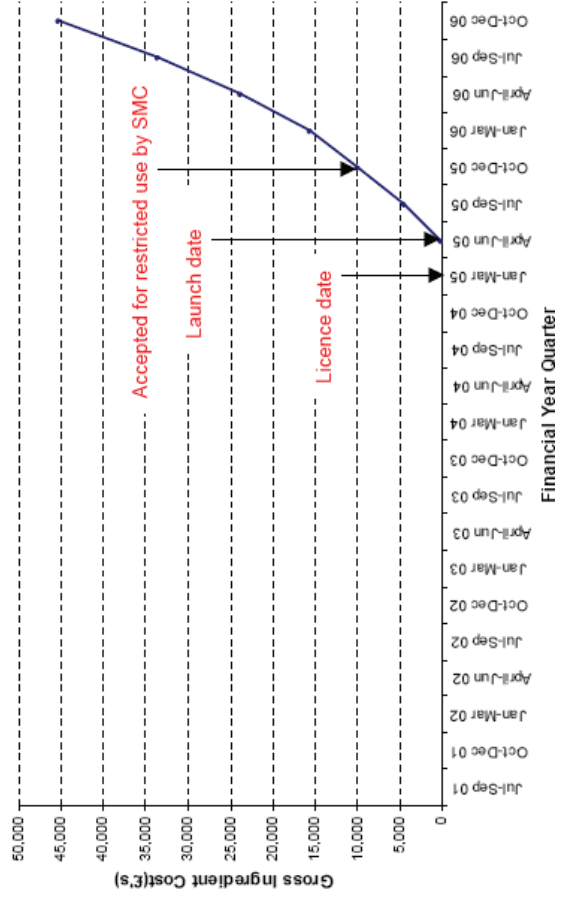
NHS Scotland- Utilisation of tiotropium bromide (Spiriva® inhaler) in Primary Care



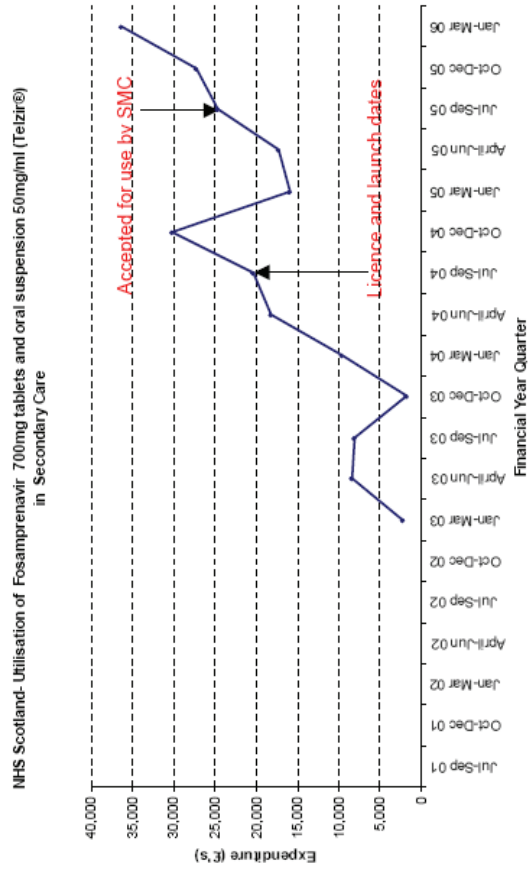
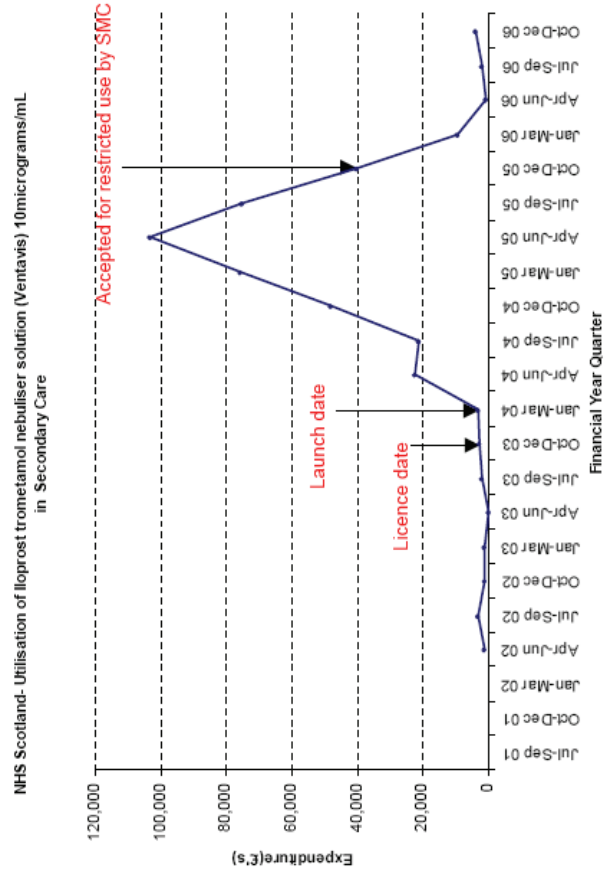
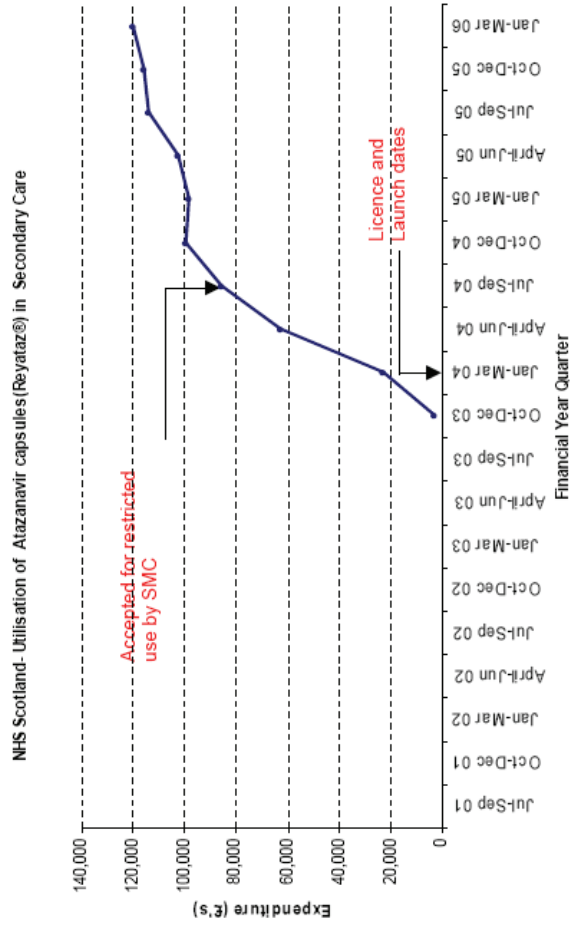
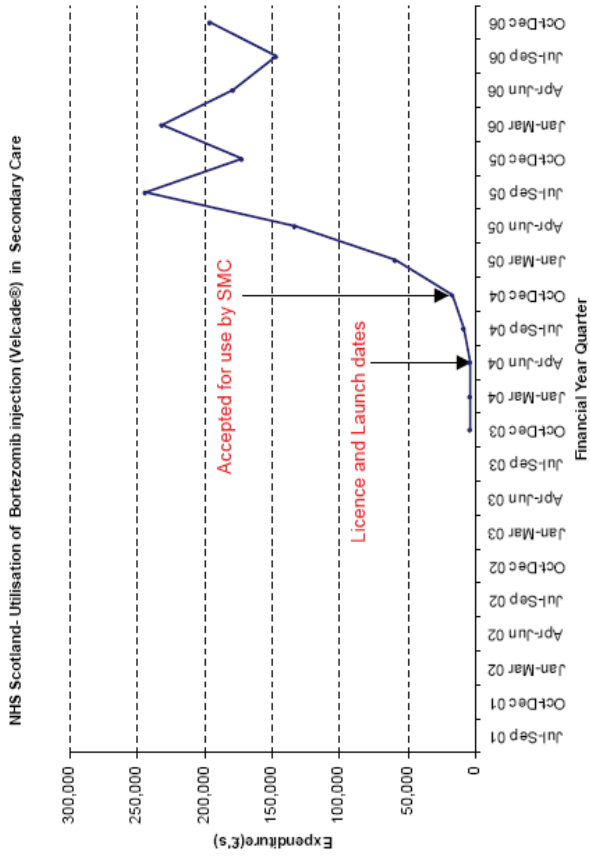
NHS Scotland- Utilisation of Vardenafil (Levitra®) in Primary Care



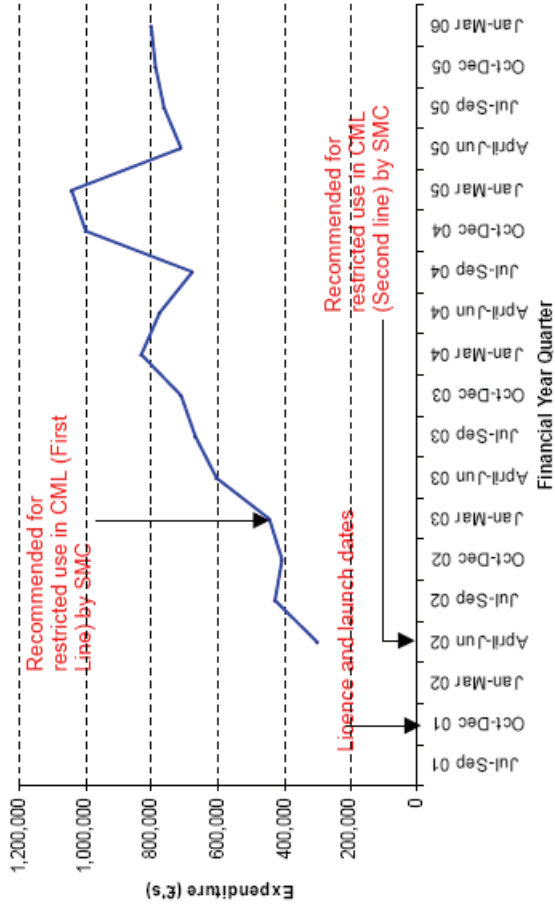
NHS Scotland - Utilisation of Zonisamide hard capsules 25 mg, 50 mg, 100 mg (Zonegran®) in Primary Care



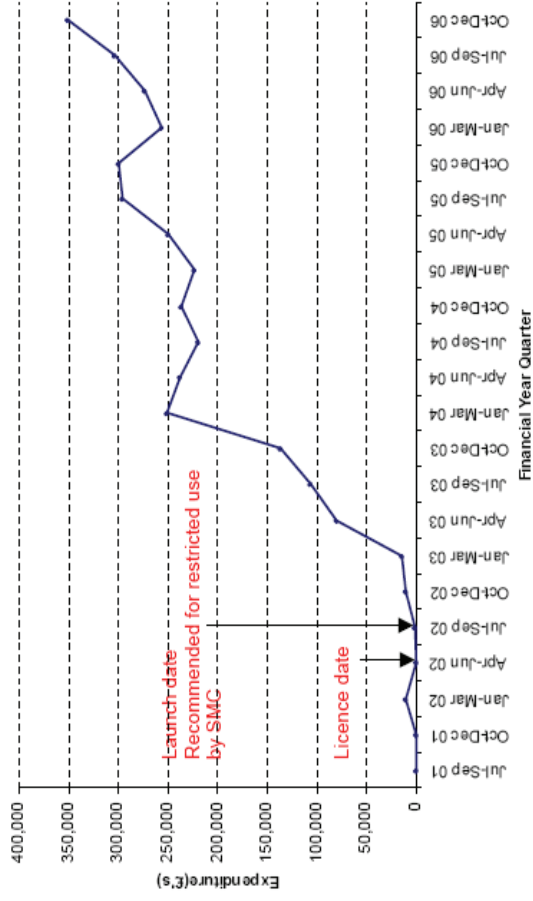
Appendix 2: – Secondary (hospital) care utilisation



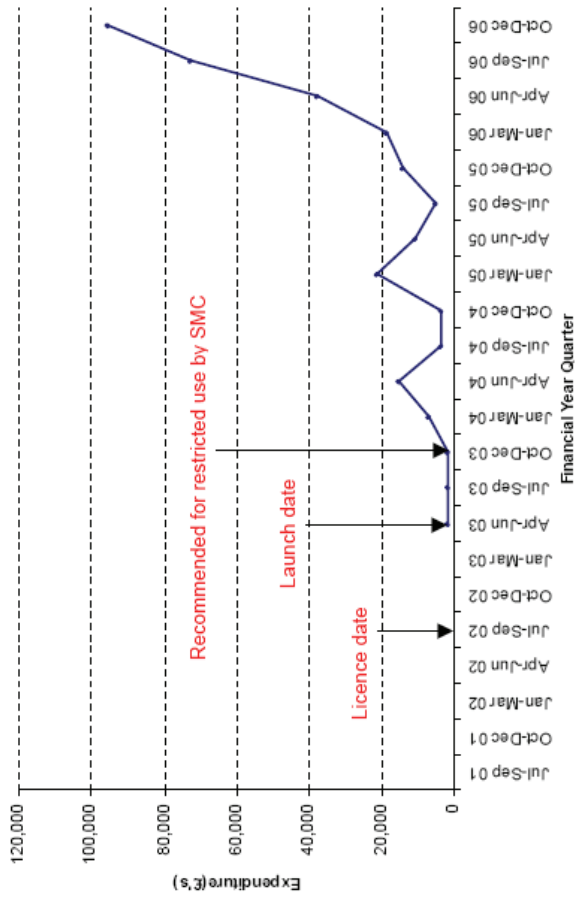
NHS Scotland -- Utilisation of Imatinib (Gleevec®) in Secondary Care



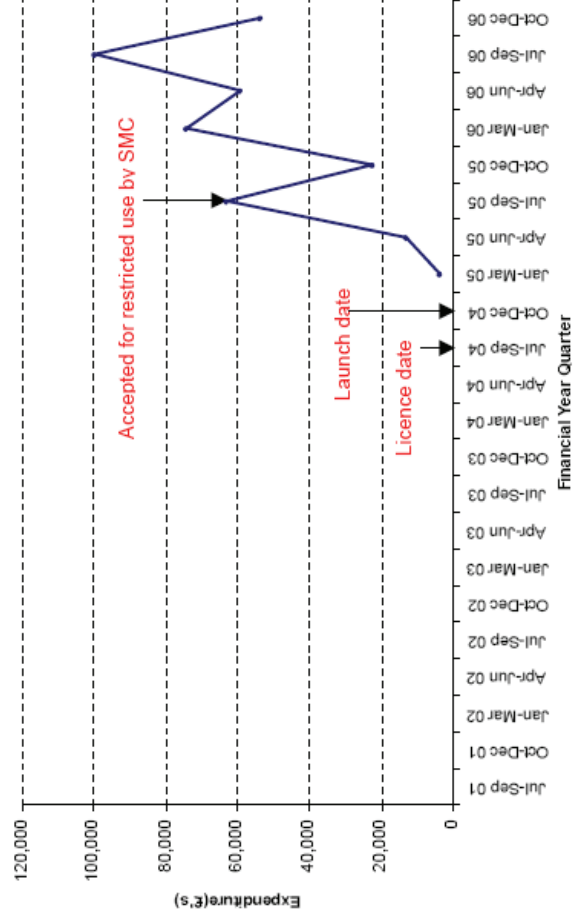
NHS Scotland- Utilisation of Pegylated interferon alfa-2a subcutaneous injection (Pegasys®) 135micrograms, 180 micrograms prefilled syringe in Secondary Care



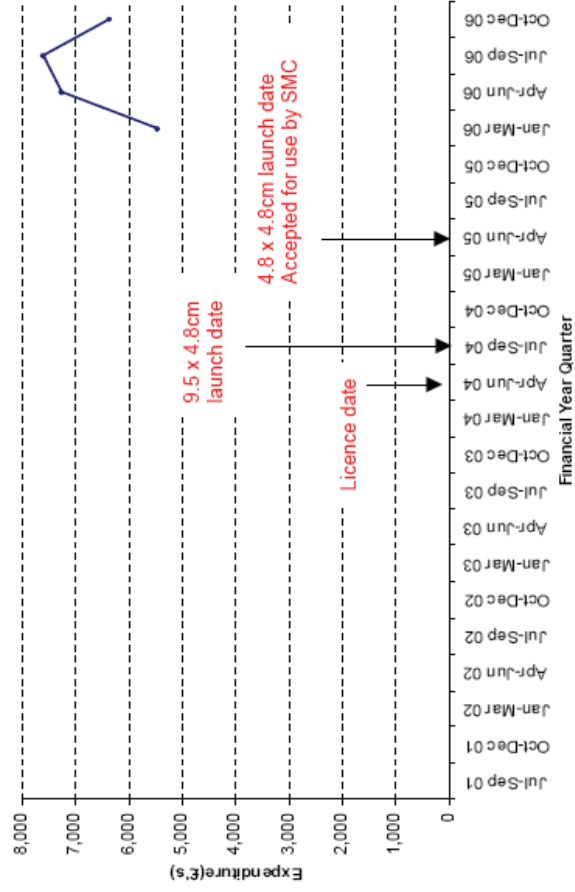
NHS Scotland- Utilisation of Pegfilgrastim injection (Neulasta®) in Secondary Care



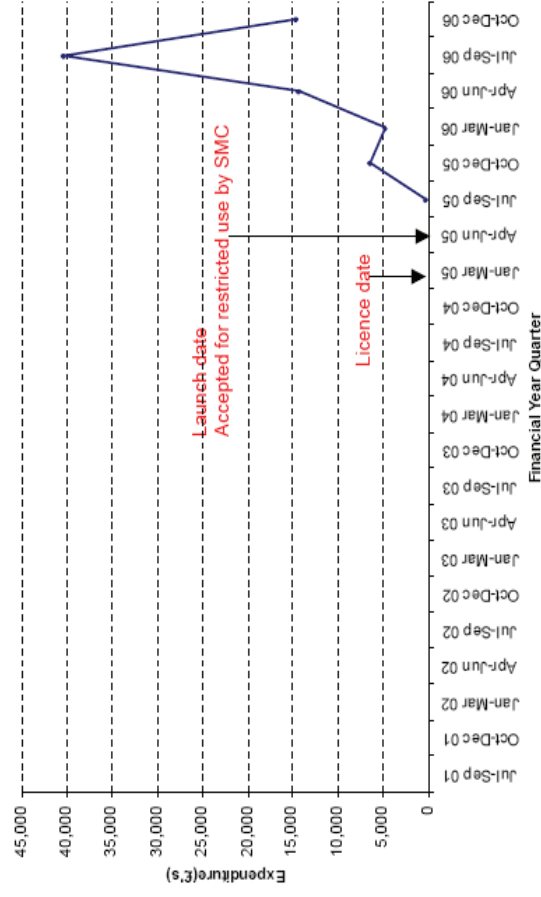
NHS Scotland- Utilisation of Pemretrexed injection (Alimta®) in Secondary Care



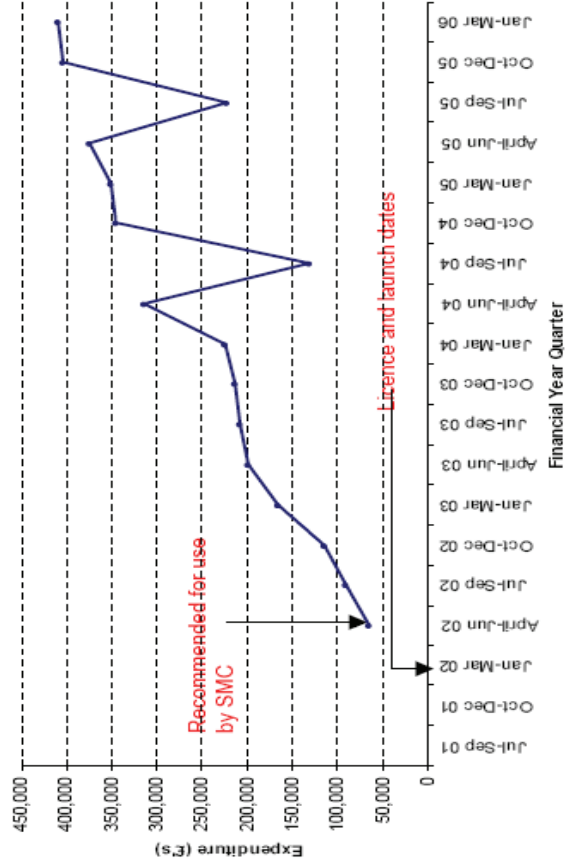
NHS Scotland - Utilisation of Human Fibrinogen 5.5mg and Human Thrombin 2.0 IU per cm² medicated sponge (TachoSil) in Secondary Care



NHS Scotland - Utilisation of Vinorelbine capsules (Navelbine® Oral) in Secondary Care



NHS Scotland - Utilisation of Tenofovir disoproxil fumarate (Virad®) tablets in Secondary Care



NHS Scotland - Utilisation of Pegylated interferon alfa-2b (VirafeonPeg®) injection in Secondary Care

