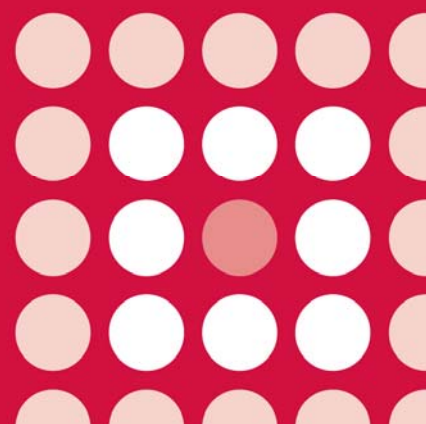




All Wales Therapeutics
and Toxicology Centre
Canolfan Therapiwteg a
Thocsicoleg Cymru Gyfan

Monitoring of Medicines appraised by NICE and AWMMSG

Welsh Analytical Prescribing Support Unit



MONITORING REPORT ON NICE AND AWMSG HEALTH TECHNOLOGY APPRAISAL UPTAKE

Purpose

This paper is intended to inform AWMSG of progress made in monitoring the usage of medicines appraised by AWMSG and the National Institute for Health and Clinical Excellence (NICE).

Summary

This paper analyses the usage of medicines appraised by AWMSG and NICE, providing data from 1 April 2006 to 30 September 2012. The information includes analysis of medicines that have been recommended and not recommended by AWMSG or NICE for use in NHS Wales. There are 89 statements of advice on the AWMSG website, each indicating a medicine that cannot be recommended due to non-submission by the company.

More detailed analysis of these and other AWMSG and NICE appraised medicines is ongoing, and will be the topic of a separate paper.

Background

Between March 2003 and September 2012, AWMSG made 142 recommendations on the use of individual medicines in Wales. Of these:

- 70 medicines are recommended
- 22 medicines are recommended with restrictions
- 21 medicines are not recommended
- 3 medicines have had their licence subsequently withdrawn following appraisal decision
- 26 medicines have had their AWMSG decision superseded by AWMSG resubmission/NICE

Until 1 October 2010, most of the medicines appraised by AWMSG were those likely to be used (or initiated) only by specialists in secondary care, reflecting the remit of AWMSG at that time (to appraise high-cost, cardiovascular and cancer medicines). The Medusa data warehouse, which holds information on medicines purchased and issued in Welsh hospitals, was therefore initially used to retrieve information on the usage of these medicines. In order to reflect the broadened remit of AWMSG, the data included in this report comprises value of issues from the Comparative Analysis System for Prescribing Audit (CASPA) combined with that from Medusa from 1 April 2006 until 30 September 2012. Therefore, unless otherwise stated, all data presented in this report refer to combined spend across primary and secondary care sectors.

Appraisal monitoring progress achieved

A database detailing all AWMSG appraisal decisions (recommendation/non-recommendation/non-submission and date decision ratified) has been developed to allow monitoring pre- and post-AWMSG Health Technology Appraisal decision. Medicine baskets have been developed for both CASPA and Medusa analysis, which are sufficiently robust to allow the accurate retrieval of data on relevant medicines, including any specific formulations.

A medicine basket has also been developed for those medicines with a NICE decision linked to a specific piece of NICE Technology Appraisal Guidance and monitored via Medusa and CASPA.

Caution in the interpretation of monitoring data

Due to limitations inherent within the data, it is not currently possible to link prescribing to treatment indication, and this is a major shortfall for accurate monitoring of appraisal recommendations. In most cases, AWMSG has undertaken an appraisal for one licensed indication of a medicine; therefore, usage data may be skewed by the fact that a medicine may have multiple indications – examples of such medicines include bortezomib, quetiapine and etanercept. This also means that some medicines may fall into more than one category (e.g. non-submission and recommended/not recommended).

Wherever possible, medicines have been classed as recommended or not recommended (including AWMSG non-submissions) and reported accordingly. There are, however, several medicines that have a positive recommendation for one or more indications, whilst being not recommended for another indication. In each situation an assessment was made to determine whether that medicine should be included in the monitoring. Where a medicine has had too many indications, or other factors have meant that monitoring would not provide useful information, the medicine has been included in the 'not monitored' section.

There are a number of medicines considered not suitable for monitoring; these have been indicated, along with the reasoning behind the decision, enabling the production of more robust data.

Combining data obtained from two different data systems provides challenges, particularly as Medusa and CASPA report data in different ways. As a result, ensuring that the medicine baskets compiled are robust with respect to medicine, strength and formulation has been time consuming.

Triangulation with previous NICE and AWMSG forecasting is required to verify whether or not appraisal uptake and compliance is as predicted. Liaison with the pharmaceutical manufacturers will aid with validation of this. Estimated costs to NHS Wales for the appraised medicines detailed within this paper are based on information from manufacturers.

AWMSG AND NICE APPRAISAL UPTAKE MONITORING INFORMATION

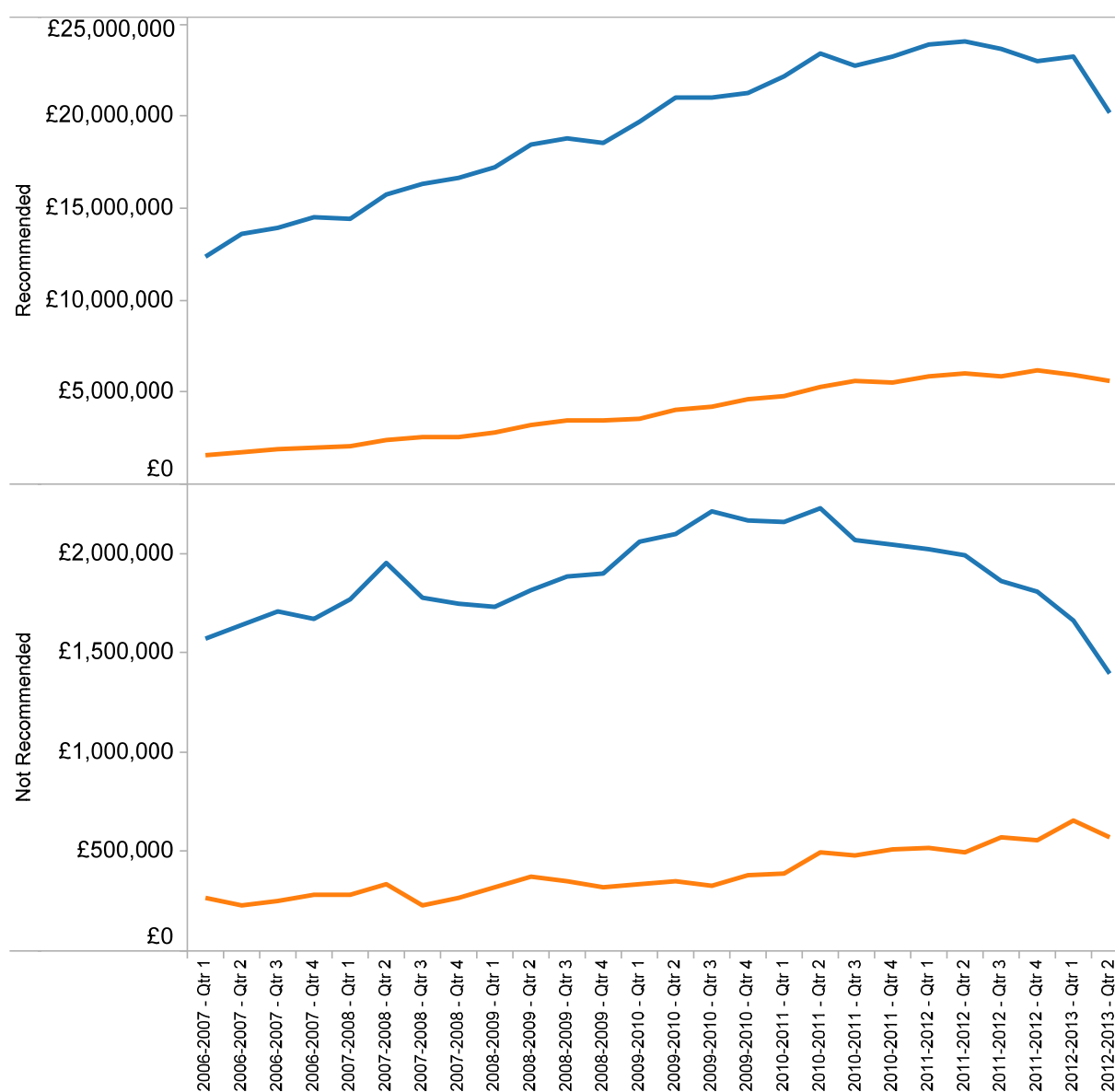
1.0 OVERVIEW

The following chart (Figure 1) shows an overview of spend on those drugs appraised by both NICE and AWMSG from April 2006 to September 2012.

In the last financial year (2011–2012), NHS Wales spent £9.3 million per year on medicines not recommended by NICE and £2.1 million per year on medicines not submitted to or not recommended by AWMSG.

NHS Wales spent £94.5 million on NICE-recommended medicines and £23.7 million on AWMSG-recommended medicines in the financial year 2011–2012.

Figure 1. Spend on medicines with AWMSG appraisal or NICE technology appraisal, broken down by recommended or non-recommended



Document Type

- AWMSG appraisal
- NICE technology appraisal

It is important to note that there are certain medicines (Table 1) that have not been included in the monitoring process, for the reasons previously outlined, and these are further detailed in the table below. The total spent on these medicines from April 2006 to September 2012 is £216.3 million.

Table 1. Drug usage not being monitored as part of the appraisal monitoring process, with an explanation

		AWMSG appraisal	NICE technology appraisal	Grand Total
Licence withdrawn	Drotrecogin Alfa		2,797,362	2,797,362
Multiple brands in same strength	Human normal immunoglobulin	10,333,853		10,333,853
	Somatropin		15,558,355	15,558,355
Multiple indications, would not provide useful information	Clopidogrel		39,956,987	39,956,987
	Enoxaparin	25,105,726		25,105,726
	Exenatide		6,094,153	6,094,153
	Fondaparinux sodium	486,984		486,984
	Losartan potassium/hydrochlorothiazide	1,099,529		1,099,529
	Quetiapine	45,940,613		45,940,613
	Quetiapine XL	8,976,392		8,976,392
	Tadalafil	8,737,320		8,737,320
	Telmisartan	4,339,155		4,339,155
	Teriparatide		201,299	201,299
Paediatric non-submission, used routinely in adults	Valsartan	26,476,541		26,476,541
	Latanoprost	20,146,394		20,146,394
Grand Total		151,642,507	64,608,156	216,250,663

Table 2 shows a breakdown of spend by NICE/AWMSG appraisal, with the total spend on all recommended and non-recommended medicines (including those not being monitored) projected to be approximately £150 million for the financial year 2012–2013.

Table 2. Annual spend broken down by appraisal type and recommendation

Document Type	Drug Recommendation	2006-2007	2007-2008	2008-2009	2009-2010	2010-2011	2011-2012	2012-2013	Grand Total
AWMSG appraisal	Recommended	7,011,189	9,358,279	12,800,477	16,260,173	21,056,166	23,672,224	11,465,350	101,623,858
	Not Recommended	1,022,665	1,099,693	1,349,500	1,379,619	1,860,081	2,128,911	1,213,451	10,053,920
	Not Monitoring	18,787,458	21,338,220	22,592,140	24,733,486	26,381,089	27,505,036	10,305,079	151,642,507
	Total	26,821,312	31,796,191	36,742,117	42,373,278	49,297,336	53,306,171	22,983,880	263,320,285
NICE technology appraisal	Recommended	54,300,274	63,052,444	72,948,915	82,855,384	91,469,850	94,494,920	43,345,668	502,467,454
	Not Recommended	6,571,459	7,222,506	7,312,463	8,516,914	8,475,565	7,653,486	3,046,995	48,799,388
	Not Monitoring	13,162,456	12,904,062	12,859,461	12,631,360	5,872,764	4,840,572	2,337,480	64,608,156
	Total	74,034,189	83,179,011	93,120,839	104,003,658	105,818,179	106,988,978	48,730,143	615,874,997
Grand Total	100,855,500	114,975,202	129,862,956	146,376,936	155,115,515	160,295,149	71,714,023	879,195,283	

N.B. 2012–2013 spend is for two quarters only

Table 3 gives a breakdown of these data by health board.

Table 3. Breakdown of spend by health board

Health Board	Drug Recommendation	2006-2007	2007-2008	2008-2009	2009-2010	2010-2011	2011-2012	2012-2013
ABMU	Recommended	12,578,320	14,493,152	16,882,969	18,843,024	21,402,584	22,809,136	7,835,223
	Not Recommended	991,307	1,120,488	1,338,114	1,810,557	1,723,318	1,912,941	634,034
	Not Monitoring	5,887,292	6,519,223	6,735,838	7,654,199	7,032,943	7,377,510	2,651,072
Aneurin Bevan	Recommended	7,408,931	9,141,962	10,859,521	14,049,227	16,676,653	17,176,317	8,002,209
	Not Recommended	933,383	1,178,392	1,104,326	1,211,972	1,466,428	1,359,624	586,200
	Not Monitoring	5,561,854	6,165,953	6,447,519	6,651,130	5,347,507	4,696,666	1,784,423
BCU	Recommended	14,328,834	16,268,008	19,188,620	21,016,910	23,307,982	24,606,388	12,231,624
	Not Recommended	1,183,434	1,370,293	1,651,813	1,815,092	1,981,675	1,754,416	837,224
	Not Monitoring	6,992,446	7,402,345	7,661,749	8,099,339	6,778,894	6,756,164	2,696,162
Cardiff and Vale	Recommended	8,592,096	11,122,690	14,508,299	16,775,427	19,552,036	21,055,104	10,349,826
	Not Recommended	1,866,873	1,794,116	1,729,396	1,901,964	1,962,231	1,787,252	856,444
	Not Monitoring	4,707,453	4,908,241	5,125,124	5,314,145	4,783,707	4,964,528	2,067,533
Cwm Taf	Recommended	3,590,798	4,537,046	5,336,098	6,543,649	7,407,973	8,752,968	4,400,307
	Not Recommended	811,867	755,955	681,498	736,508	880,915	903,715	368,166
	Not Monitoring	3,028,198	3,141,541	3,379,432	3,488,005	3,149,961	3,279,419	1,447,109
Hywel Dda	Recommended	7,531,955	8,581,109	10,367,793	12,430,514	13,841,733	14,939,673	7,590,903
	Not Recommended	1,126,931	1,159,659	1,211,675	1,368,105	1,273,367	1,211,354	640,442
	Not Monitoring	4,640,191	4,923,077	4,887,583	4,886,794	4,175,674	4,290,699	1,636,326
Powys	Recommended	1,165,321	1,511,667	1,630,623	1,845,095	2,107,476	2,104,313	999,532
	Not Recommended	412,643	444,859	456,970	463,845	413,172	358,434	163,100
	Not Monitoring	1,126,949	1,171,906	1,203,602	1,249,701	952,388	965,887	359,687
Velindre	Recommended	6,115,209	6,755,088	6,975,469	7,611,710	8,229,579	6,723,245	3,401,394
	Not Recommended	267,686	498,438	488,171	588,492	634,539	494,662	174,835
	Not Monitoring	5,530	9,996	10,754	21,533	32,779	14,735	247
Grand Total		100,855,500	114,975,202	129,862,956	146,376,936	155,115,515	160,295,149	71,714,023

Drug Recommendation
■ Recommended
■ Not Recommended
■ Not Monitoring
■ Total

This information shows that all Health Boards are prescribing certain medicines which have been appraised as not recommended by NICE and AWMSG. This may be via Individual Patient Funding Requests (IPFR) and can be verified by local intelligence.

It is also important to consider here that population, deprivation, and speciality prescribing should be accounted for. For further details, please refer to Appendices 1 and 2.

Appendix 1 details usage of all medicines appraised by NICE and AWMSG across NHS Wales.

Appendix 2 details usage of all medicines appraised by NICE and AWMSG and not recommended across NHS Wales.

2.0 AWMSG AND NICE APPRAISED MEDICINES – RECOMMENDED

This section highlights medicines which have been recommended in appraisal by AWMSG and NICE.

2.1 Alteplase (Actilyse® Cathflo® 2 mg)

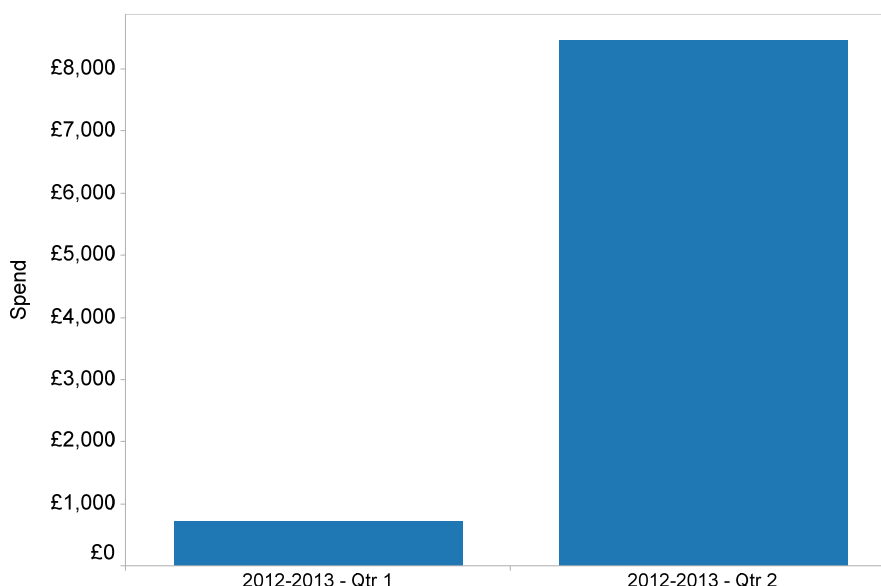
AWMSG appraisal indication – Thrombolytic treatment of occluded central venous access devices, including those used for haemodialysis.

AWMSG recommended – January 2012.

Estimated cost to NHS Wales – Cost-neutral.

The usage of this medicine has rapidly increased since its positive appraisal. It is only used within Cardiff and Vale University Health Board as of January 2013, costing approximately £36,000 per year (Figure 2).

Figure 2. Alteplase (Actilyse® Cathflo® 2 mg) spend



2.2 Aripiprazole (Abilify®) oral tablet

AWMSG appraisal indication – Treatment of moderate to severe manic episodes in Bipolar I Disorder and for the prevention of a new manic episode in certain patients.

AWMSG recommended – August 2009.

Estimated cost to NHS Wales – If aripiprazole were to replace risperidone, the additional cost would be an estimated £247,608 in 2009, rising to £1.4 million in 2013. Replacing quetiapine with aripiprazole will not produce the originally estimated savings, as quetiapine has lost its patent since estimates were made.

Aripiprazole is a more expensive treatment than older agents and is now costing NHS Wales £7.2 million. The usage of this medicine has rapidly increased since its recommendation, although it was already in frequent use prior to appraisal.

Note that it is licensed for other indications, although it has not been appraised for these (one indication is awaiting a NICE technology appraisal). Figures 3 and 4 show the extent of usage across NHS Wales and within Health Boards respectively.

Figure 3. All Wales aripiprazole (Abilify®) oral tablet spend by quarter (Dark green bar indicates appraisal by AWMSG or NICE in the quarter)

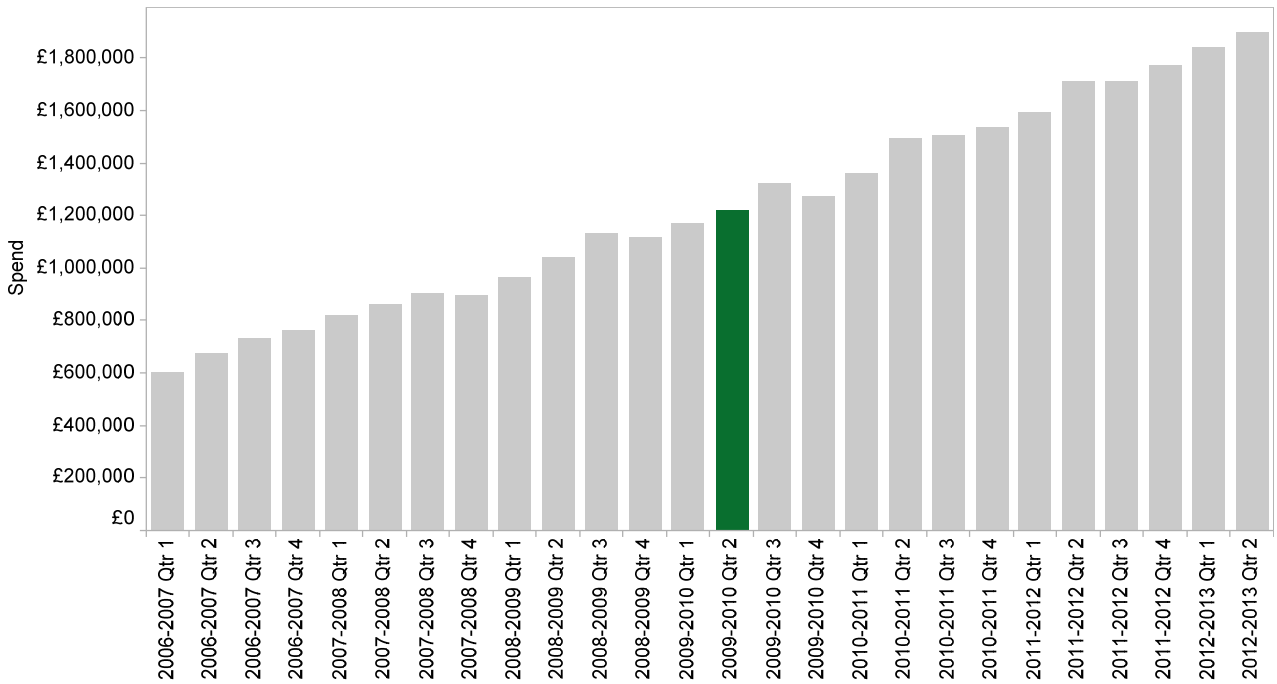
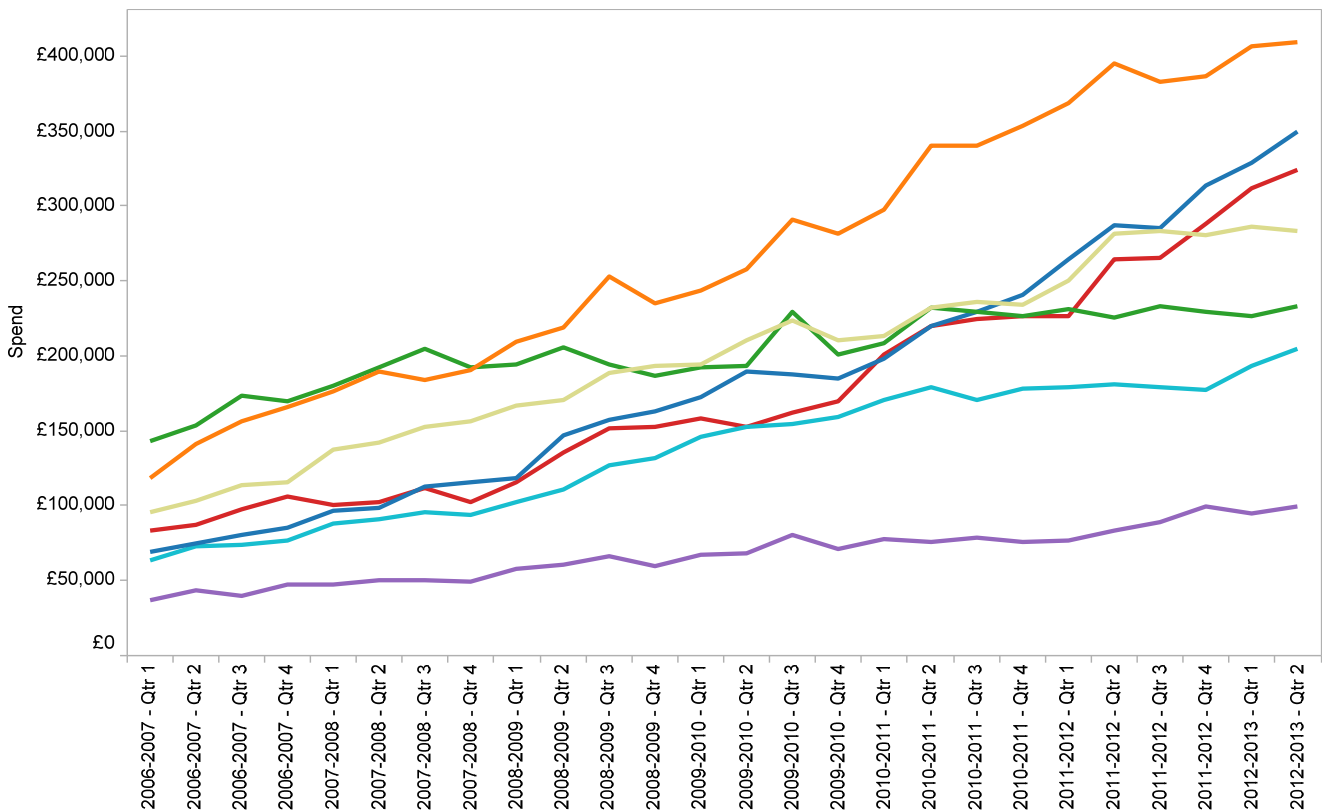


Figure 4. Health board aripiprazole (Abilify®) oral tablet spend by quarter



- Health Board**
- ABMU
 - Aneurin Bevan
 - BCU
 - Cardiff and Vale
 - Cwm Taf
 - Hywel Dda
 - Powys

2.3 Cinacalcet (Mimpara®)

NICE technology appraisal indication – Treatment of secondary hyperparathyroidism in patients with end-stage renal disease on maintenance dialysis therapy.

NICE recommended – January 2007.

Estimated cost to NHS Wales – £500,000 per year (based on an average dosage).

As can be seen in Figure 5, this medicine was welcomed for the treatment of renal patients, given the lack of alternative treatments. Figure 6 shows the differences in adoption of this guidance by Health Boards. Cinacalcet also has a licence for hypercalcaemia of primary hyperparathyroidism or parathyroid carcinoma, which has not been appraised and is likely to account for a small proportion of the total usage.

**Figure 5. All Wales cinacalcet (Mimpara®) spend by quarter
(Dark green bar indicates appraisal by AWMSG or NICE in the quarter)**

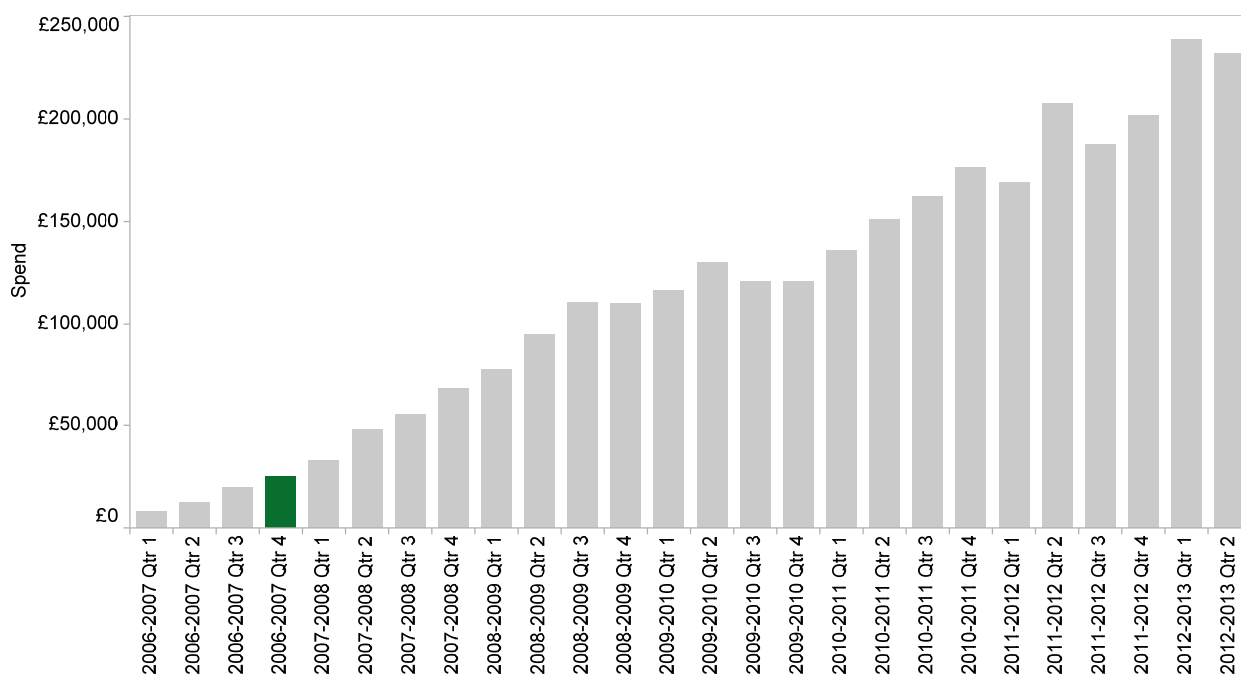
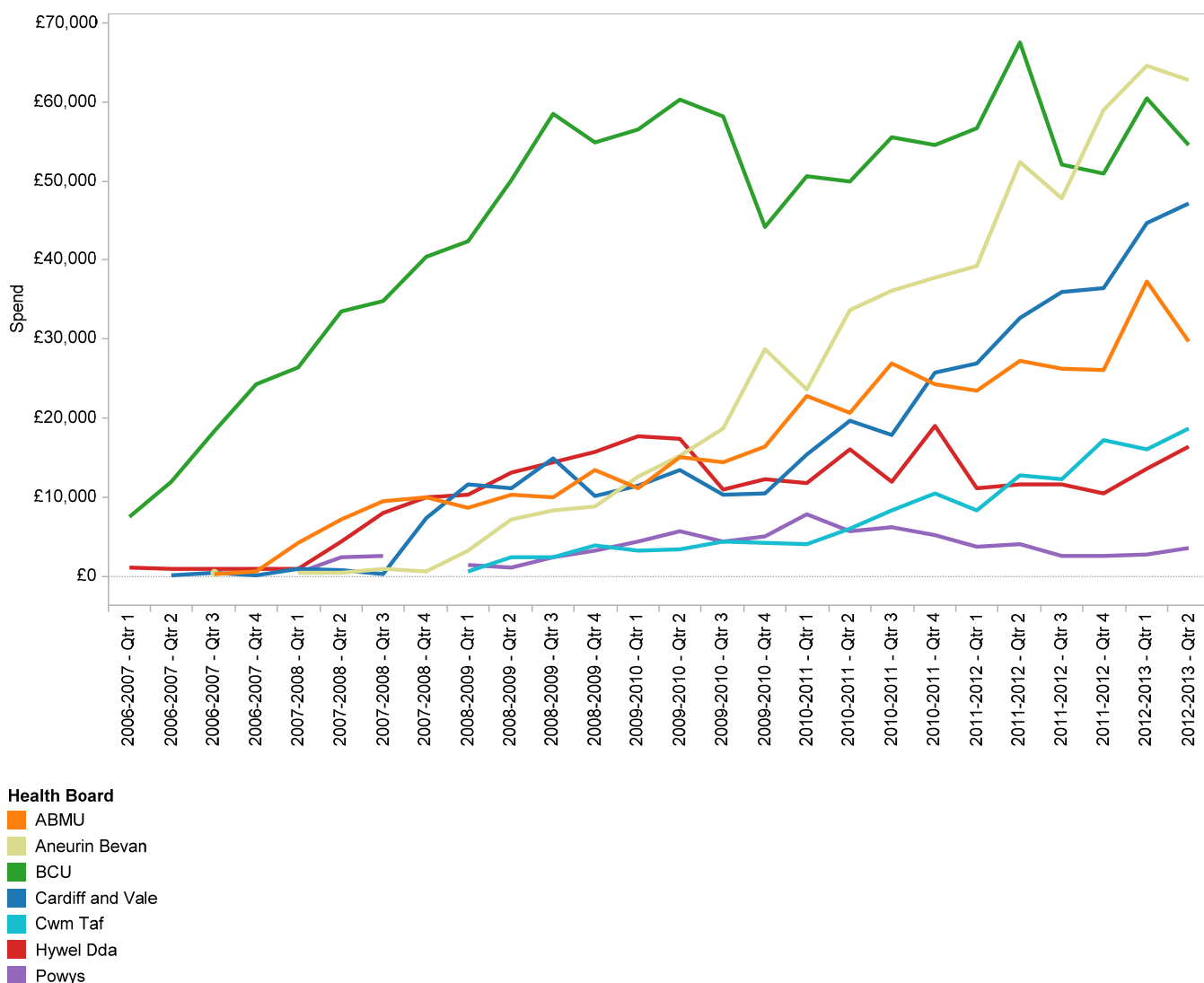


Figure 6. Health board cinacalcet (Mimpara®) spend by quarter



2.4 Letrozole (Femara®)

NICE technology appraisal indication – Treatment of early invasive breast cancer in postmenopausal women who have received prior standard adjuvant tamoxifen therapy.

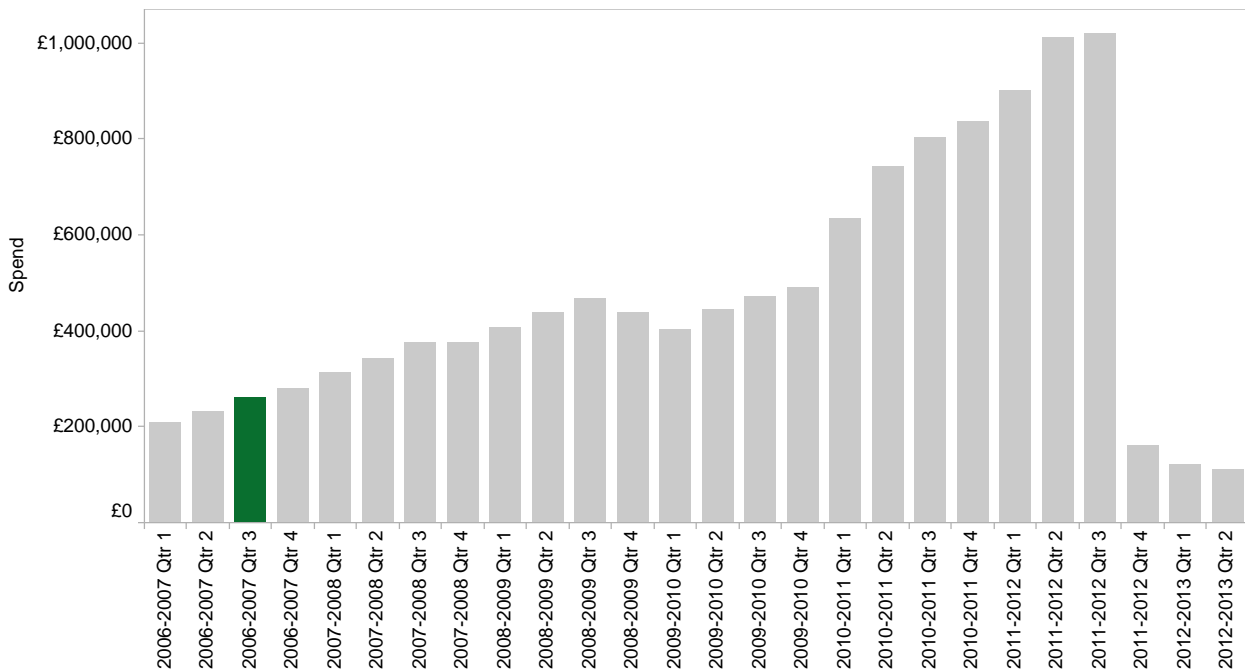
NICE recommended – November 2006.

Estimated cost to NHS Wales – Originally £2.3 million based on NICE estimates in 2006.

Uptake of letrozole increased considerably following the NICE recommendation (Figure 7). The saving of £3.6 million since the last quarter of 2011–2012 is due to the launch of generic letrozole, costing £1,000 per patient per year less than the branded product. Letrozole is now licensed for several indications.

It is not possible to monitor usage by quantity issued accurately through the Medusa system; however, CASPA data suggests usage of letrozole is still increasing in primary care. In the year 2012–2013, the number of prescriptions dispensed has increased by 18.5%.

**Figure 7. All Wales letrozole (Femara®) spend by quarter
(Dark green bar indicates appraisal by AWMSG or NICE in the quarter)**



2.5 Midazolam – buccal (Buccolam®)

AWMSG appraisal indication – Treatment of prolonged, acute, convulsive seizures in infants, toddlers, children and adolescents (from 3 months to 18 years).

AWMSG recommended – June 2012.

A buccal preparation of midazolam has been required for clinical governance safety purposes for some time, as the use of an unlicensed product and lack of an alternative safe and effective licensed medicine has been a cause for concern.

Estimated cost to NHS Wales – £240,000 per year. An overall saving to NHS Wales is expected from a reduction in the use of unlicensed, more expensive “specials” preparations of midazolam in the community.

Spend on unlicensed midazolam preparations in primary care reached £145,000 in the quarter to March 2011. It accounted for approximately £105,000 in the quarter to December 2011, when the licensed preparation was first used in Wales. It is hoped that use of the unlicensed preparations will continue to decrease.

Figure 8 shows NHS Wales uptake and Figure 9 shows the variation by health board.

Figure 8. All Wales buccal midazolam (Buccolam®) spend by quarter (Dark green bar indicates appraisal by AWMSG or NICE in the quarter)

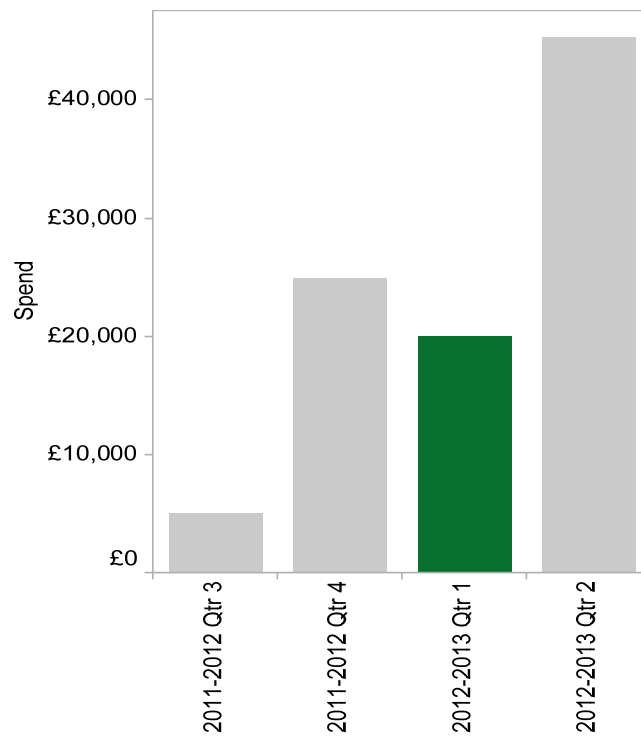
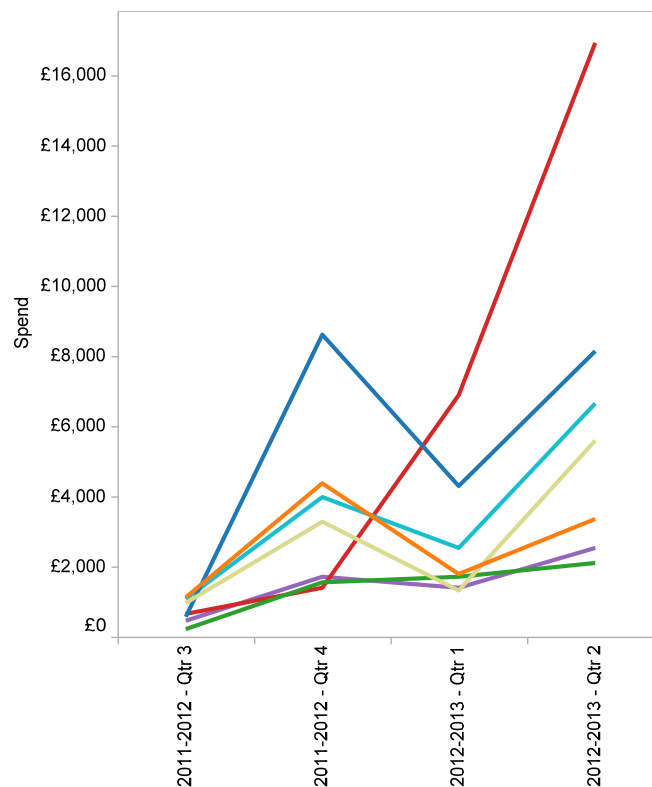


Figure 9. Health board buccal midazolam (Buccolam®) spend by quarter



- Health Board**
- ABMU
 - Aneurin Bevan
 - BCU
 - Cardiff and Vale
 - Cwm Taf
 - Hywel Dda
 - Powys

2.6 Ranibizumab (Lucentis®)

NICE has completed two technology appraisals on ranibizumab:

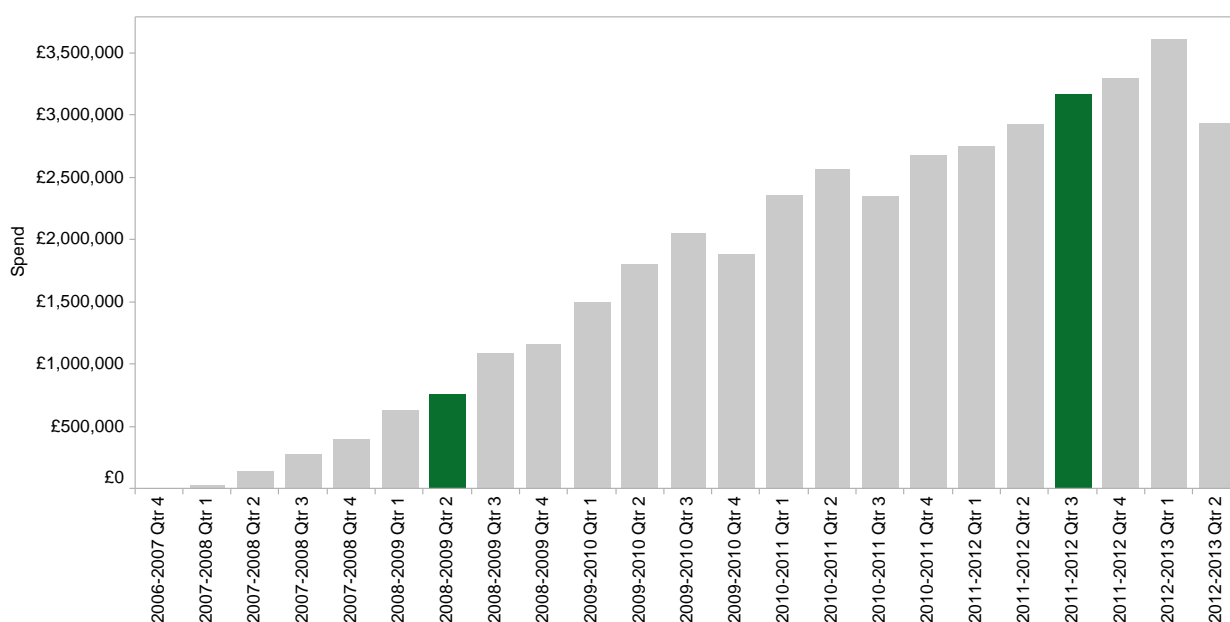
NICE technology appraisal indication – Treatment of wet age-related macular degeneration. NICE recommended the use of ranibizumab if certain criteria were met – August 2008.

NICE technology appraisal indication – Treatment of diabetic macular oedema and for macular oedema secondary to branch retinal vein occlusion.

NICE did not recommend its use for this indication – November 2011.

Figure 10 shows the uptake of ranibizumab pre- and post- both NICE decisions.

Figure 10. All Wales ranibizumab (Lucentis®) spend by quarter (Dark green bars indicate appraisal by AWMSG or NICE in the quarter)



In certain parts of the UK, bevacizumab is being used in preference to ranibizumab for the treatment of wet age-related macular degeneration. This is an unlicensed indication. Prescribing data for bevacizumab are reported in section 3.3.

2.7 Thalidomide (Thalidomide Pharmion®)

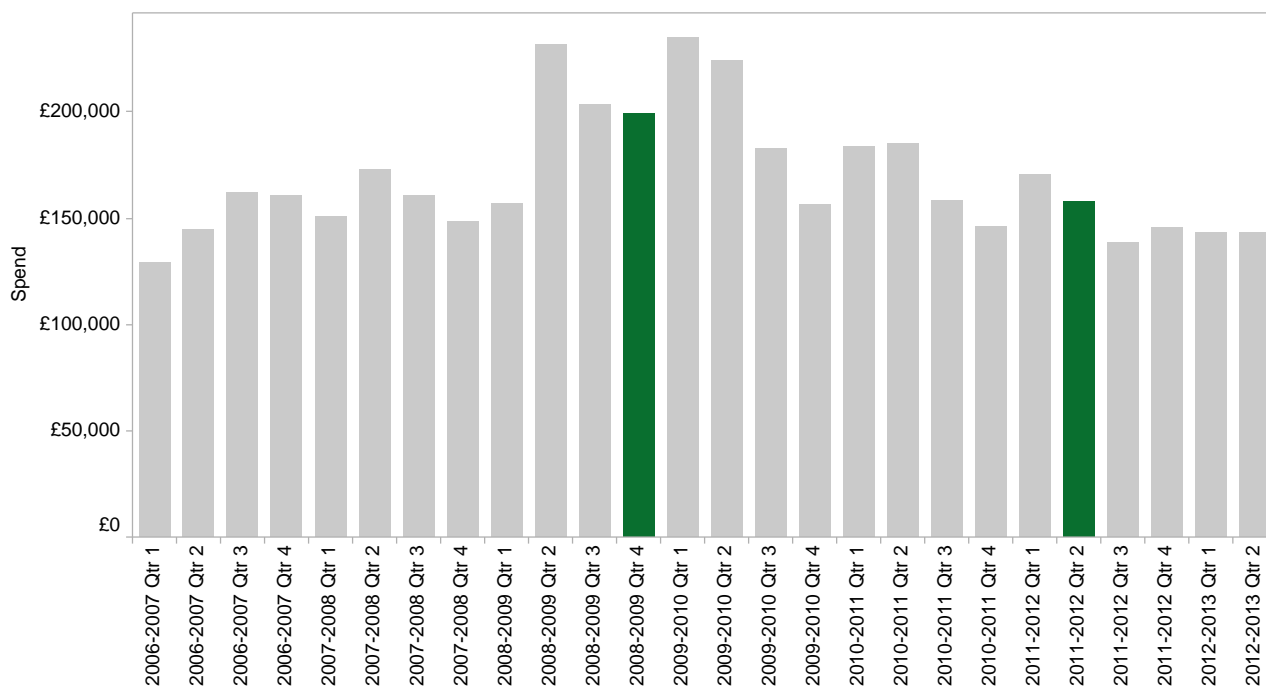
AWMSG appraisal indication – In combination with melphalan and prednisolone as first-line treatment of patients with untreated multiple myeloma, aged 65 and over, or for those ineligible for high-dose chemotherapy.

AWMSG recommended – March 2009 (advice superseded by a NICE recommendation in July 2011).

Figure 11 shows uptake of thalidomide post AWMSG and NICE recommendations.

Estimated cost to NHS Wales – £1.3 million per year, based on 128 patients in Wales likely to be prescribed this treatment. At the peak of prescribing, treatment cost was £920,000 per year; however, usage decreased in the second quarter of 2012–2013.

**Figure 11. All Wales thalidomide (Thalidomide Pharmion®) spend by quarter
(Dark green bars indicate appraisal by AWMSG or NICE in the quarter)**



3.0 AWMSG AND NICE APPRAISED MEDICINES – NOT RECOMMENDED

This section highlights some AWMSG/NICE appraised medicines which were not recommended.

3.1 Aliskiren (Rasilez®)

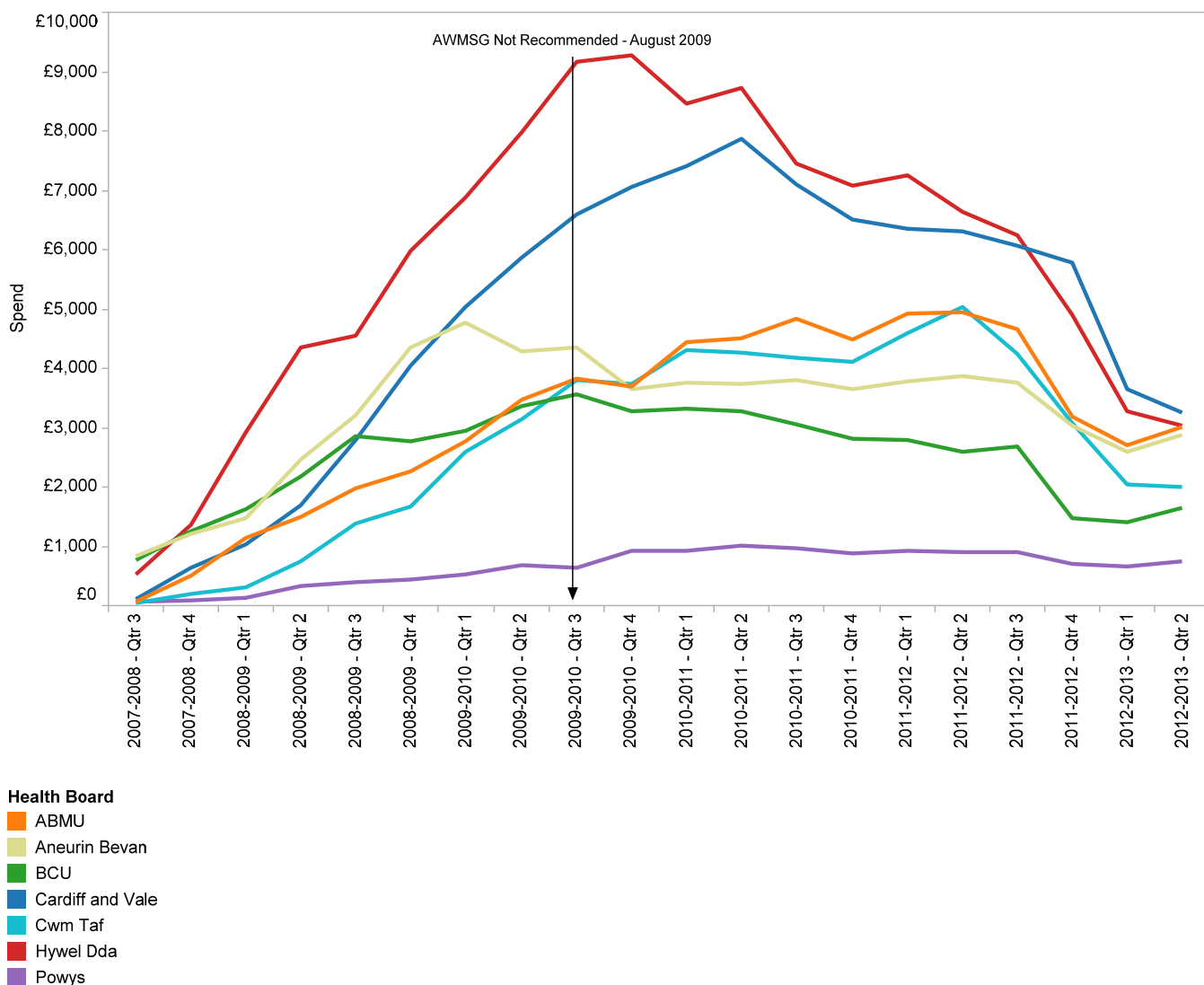
AWMSG appraisal indication – Treatment of essential hypertension.

AWMSG not recommended – August 2009.

There was significant prescribing of aliskiren prior to the AWMSG appraisal non-recommendation, which peaked between June and September 2010 and then started to fall around twelve months after the negative appraisal by AWMSG (Figure 12).

Figure 12 shows the variation in early uptake and discontinuation between health boards.

Figure 12. Health board aliskiren (Rasilez®) spend by quarter



3.2 Linagliptin (Trajenta®)

AWMSG appraisal indication – Treatment of type 2 diabetes mellitus to improve glycaemic control in adults:

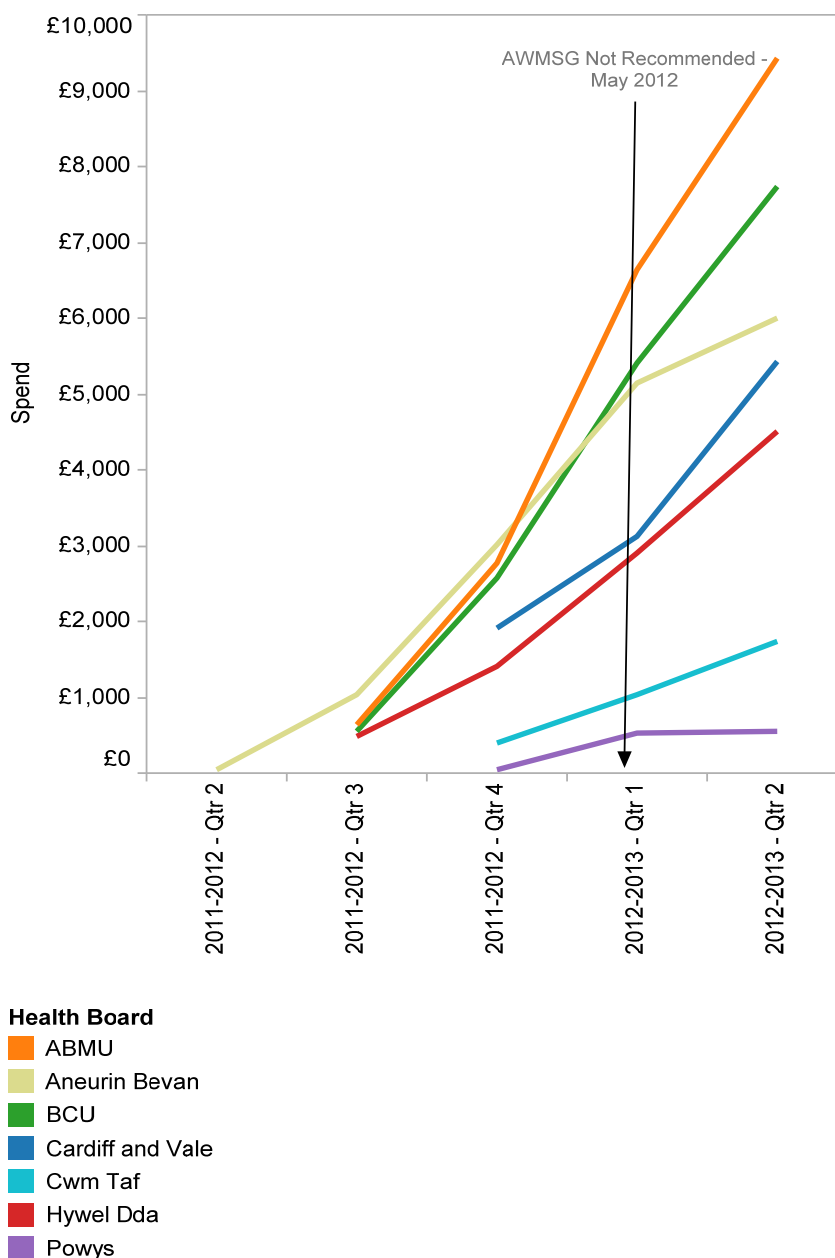
- as monotherapy in patients inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to intolerance, or contraindicated due to renal impairment;
- as combination therapy in combination with metformin when diet and exercise plus metformin alone do not provide adequate glycaemic control; or
- in combination with a sulphonylurea and metformin when diet and exercise plus dual therapy with these medicinal products do not provide adequate glycaemic control.

AWMSG not recommended – May 2012.

Despite its non-recommendation, usage has risen since the appraisal (Figure 13).

Total cost to NHS Wales is currently £140,000 per year.

Figure 13. Health board linagliptin (Trajenta®) spend by quarter

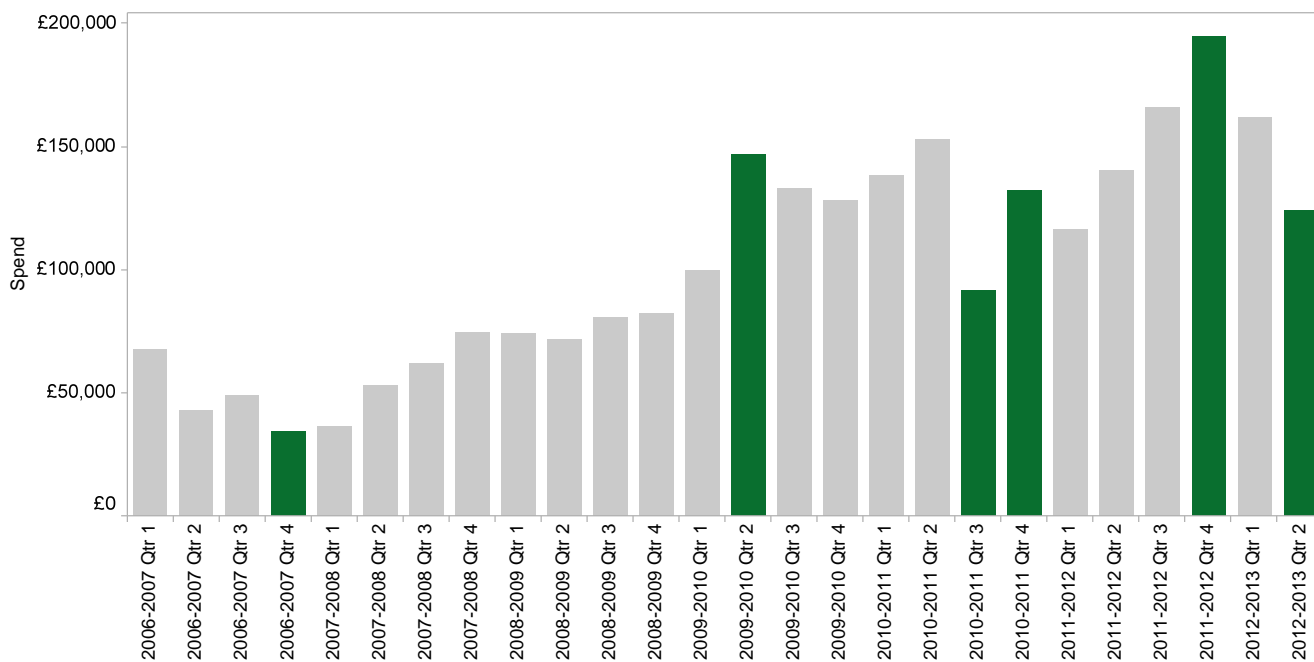


3.3 Bevacizumab (Avastin®)

Bevacizumab is an antineoplastic agent with several licensed indications for chemotherapy. There are six NICE technology appraisals linked to the agent. All six technology appraisals have not recommended the use of the agent.

Figure 14 shows the dates of the six non-recommendations; the cost of this medicine however remains at £500,000 per year. Three Health Boards are still prescribing this agent, the majority being prescribed within Velindre NHS Trust.

Figure 14. All Wales spend on bevacizumab (Avastin®) by quarter (Dark green bars indicate appraisal by AWMSG or NICE in the quarter)



Appendix 1 - Usage of all medicines appraised by NICE and AWMSG across NHS Wales

Monitored Drug	FYear							Drug Recommendation
	2006-2007	2007-2008	2008-2009	2009-2010	2010-2011	2011-2012	2012-2013	
Abacavir/Lamivudine	116,964	214,722	259,110	245,474	232,224	236,874	130,097	Recommended
Abatacept			17,409	31,317	21,410	153,016	109,484	Recommended
Adalimumab	623,415	874,916	1,581,165	2,156,371	1,975,791	1,564,642	329,016	Recommended
Adefovir Dipivoxil	44,580	37,816	49,385	39,050	22,565	18,394	8,323	Recommended
Agalsidase alfa				27,357	4,671	16,379	22,679	Recommended
Agalsidase beta		132,640	261,897	9,927				Recommended
Agomelatine				6,347	21,457	25,011	10,108	Recommended
Alglucosidase alpha	97,446	183,198	698,091	383,295	189,103	179,454		Recommended
Aliskiren		7,536	60,267	117,504	126,612	111,303	32,755	Recommended
Alitretinoin			3,405	51,222	164,733	231,737	122,742	Recommended
Alteplase Cathflo							9,180	Recommended
Amantadine Hydrochloride		34	161	276	553	576	346	Recommended
Ambrisentan							1,618	Recommended
Amifampridine					68,572	70,839	27,225	Recommended
Anagrelide Hydrochloride	273,438	364,141	419,702	453,733	503,721	524,151	258,209	Recommended
Anastrozole	2,513,669	2,803,092	3,241,163	3,652,047	3,437,503	1,143,220	138,245	Recommended
Anidulafungin			10,809	5,248		8,561	4,320	Recommended
Apixaban							12,300	Recommended
Aripiprazole - Injection			11	23	156	142	130	Recommended
Aripiprazole Tablets	2,773,366	3,488,474	4,261,280	4,987,061	5,895,938	6,792,848	3,741,263	Recommended
Atazanavir	402,401	431,869	497,464	526,868	539,298	374,775	94,210	Recommended
Atomoxetine Hydrochloride	249,180	260,961	270,757	316,222	341,515	373,958	186,472	Recommended
Atorvastatin chewable tablets						246	1,180	Recommended
Azacitidine	5,459	4,059	17,763	33,322	83,747	630,080	413,870	Recommended
Azilsartan medoxomil							17	Recommended
Azithromycin eye drops							114	Recommended
Aztreonam lysine				3	24,255	12,319	2,567	Recommended
Basiliximab	82,630	116,599	90,179	91,834	113,762	134,158	51,554	Recommended
Bendamustine		1,719	2,633	0	41,450	209,481	110,926	Recommended
Bevacizumab	193,615	226,101	308,619	507,672	515,019	616,920	285,921	Recommended
Bilastine						15	15	Recommended
Bivalirudin	3,643	2,550		61,303	124,310	253,406	128,786	Recommended
Boceprevir							26,904	Recommended
Bortezomib	316,755	618,917	808,555	1,031,579	1,248,117	1,525,688	845,856	Recommended
Bosentan	41,644	27,160	35,855	42,671	59,165	66,137	34,133	Recommended
Botulinum	215,008	217,025	265,698	304,155	318,068	374,996	180,147	Recommended
Bromfenac						34	102	Recommended
Buprenorphine Hydrochloride	678,371	725,505	783,863	929,963	996,733	1,015,225	509,614	Recommended
Buprenorphine/Naloxone	8,010	27,306	71,149	103,016	110,469	98,771	41,710	Recommended
Capecitabine	1,235,514	1,341,187	1,527,625	1,505,108	1,538,657	1,666,696	782,412	Recommended
Capsaicin patch						756	4,032	Recommended
Carmustine	12,227		5,983	10,791	23,084	14,019		Recommended
Caspofungin	737,265	744,679	824,786	748,309	869,473	900,264	454,791	Recommended
Certolizumab pegol				0	15,980	37,216	0	Recommended
Cetuximab	452,142	226,595	301,811	388,168	732,738	851,274	307,339	Recommended
Cilostazol	75,649	79,896	90,337	101,462	113,712	106,393	44,819	Recommended
Cinacalcet Hydrochloride	66,048	204,208	392,180	487,981	625,009	766,084	471,099	Recommended
Ciprofloxacin ear drops		47	0	27		683	427	Recommended
Clofarabine	28,200	180,621	2,820	10,840				Recommended
Clonazepam oral solution	26,996	22,254	26,374	11,239	4,052	22,729	34,122	Recommended
Clopidogrel	9,849,644	9,623,029	9,477,618	8,393,582	1,437,131	744,040	431,943	Recommended
Colecalciferol						7,209	47,708	Recommended
Colesevelam		2,211	16,005	37,424	59,046	67,078	36,665	Recommended
Collagenase clostridium histolyticum						3,900	22,620	Recommended

Monitored Drug	FYear							Drug Recommendation
	2006-2007	2007-2008	2008-2009	2009-2010	2010-2011	2011-2012	2012-2013	
Dabigatran			3,758	3,358	44,526	76,671	84,834	Recommended
Darbepoetin Alfa	2,984,849	2,121,461	1,859,264	1,501,578	822,260	506,307	229,227	Recommended
Darunavir	3,553	27,264	87,299	221,703	429,528	578,650	176,022	Recommended
Dasatinib	27,131	351,547	440,216	814,836	588,310	200,258	42,885	Recommended
Deferasirox		29,215	147,685	319,430	292,814	307,850	155,014	Recommended
Degarelix		0	0	2,643	6,097	5,828	2,572	Recommended
Delta-9-tetrahydrocannabinol/canna..	26,393	37,296	49,639	34,579	58,197	62,125	29,325	Recommended
Denosumab					28,274	282,554	203,369	Recommended
Dexamethasone intravitreal implant						7,308	9,396	Recommended
Dexamfetamine Sulphate	29,729	31,997	29,323	27,415	62,805	111,922	63,455	Recommended
Dexmedetomidine						1,503	7,197	Recommended
Dexrazoxane						0		Recommended
Docetaxel	1,659,553	2,654,617	2,714,326	3,254,217	2,917,250	545,930	152,733	Recommended
Donepezil Hydrochloride	2,220,099	2,413,283	2,664,440	2,666,725	2,561,809	2,591,189	490,957	Recommended
Doxorubicin Hydrochloride	344,311	513,838	606,543	488,072	376,221	329,669	11,459	Recommended
Dronedarone					63,367	141,605	48,497	Recommended
Drotrecogin Alfa	780,288	635,826	482,422	443,068	344,240	111,518		Recommended
Efalizumab	1,354	26,581	76,309	778				Recommended
Efavirenz/Emtricitabine /Tenofovir di..		2,210	111,851	1,713,480	2,571,860	2,396,466	624,305	Recommended
Eltrombopag					24,091	15,698		Recommended
Emtricitabine	14,899	7,986	4,528	3,736	8,603	17,692	4,258	Recommended
Emtricitabine/rilpivirine/tenofovir						636		Recommended
Emtricitabine/tenofovir	732,621	1,122,406	1,776,807	1,467,566	1,688,774	1,693,699	415,950	Recommended
Enfuvirtide	25,498	18,523			2,606	179		Recommended
Enoxaparin	3,166,936	3,533,584	3,882,491	4,038,089	4,354,238	4,124,438	2,005,951	Recommended
Entecavir		2,646	5,587	15,003	18,397	17,887	10,389	Recommended
Epoetin	4,424	2,505	3,209	1,099				Recommended
Epoetin Alfa	496,459	762,228	1,076,273	714,828	839,835	899,340	377,737	Recommended
Epoetin Beta	2,969,692	2,718,874	2,170,599	1,490,277	712,269	306,288	48,762	Recommended
Epoetin Zeta						272		Recommended
Eribulin						5,634	35,380	Not Recommended
Erlotinib	108,507	169,835	344,471	766,955	799,155	897,854	432,609	Not Recommended
Eslicarbazepine Acetate				2,149	36,530	86,367	49,358	Not Recommended
Esomeprazole		7,836	8,350	328	34	-6	0	Not Recommended
Etanercept	1,912,412	2,272,096	2,452,476	2,630,496	2,634,545	2,476,950	583,567	Not Recommended
Etravirine		13,490	40,744	59,743	84,932	89,761	16,821	Not Recommended
Everolimus					44,872	167,095	37,672	Not Recommended
Exemestane	483,702	704,755	865,214	947,831	966,005	731,421	87,285	Not Recommended
Exenatide		95,737	534,540	1,370,566	1,676,783	1,589,473	827,053	Not Recommended
Ezetimibe	3,215,464	4,267,679	4,988,750	5,328,752	5,308,139	4,658,678	1,958,439	Not Recommended
Febuxostat				105	21,738	57,647	42,233	Not Recommended
Fentanyl nasal spray				125	3,634	7,553	6,375	Not Recommended
Ferric Carboxymaltose			9,154	71,331	141,977	222,705	172,861	Not Recommended
Filgrastim	751,289	611,689	571,866	554,892	464,125	394,895	160,956	Not Recommended
Fingolimod							2,580	Not Recommended
Fludarabine Phosphate	409,093	345,380	307,510	283,656	241,404	181,557	37,817	Not Recommended
Fluorouracil/salicylic acid						1,226	1,915	Not Recommended
Fondaparinux sodium	36,304	35,735	46,437	41,312	117,212	144,582	65,402	Not Recommended
Fulvestrant	67,354	102,775	190,359	198,832	355,204	327,029	98,735	Not Recommended
Galantamine	676,913	785,204	788,319	765,364	674,714	545,322	183,465	Not Recommended
Gefitinib					127,597	212,102	165,378	Not Recommended
Gemcitabine	1,471,952	1,504,888	1,725,957	682,622	268,797	159,721	66,828	Not Recommended
Glatiramer Acetate	51,381	53,615	80,406	138,126	168,438	221,117	62,538	Not Recommended
Golimumab						4,468	21,134	Not Recommended
Human normal immunoglobulin	1,267,814	1,526,331	1,418,906	1,767,212	1,761,052	1,750,364	842,173	Not Recommended
Hydroxycarbamide	20,242	22,368	19,838	24,051	33,012	29,050	16,512	Not Recommended

Monitored Drug	FYear							Drug Recommendation
	2006-2007	2007-2008	2008-2009	2009-2010	2010-2011	2011-2012	2012-2013	
Icatibant acetate					4,987	6,222		Recommended
Imatinib Mesilate	2,875,766	2,130,672	2,189,932	2,067,777	1,583,720	1,486,577	663,977	Recommended
Infliximab	3,397,042	4,113,918	5,319,913	5,897,385	6,211,756	6,426,227	3,299,814	Recommended
Inositol Nicotinate	75,576	72,859	67,136	56,254	47,917	36,038	13,911	Recommended
Insulin Glargine	4,257,241	4,834,043	5,406,734	5,613,856	5,835,564	6,354,832	3,177,066	Recommended
Irinotecan	847,732	806,797	882,166	562,828	139,968	102,753	30,420	Recommended
Ivabradine	27,159	86,709	158,584	219,093	325,025	496,866	302,085	Recommended
Lapatinib			9,442	112,964	206,672	129,057	44,648	Recommended
Laronidase	211,196	205,005	144,423	7,412				Recommended
Latanoprost	3,343,125	3,371,814	3,327,147	3,134,591	3,021,964	2,949,523	998,230	Recommended
Lenalidomide	0	21,646	90,680	1,488,280	2,328,804	2,825,191	1,330,923	Recommended
Letrozole	983,237	1,409,410	1,752,862	1,814,686	3,021,288	3,096,374	232,481	Recommended
Linagliptin						14,698	59,996	Recommended
Liposomal cytarabine	16,036	13,604	4,113	5,065	6,535	1,469	0	Recommended
Liraglutide				216,101	1,540,685	3,067,011	1,911,883	Recommended
Losartan potassium/hydrochlorothia..	262,094	235,812	195,454	190,076	114,276	68,991	32,826	Recommended
Maraviroc				8,887	23,928	42,275	12,459	Recommended
Memantine Hydrochloride	254,478	240,464	238,592	270,851	254,480	532,846	428,007	Recommended
Mercaptopurine oral suspension	18,163	20,486	10,680	3,408	2,569	2,886	3,781	Recommended
Methadone Hydrochloride	413,617	756,513	944,810	1,021,765	981,013	755,289	340,965	Recommended
Methoxy polyethylene glycol-epoetin..		21,577	134,630	108,872	95,202	49,335		Recommended
Micafungin			1,152		13,563		12,935	Recommended
Midazolam buccal suspension	3,129	4,403	2,353	4,658	4,227	33,133	65,228	Recommended
Miglustat	10,528	-1,093						Recommended
Mitotane	2,003	17,238	28,845	18,420	36,034	39,116	9,452	Recommended
Mycophenolate Mofetil	1,305,285	1,648,794	1,888,999	2,082,594	2,343,598	1,477,646	610,917	Recommended
Mycophenolic acid	56,980	86,789	118,964	173,167	189,256	292,175	184,477	Recommended
Naftidrofuryl oxalate	118,326	100,323	77,455	56,874	51,157	66,931	33,868	Recommended
Naltrexone Hydrochloride	18,786	16,691	24,143	32,458	61,374	78,805	43,868	Recommended
Natalizumab		7,967	59,288	96,608	150,705	284,755	155,191	Recommended
Nelarabine		14,086			7,193			Recommended
Nepafenac						254	78	Recommended
Nicotinic acid/laropiprant				2,525	16,575	31,344	20,127	Recommended
Nilotinib		0	73,867	79,391	69,205	173,068	227,106	Recommended
Olanzapine depot						3,987	9,632	Recommended
Omalizumab	50,564	79,458	163,374	333,878	627,656	841,152	459,055	Recommended
Oseltamivir Phosphate	3,110	2,504	8,869	776	113,414	5,582	3,904	Recommended
Oxaliplatin	2,078,918	846,714	445,196	173,277	244,692	72,356	89,762	Recommended
Paclitaxel albumin					10,406	12,140	4,428	Recommended
Paliperidone		2,043	8,078	9,174	7,965	11,818	6,143	Recommended
Paliperidone palmitate prolonged rel..						6,267	6,707	Recommended
Panitumumab				9,036	36,929	6,385		Recommended
Paricalcitol		0	717	4,591	11,932	19,329	7,438	Recommended
Pazopanib					16,596	616,935	294,865	Recommended
Pegfilgrastim	349,777	565,873	763,460	823,353	816,420	767,354	386,947	Recommended
Peginterferon Alfa	404,806	501,988	431,142	650,106	714,651	585,771	279,686	Recommended
Pegvisomant	1,763							Recommended
Pemetrexed	35,015	147,439	270,801	378,715	1,024,941	1,437,451	507,362	Recommended
Pentoxifylline	95,518	83,550	74,307	69,629	66,905	67,777	29,710	Recommended
Pharmalgen	1,765	1,680	1,740	1,990	1,486	617	549	Recommended
Pimecrolimus	63,450	52,408	52,027	51,200	56,124	63,313	28,453	Recommended
Plerixafor			3	33,939	155,272	345,499	152,305	Recommended
Pramipexole prolonged release				58,238	475,915	720,602	379,961	Recommended
Prasugrel				13,047	73,962	164,404	123,354	Recommended
Prucalopride					9,077	102,515	98,231	Recommended

Monitored Drug	FYear							Drug Recommendation
	2006-2007	2007-2008	2008-2009	2009-2010	2010-2011	2011-2012	2012-2013	
Quetiapine	5,169,851	6,345,930	6,877,654	7,595,926	7,987,266	8,801,774	3,162,213	Recommended
Quetiapine XL			241,746	1,525,083	2,392,516	3,241,301	1,575,746	Recommended
Rabbit anti-human thymocyte immu..		10,779	21,767					Not Recommended
Raloxifene Hydrochloride	542,217	473,003	407,445	353,489	305,498	262,586	112,120	Recommended
Raltegravir		9,626	43,547	164,225	340,386	246,676	82,036	Recommended
Raltitrexed	770	379	1,600	1,583	26,342	17,616	14,848	Recommended
Ramipril (oral solution)	2,586	28,442	54,307	77,026	52,585	38,736	17,310	Recommended
Ranibizumab	894	822,146	3,638,226	7,217,721	9,942,333	12,142,004	6,548,615	Recommended
Ranolazine			185	25,253	56,313	106,403	77,503	Recommended
Retigabine						3,036	10,562	Recommended
Ribavirin	391,416	490,317	453,657	466,918	477,109	319,216	64,150	Recommended
Rifaximin			500	1,988	2,885	12,594	15,758	Recommended
Riluzole	269,273	264,591	235,831	280,627	337,643	380,696	180,065	Recommended
Rituximab	3,852,867	4,202,103	4,725,728	6,133,153	6,784,918	8,148,698	3,782,860	Recommended
Rivaroxaban			239	65,777	230,958	205,650	85,740	Recommended
Rivastigmine	258,504	346,524	397,035	544,144	616,652	679,945	311,747	Recommended
Romiplostim					23,859	226,299	159,638	Recommended
Ropinirole M/R			205,321	743,939	888,578	456,093	237,252	Recommended
Rosuvastatin	5,247,636	5,331,128	5,237,262	5,605,988	5,641,227	5,238,937	2,209,558	Recommended
Rufinamide		532	10,229	29,739	47,412	79,792	47,486	Recommended
Rufinamide oral suspension							1,622	Recommended
Rupatadine oral solution				669	1,922	2,982	1,825	Recommended
Saxagliptin				14,215	254,789	640,683	508,317	Recommended
Sevelamer carbonate powder for or..	111,734	100,167	82,675	67,212	79,463	70,605	38,788	Recommended
Sildenafil oral 20mg	7,662	54,231	32,879	121,297	186,575	164,147	101,800	Recommended
Sirolimus	326,082	334,569	408,500	393,475	368,648	331,003	160,022	Recommended
Sitagliptin		49,992	289,189	996,756	2,296,305	3,529,259	2,090,429	Recommended
Sodium Oxybate		2,160	5,400	11,835	23,544	31,608	31,104	Recommended
Sodium Phenylbutyrate	17,092	27,411	30,995	48,174	61,456	44,993	22,726	Recommended
Sodium Valproate		1,477	7,931	16,667	33,454	48,618	26,637	Recommended
Somatropin	2,491,172	2,510,054	2,299,713	2,398,587	2,398,670	2,383,959	1,076,200	Recommended
Sorafenib	2,943	49,294	73,403	90,464	38,147	78,152	23,844	Recommended
Stiripentol	901	4,536	5,392	21,347	25,842	34,303	18,358	Recommended
Strontium Ranelate	285,350	373,282	472,736	524,377	529,242	575,532	271,233	Recommended
Sunitinib	70,606	366,408	732,897	1,977,784	2,458,888	2,428,456	997,166	Recommended
Tacrolimus	237,758	410,298	499,587	475,960	678,464	846,167	380,247	Recommended
Tacrolimus (topical)	15,914	16,389	14,118	13,999	15,766	19,343	6,377	Recommended
Tacrolimus MR	219,178	364,616	482,801	504,298	648,969	792,112	412,005	Recommended
Tadalafil	804,642	1,042,644	1,258,616	1,569,237	1,716,966	1,646,311	698,902	Recommended
Tapentadol fim coated tabs						4,731	6,249	Recommended
Tapentadol prolonged release						17,549	23,331	Recommended
Tegafur uracil	10,754	25,170	34,293	24,258	14,718	1,906	912	Recommended
Telaprevir						32	94,072	Recommended
Telmisartan	552,127	609,645	646,876	742,414	750,139	711,093	326,862	Recommended
Temozolomide IV soln	324,793	525,947	428,209	477,135	338,154	212,235	54,255	Recommended
Temsirolimus		0	3,496	42,653	212			Recommended
Tenofovir disoproxil	284,240	266,862	242,708	267,277	272,570	281,442	101,200	Recommended
Teriparatide	41,353	39,416	65,167	25,557	15,941	11,582	2,284	Recommended
Thalidomide	596,721	632,780	791,534	798,063	673,852	612,231	285,899	Recommended
Ticagrelor					50	230	3,746	Recommended
Tipranavir capsules	4,043	1,168	584	22		7		Recommended
Tocilizumab				2,473	110,089	468,820	412,654	Recommended
Tocofersolan				996	1,146	1,637	1,418	Recommended
Topotecan	85,667	70,343	138,897	212,994	120,178	162,463	11,753	Recommended
Trabectedin		0	7,233	20,333	130,934	166,102	116,899	Recommended
Trastuzumab	5,106,069	6,932,998	6,731,570	6,524,571	7,189,660	7,434,007	3,936,614	Recommended
Triptorelin pamoate SR						4,140	3,726	Recommended
Ulipristal acetate				220	1,898	3,899	3,232	Recommended
Ustekinumab				17,444	76,916	53,250		Recommended
Valganciclovir	462,514	430,709	486,169	462,411	616,898	626,335	345,080	Recommended
Valsartan	4,184,566	4,636,724	4,696,813	4,129,547	4,165,461	4,066,657	596,773	Recommended
Varenicline Tartrate	65,707	1,344,642	1,447,114	1,574,851	1,752,091	1,635,408	751,756	Recommended
Vildagliptin			12,909	84,272	160,058	164,953	80,906	Recommended
Vinorelbine	143,853	181,216	240,233	265,752	246,725	357,178	196,806	Recommended
Zanamivir	368		164	254	6,579	291	85	Recommended

Appendix 2 – Usage of all medicines appraised by NICE and AWMSG and not recommended across NHS Wales

Monitored Drug	Primary	Secondary	Grand Total
Agomelatine	£8,010.00	£2,098.11	£10,108.11
Aliskiren	£32,561.90	£193.45	£32,755.35
Amantadine Hydrochloride	£345.60		£345.60
Amifampridine	£27,225.00		£27,225.00
Aripiprazole - Injection		£129.72	£129.72
Azilsartan medoxomil	£16.80		£16.80
Azithromycin eye drops	£76.89	£37.32	£114.21
Aztreonam lysine	£2,566.50		£2,566.50
Bevacizumab		£285,920.77	£285,920.77
Bilastine	£15.09		£15.09
Bosentan	£1,510.21	£32,623.11	£34,133.32
Bromfenac	£102.00		£102.00
Caspofungin		£454,790.69	£454,790.69
Cilostazol	£43,739.38	£1,079.34	£44,818.72
Ciprofloxacin ear drops	£426.64		£426.64
Clonazepam oral solution	£31,308.08	£2,813.70	£34,121.78
Colesevelam	£36,140.43	£524.15	£36,664.58
Dasatinib		£42,884.88	£42,884.88
Degarelix	£1,036.22	£1,536.03	£2,572.25
Delta-9-tetrahydrocannabinol/cannabidiol	£28,875.00	£450.00	£29,325.00
Dexamethasone intravitreal implant		£9,396.00	£9,396.00
Eribulin		£35,379.60	£35,379.60
Everolimus		£37,671.97	£37,671.97
Fludarabine Phosphate		£37,817.20	£37,817.20
Fulvestrant	£3,656.87	£95,078.52	£98,735.39
Glatiramer Acetate	£2,680.20	£59,857.80	£62,538.00
Hydroxycarbamide	£3,510.02	£13,001.97	£16,511.99
Inositol Nicotinate	£13,813.00	£97.99	£13,910.99
Ivabradine	£280,792.68	£21,292.04	£302,084.72
Lapatinib		£44,648.28	£44,648.28
Linagliptin	£59,669.29	£326.88	£59,996.17
Liposomal cytarabine		£0.00	£0.00
Micafungin		£12,934.58	£12,934.58
Mitotane	£590.97	£8,860.99	£9,451.96
Nepafenac	£77.58		£77.58
Nicotinic acid/laropiprant	£19,717.45	£410.00	£20,127.45
Olanzapine depot		£9,632.34	£9,632.34
Paliperidone	£6,142.54		£6,142.54
Paricalcitol	£694.40	£6,743.65	£7,438.05
Pentoxifylline	£26,962.73	£2,747.64	£29,710.37
Raltitrexed		£14,847.94	£14,847.94
Rosuvastatin	£2,186,389.73	£23,168.00	£2,209,557.73
Rupatadine oral solution	£1,824.57		£1,824.57
Sevelamer carbonate powder for oral solution	£990.92	£37,796.77	£38,787.69
Sodium Oxybate	£15,120.00	£15,984.00	£31,104.00
Sorafenib		£23,843.75	£23,843.75
Stiripentol	£3,029.35	£15,328.30	£18,357.65
Tapentadol fim coated tabs	£5,344.15	£904.79	£6,248.94
Temozolomide IV soln		£54,255.22	£54,255.22
Tocofersolan	£1,418.31		£1,418.31
Triptorelin pamoate SR	£3,726.00		£3,726.00
Ulipristal acetate	£3,231.80		£3,231.80
Grand Total	£2,853,338.30	£1,407,107.50	£4,260,445.80