

All Wales Medicines Strategy Group

Grŵp Strategaeth Meddyginiaethau Cymru Gyfan



Monitoring Usage in Wales of Medicines Appraised by NICE and AWMSG

October 2014

This report has been prepared by the Welsh Analytical Prescribing Support Unit (WAPSU), part of the All Wales Therapeutics and Toxicology Centre (AWTTC), and has subsequently been endorsed by the All Wales Medicines Strategy Group (AWMSG).

Please direct any queries to AWTTC:

All Wales Therapeutics and Toxicology Centre
University Hospital Llandough
Penlan Road
Llandough
Vale of Glamorgan
CF64 2XX

awttc@wales.nhs.uk

029 2071 6900

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EXECUTIVE SUMMARY

- Between April 2003 and 31 March 2014, AWMSG undertook 199 appraisals; 162 resulted in a positive recommendation for a specific indication, 37 resulted in a negative recommendation for a specific indication. During the same period AWMSG issued 202 “Statements of Advice”, confirming that a medicine cannot be endorsed for use within NHS Wales because the marketing authorisation holder did not submit an application for appraisal; 140 are currently active.
- Up to 31 March 2014, NICE has undertaken 308 appraisals, of which 234 are currently active.
- As of March 2014, 232 medicines have a positive recommendation for use by either NICE and/or AWMSG for one or more indications, costing NHS Wales £173,966,196 for the financial year 2013–2014.
- Of the medicines with a positive recommendation from NICE and/or AWMSG, 13 have not been used within NHS Wales in the last three years.
- As of March 2014, there were 55 medicines with one or more negative recommendations by NICE/AWMSG. NHS Wales spend on the 20 medicines that only have a negative recommendation for their indication(s) was £2,382,974 for the financial year 2013–2014.
- NHS Wales spend on the 26 medicines with only a Statement of Advice for their indication(s) was £1,393,313 for the financial year 2013–2014.
- Further analysis has been undertaken on three areas due to their high cost to NHS Wales and/or current therapeutic interest: cytokine modulators, medicines used in the prevention and treatment of osteoporosis, and medicines used in the management of diabetes.

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1.0 BACKGROUND

Medicines are funded by NHS Wales following advice from two sources: the National Institute for Health and Care Excellence (NICE) and the All Wales Medicines Strategy Group (AWMSG). Health boards are expected to follow the advice from these bodies and provide the recommended treatment where appropriate. Recommendations should be implemented within three months of the issuance of NICE advice or the ratification by the Minister for Health and Social Services of the AWMSG recommendation.

AWMSG has a remit to appraise newly licensed medicines, including licence extensions and new formulations of existing medicines. NICE advice supersedes AWMSG advice; therefore AWMSG does not usually appraise medicines where NICE advice is expected within 12 months. If the holder of the marketing authorisation does not submit an application for appraisal (non-submission), AWMSG will issue a Statement of Advice, confirming that a medicine cannot be endorsed for use within NHS Wales.

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. From October 2010, the remit was expanded to include the appraisal of all new medicines not on the NICE work programme.

A database detailing all NICE and AWMSG appraisal recommendations and AWMSG non-submissions has been developed by the Welsh Analytical Prescribing Support Unit (WAPSU) to facilitate their monitoring. Each NICE/AWMSG recommendation and non-submission is linked to the specific medicine (including formulation and brand where appropriate) to enable accurate retrieval of the appropriate prescribing data.

Two systems are used to retrieve medicines usage data:

- The Comparative Analysis System for Prescribing Audit (CASPA) version 1.0.4.8 (NHS Wales Shared Services Partnership [NWSSP]). This software provides a record of all WP10 prescriptions (issued by GPs in Wales for patients receiving NHS treatment) and WP10HP prescriptions (issued by hospital clinicians in NHS Wales) forwarded to Prescribing Services, NWSSP, for processing and payment following dispensing¹.
- The Medusa data warehouse, which holds information on medicines issued by all hospitals in Wales².

The data from the two systems have been combined to allow analysis of both sectors in NHS Wales.

The report monitors medicines appraised between April 2003 and 31 March 2014, and also those where an AWMSG Statement of Advice due to non-submission has been issued. Medicines usage data are reported for the period 1 April 2011 to 31 March 2014.

2.0 CAUTION IN THE INTERPRETATION OF MONITORING DATA

- Due to the limitations of both systems used to collect medicines usage data, it is not currently possible to link the prescribing of a specific medicine to a specific indication. As many of the medicines monitored have more than one indication, this is a major problem when trying to monitor appraisal recommendations and non-submissions.
- The Medusa data warehouse is reliant on data input by individual hospital pharmacy departments. If the data on a medicine are input under an alternative name to the usual generic or brand name, it may not be identified at extraction.
- For the first time the report includes medicines supplied by homecare, recorded through the hospital system; medicines supplied through other homecare providers are not included in this report.
- Medicines supplied through hospitals in England or on FP10HP (issued by hospital clinicians in NHS England) to patients resident in Wales, which do not get issued via Medusa or recorded through CASPA, are not included in this report.
- Combining data obtained from two different software systems provides challenges, particularly as CASPA and Medusa report data via different measurement criteria. Hence, in order to amalgamate data, total cost of medicine usage is reported. Where primary care data are monitored, the number of items (prescriptions) may also be used.
- Many of the medicines being monitored are linked to more than one NICE or AWMSG appraisal. Several medicines therefore have a positive recommendation for one indication and a negative recommendation or Statement of Advice for another indication. Where possible, medicines have been classed as recommended, not recommended and AWMSG Statement of Advice, and reported accordingly.
- Some of the medicines being monitored have multiple indications, some of which, due to the remit of NICE and AWMSG, may not have met the criteria for appraisal. This means that these medicines may be in use for indications other than those appraised. These medicines have been included in the relevant sections of the report, but have been highlighted and excluded from the more detailed analysis.
- AWMSG has appraised several new liquid preparations that have been licensed for use. Many of these preparations may have been available as liquid specials prior to the introduction of the licensed product. Liquid specials formulated in different strengths to the licensed product can be excluded from the analysis; however, it is not always possible on CASPA or Medusa to determine whether a product is a special or a licensed product where the strengths are the same.
- Generic prescribing is encouraged in primary care and nearly all medicines are recorded generically on the Medusa system. Therefore, where an appraisal and indication relates to a particular brand, it is not always possible to accurately determine usage against a particular appraisal.
- It is important to be aware that population size and demographics, as well as individual medical and surgical specialties, will influence prescribing; this should be taken into consideration when reading this report.

3.0 APPRAISALS OVERVIEW

This report classifies a medicine according to its appraisal status (i.e. recommendation, negative recommendation, Statement of Advice) on 31 March 2014. Appendix 1 provides a full list of all medicines that have undergone appraisal by NICE/AWMSG and the appraisal recommendation, and those medicines that have received a Statement of Advice, confirming that they could not be endorsed for use for a particular indication due to company non-submission.

Between April 2003 and 31 March 2014, AWMSG undertook 199 appraisals on 156 medicines. Of these:

- 162 appraisals resulted in a positive recommendation (full or in part) for a specific indication;
- 37 appraisals resulted in a negative recommendation for a specific indication.

Twenty-seven appraisals undertaken by AWMSG have subsequently been superseded by NICE Technology Appraisals (TAs).

During the same period, 202 Statements of Advice were issued confirming a medicine could not be endorsed for use for a particular indication due to company non-submission for appraisal. Of those, nine Statements of Advice have been superseded by NICE, and 38 have subsequently undergone AWMSG appraisal and received a positive recommendation. Six medicines are currently undergoing AWMSG appraisal and nine have subsequently met exclusion criteria for appraisal. Thus, there are 140 AWMSG Statements of Advice currently active.

Up to 31 March 2014, NICE had undertaken 308 TAs, including reviews and terminated appraisals, of which 234 are currently active; however, 26 of those appraisals cover medical technologies and procedures rather than medicines. A medicine may be included in more than one appraisal (similar to the AWMSG appraisal process) and some appraisals cover more than one medicine. A number of NICE TAs have been excluded from the report due to their broad remit. These are listed in Appendix 2.

4.0 MEDICINES WITH A NICE/AWMSG RECOMMENDATION

As of March 2014, 232 medicines have a positive recommendation for use by either NICE and/or AWMSG for one or more indications. The NHS Wales spend for the financial year 2013–2014 on these medicines was £173,966,196.

Of those 232 medicines, 16 have also received one or more negative recommendations from NICE or AWMSG, and 29 have been subject to one or more Statements of Advice issued by AWMSG, confirming that the medicine cannot be endorsed for use within NHS Wales due to a non-submission.

Table 1 details 15 medicines with a positive recommendation from NICE/AWMSG, which have the highest spend in NHS Wales for the financial year 2013–2014. Ten of these medicines have been subject to more than one NICE and/or AWMSG appraisal for multiple indications. Four of the 15 medicines are cytokine modulators and three are used in the management of diabetes.

Table 1. NICE/AWMSG recommended medicines with highest spend

Medicine	NICE/AWMSG positive recommendations NICE publication/ministerial ratification date	Spend (£) 2013–2014
Ranibizumab	TA155 (August 2008) TA274 (April 2013) TA283 (May 2013) TA298 (November 2013)	10,936,200
Trastuzumab*	TA34 (March 2002) TA107 (August 2006) TA208 (November 2010) AWMSG reference no. 1066 (16/05/2012) AWMSG reference no. 1409 (25/10/2012)	10,758,995
Etanercept*	TA35 (March 2002) TA103 (July 2006) TA130 (October 2007) TA143 (May 2008) TA195 (August 2010) TA199 (August 2010) AWMSG reference no. 1437 (06/12/2013)	8,554,161
Rituximab	TA65 (September 2003) TA137 (February 2008) TA174 (July 2009) TA193 (July 2010) TA195 (August 2010) TA226 (June 2011) TA243 (January 2012) TA308 (March 2014)	8,513,593
Adalimumab*	TA130 (October 2007) TA143 (May 2008) TA146 (June 2008) TA187 (May 2010) TA195 (August 2010) TA199 (August 2010) AWMSG reference no. 8 (25/04/2012) AWMSG reference no. 1381 (29/07/2013) AWMSG reference no. 1977 (14/08/2013) AWMSG reference no. 749 (14/08/2013)	7,893,431
Infliximab*	TA130 (October 2007) TA134 (January 2008) TA163 (December 2008) TA187 (May 2010) TA195 (August 2010) TA199 (August 2010)	7,776,433
Insulin glargine	TA53 (December 2002) AWMSG reference no. 1673 (18/03/2013)	6,448,050
Sitagliptin	AWMSG reference no. 1655 (25/10/2012)	5,050,434
Aripiprazole oral	AWMSG reference no. 27 (22/07/2009) TA213 (January 2011) TA292 (July 2013)	4,919,622
Liraglutide	TA203 (October 2010)	4,834,489
Imatinib*	TA70 (October 2003) TA86 (October 2004) TA251 (April 2012)	4,226,042
Enoxaparin	AWMSG reference no. 125 (28/05/2010)	3,920,357
Lenalidomide	TA171 (June 2009)	3,628,184
Ezetimibe	TA132 (November 2007)	3,282,540
Tacrolimus capsules	TA85 (September 2004) TA99 (April 2006)	2,871,982

*Indicates medicines that also have a NICE/AWMSG negative recommendation or AWMSG Statement of Advice due to a non-submission for a specific indication.

4.1 NICE/AWMSG recommended medicines not being used by NHS Wales

Of the medicines with a positive recommendation from NICE/AWMSG, 13 medicines have no spend attributed to them in NHS Wales in the last 3 years. Table 2 lists those medicines, including the details of the NICE/AWMSG appraisals linked to them. It would be necessary to work with individual health boards and clinicians to try to identify why these medicines have not been used.

Table 2. Medicines with a positive recommendation from NICE/AWMSG and zero spend

Medicine	NICE/AWMSG guidance	NICE publication/ ministerial ratification date
Ceftaroline fosamil (Zinforo [®])	AWMSG reference no. 1065	29/07/2013
Colistimethate sodium dry powder inhaler (Colobreathe [®])	TA276	March 2013
Daclizumab	TA85	September 2004
	TA99	April 2006
Dihydroartemisinin/piperaquine phosphate (Eurartesim [®])	AWMSG reference no. 1228	07/08/2012
Epoetin theta (Eporatio [®])	AWMSG reference no. 592	17/11/2010
Ferumoxytol (Rienso [®])	AWMSG reference no. 145	29/07/2013
Iloprost trometamol nebuliser solution (Ventavis [®])	AWMSG reference no. 163	13/03/2007
Mecasermin (Increlex [®])	AWMSG reference no. 196	03/11/2009
Pixantrone (Pixuvri [®])	TA306	February 2014
Sodium phenylbutyrate (Ammonaps [®]) (Pheburane [®])	AWMSG reference no. 280	14/05/2004
	AWMSG reference no. 2227	06/12/2013
Tegafur/gimeracil/oteracil (Teysuno [®])	AWMSG reference no. 928	02/12/2013
Teriflunomide (Aubagio [®])	TA303	January 2014
Tobramycin dry powder inhaler (TOBI Podhaler [®])	TA276	March 2013

4.2 AWMSG recommended medicines – company estimate versus actual spend

As part of a submission for appraisal by AWMSG, the company is required to estimate the cost to NHS Wales of the particular medicine for the indication being appraised. Analysis has been undertaken to compare the actual spend by NHS Wales with the company estimated spend for a selected group of medicines, which have received a positive recommendation from AWMSG between 1 April 2011 and 31 March 2013. The medicines selected are newly licensed products or formulations, which do not have established use for another indication.

Table 3 provides a summary of both the company estimated and the actual spend on these medicines in NHS Wales. The information shows that for some medicines there is a large difference between the estimated and the actual spend. Estimated spend is subject to uncertainty, which could be around the predicted level of uptake of a new medicine, the methods used to derive the number of patients eligible for treatment, or the number of patients who are likely to be switched from the comparator medicine to the new medicine, particularly where an indication has previously been managed with an unlicensed medicine.

Data on actual spend are collected quarterly, so the date within the quarter that the appraisal recommendation is published and the speed of uptake of a particular recommendation can affect the calculation of actual spend.

Table 3. Company estimated versus actual spend on AWMSG recommended medicines

Medicine	Ministerial ratification date	Company estimated spend		Actual spend (percent of estimate)	
		Year 1	Year 2	Year 1	Year 2
Tacrolimus modified release tablets	01/09/2011	£376,096	£714,582	£25,734 (6.8%)	£30,728 (4.3%)
Ferric carboxymaltose	01/09/2011	£196,539	£271,602	£302,413 (153.9%)	£395,538 (145.6%)
Collagenase <i>Clostridium histolyticum</i> (Xiapex [®])	20/12/2011	£71,136	£141,024	£80,340 (112.9%)	£239,460 (169.8%)
Tapentadol modified release tablets	09/01/2012	£32,940	£161,040	£49,967 (151.7%)	£118,787 (73.8%)
Esomeprazole IV solution	25/04/2012	£1,565	£1,565	£0 (0%)	£37 (2.4%)
Fluorouracil/salicylic acid	19/06/2012	£37,741	£72,662	£17,073 (45.2%)	-
Rilpivirine	23/07/2012	£56,074	£126,776	£11,938 (21.3%)	-
Rifaximin 200 mg tablet	23/07/2012	£7,520	£7,520	£126,003 (1,675.6%)	-
Dexmedetomidine	07/08/2012	£124,108	£186,304	£55,531 (44.7%)	-
Dihydroartemisinin/piperaquine phosphate	07/08/2012	£1,200	£1,200	£0 (0%)	-
Rufinamide oral suspension	25/10/2012	£18,612	£18,612	£9,863 (53.0%)	-
Eslicarbazepine acetate	09/11/2012	£116,510	£136,089	£215,707 (185.1%)	-
Paliperidone palmitate depot injection	09/11/2012	£167,523	£1,875,082	£299,986 (179.1%)	-
Ramipril oral solution	09/11/2012	£14,400	£14,400	£46,238 (321.1%)	-
Fidaxomicin	11/12/2012	£157,400	£243,874	£87,399 (55.5%)	-
Argatroban	16/01/2013	£379,115	£379,115	£63,866 (16.8%)	-

The actual spend on tacrolimus modified release tablets, esomeprazole IV solution, fluorouracil/salicylic acid, rilpivirine, dexmedetomidine, dihydroartemisinin/piperaquine phosphate, rufinamide oral suspension, fidaxomicin, and argatroban are less than company estimates, whilst the actual spend for ferric carboxymaltose, collagenase *Clostridium histolyticum* (Xiapex[®]), rifaximin 200 mg tablets, eslicarbazepine acetate, paliperidone palmitate depot injection and ramipril oral solution are higher than company estimates.

5.0 MEDICINES WITH A NICE/AWMSG NEGATIVE RECOMMENDATION

As of March 2014, there were 55 medicines with one or more negative recommendations by NICE/AWMSG. Of these medicines, 16 also have a positive recommendation for another indication, and one is included as an option in a NICE clinical guideline (CG); these 17 medicines are therefore excluded from further analysis. A further two medicines, rosuvastatin and valsartan tablets, have established use for other indications and have therefore also been excluded from further analysis. Sixteen of the medicines with negative recommendations had no spend attributed to them for the financial year 2013–2014. Analysis of primary care and secondary care spend has been undertaken on the remaining 20 medicines.

Expenditure on these 20 medicines with negative recommendations from NICE/AWMSG was £2,382,974 for the financial year 2013–2014, the majority of which, £2,136,002, was secondary care prescribing and via WP10HP. Table 4 shows secondary care and WP10HP spend on the 19 medicines with negative recommendations prescribed within hospitals in Wales (the remaining medicine was prescribed in primary care only). Table 5 shows secondary care and WP10HP spend broken down by health board. The variation in use may reflect particular specialties rather than different prescribing behaviours and interpretation of guidance.

Table 4. Secondary care and WP10HP spend (£) for the financial year 2013–2014 on medicines with a negative recommendation

Medicine	Secondary care	WP10HP	Total
Aliskiren	265	0	265
Amantadine hydrochloride	1,192	491	1,683
Bevacizumab	824,331	0	824,331
Cabazitaxel	17,741	0	17,741
Cilostazol	1,442	33	1,475
Crizotinib	5,627	0	5,627
Dasatinib	115,493	508,951	624,444
Dexrazoxane	6,750	0	6,750
Eribulin	72,561	0	72,561
Fulvestrant	180,954	0	180,954
Histamine dihydrochloride	317	0	317
Inositol nicotinate	641	0	641
Ofatumumab	7,980	0	7,980
Olanzapine depot injection	27,170	0	27,170
Panitumumab	1,821	0	1,821
Paricalcitol	7,520	0	7,520
Pentoxifylline	5,081	791	5,872
Ruxolitinib	274,860	0	274,860
Sorafenib	73,990	0	73,990
Total	1,625,736	510,266	2,136,002

The majority of spend is for bevacizumab (39%) and dasatinib (29%), and the majority of the dasatinib spend was on WP10HP.

Bevacizumab has been the subject of eight NICE TAs, all of which do not recommend the use of the medicine for the indications appraised. Despite that, spend on bevacizumab for the financial year 2013–2014 has increased by 34% compared to the financial year 2011–2012.

Dasatinib has been subject to three AWMSG appraisals; two of the appraisals did not recommend dasatinib for use for the indications appraised, whilst one recommended it for restricted use in specific circumstances (ratified January 2008). This appraisal, along with one of the other two appraisals, has since been superseded by a NICE TA; both TAs did not recommend dasatinib for use for the indications appraised. Therefore spend on this medicine may be as a result of the previous positive AWMSG recommendation. Spend on dasatinib for the financial year 2013–2014 has reduced by 32% compared to the financial year 2011–2012.

The funding for these medicines for the indications with negative recommendations from NICE or AWMSG may have been via Individual Patient Funding Requests (IPFRs).

Table 5. Breakdown of secondary care and WP10HP spend (£) by health board for the financial year 2013–2014 on medicines with negative recommendations.

Medicine	ABMU	Aneurin Bevan	BCU	Cardiff and Vale	Cwm Taf	Hywel Dda	Powys	Velindre
Aliskiren	26	0	53	60	0	126	0	0
Amantadine hydrochloride	179	622	512	200	47	108	15	0
Bevacizumab	494,664	4,787	137,906	22,950	30,337	65,785	0	67,902
Cabazitaxel	0	0	0	0	0	0	0	17,741
Cilostazol	644	0	247	0	103	481	0	0
Crizotinib	0	0	0	0	0	0	0	5,627
Dasatinib	138,030	223,025	137,640	109,316	0	16,433	0	0
Dexrazoxane	6,750	0	0	0	0	0	0	0
Eribulin	0	5,415	15,162	0	12,996	1,733	0	37,255
Fulvestrant	38,240	6,896	44,509	0	8,777	37,396	0	45,136
Histamine dihydrochloride	317	0	0	0	0	0	0	0
Inositol nicotinate	156	0	406	0	0	79	0	0
Ofatumumab	1,200	0	0	4,200	0	2,580	0	0
Olanzapine depot injection	1,870	0	267	5,529	5,611	13,893	0	0
Panitumumab	0	0	0	0	0	0	0	1,821
Paricalcitol	0	0	7,520	0	0	0	0	0
Pentoxifylline	1,817	308	1,148	1,209	1,053	337	0	0
Ruxolitinib	0	0	116,748	0	0	158,112	0	0
Sorafenib	0	0	46,495	27,495	0	0	0	0
Total	683,893	241,053	508,613	170,959	58,924	297,063	15	175,482

Table 6 lists primary care usage of medicines with a negative recommendation from NICE/AWMSG broken down by health board and also includes total spend on these medicines in primary care weighted by population. The table shows that spend varies across the health boards from £46 to £114 per 1,000 patient population.

Table 6. Breakdown of primary care spend (£) by health board for the financial year 2013–2014 of medicines with a negative recommendation from NICE/AWMSG

Medicine	ABMU	Aneurin Bevan	BCU	Cardiff and Vale	Cwm Taf	Hywel Dda	Powys	Wales
Aliskiren	9,885	11,288	6,623	11,325	7,479	11,967	2,476	61,043
Amantadine hydrochloride	8,291	5,861	13,080	2,976	2,792	6,602	3,315	42,917
Cilostazol	10,464	9,164	22,303	968	7,024	17,107	435	67,465
Fulvestrant	3,657	0	1,045	0	0	0	0	4,702
Inositol nicotinate	2,891	7,389	4,547	4,020	1,611	1,549	1,001	23,008
Paricalcitol	0	0	69	0	0	0	0	69
Pentoxifylline	8,694	8,253	9,043	4,074	9,433	7,315	925	47,737
Racecadotril granules for suspension	0	4	11	0	8	8	0	31
Total (£)	43,882	41,959	56,721	23,363	28,347	44,548	8,152	246,972
Population (March 2014)	544,401	598,453	706,232	506,071	303,824	391,319	138,331	3,188,631
Spend (£) per 1,000 population	81	70	80	46	93	114	59	77

ABMU: Abertawe Bro Morgannwg University
 BCU: Betsi Cadwaladr University

It should be noted that although these medicines are not recommended for use by AWMSG or NICE, discontinuing them will not necessarily realise significant savings, as alternative medicines may be need to be considered in certain situations.

6.0 MEDICINES WITH AN AWMSG STATEMENT OF ADVICE

As of March 2014 there were 140 active Statements of Advice, issued by AWMSG, not endorsing the use of 121 medicines for one or more specific indications, due to company non-submission for appraisal:

- There are 56 medicines with one or more Statements of Advice that have not been prescribed within NHS Wales during 2013–2014. The All Wales Therapeutics and Toxicology Centre (AWTTC) appraisal database reports that many of these non-submissions are due to the fact that the company has no plans to launch the product in the UK.
- There are 29 medicines with a Statement of Advice for a specific indication/sub-group of the population that also have a positive recommendation from NICE/AWMSG for a different indication. There is also one medicine with a Statement of Advice for a specific indication that also has a negative recommendation from AWMSG for a different indication. These medicines are monitored in the recommendation and negative recommendation sections of the report.
- There are 35 medicines with a Statement of Advice for a particular indication/sub-group of the population, e.g. children, that have been used within NHS Wales. Of these, nine are licensed for other indications that have not been through the NICE/AWMSG appraisal process as they do not meet the criteria for appraisal. It is not possible to establish whether usage is attached to the indication covered by the Statement of Advice, so more detailed analysis excludes these medicines. Table 7 lists those excluded medicines and the reason for exclusion.

Table 7. Medicines with an AWMSG Statement of Advice for a specific indication, with established use for other indications

Medicine	Comments
Caspofungin (Cancidas [®])	Statement of Advice is for paediatric use – established use in adults
Exenatide (Byetta [®])	Established use for indications not covered by Statement of Advice
Human normal immunoglobulin (Aragam [®] , Kiovig [®] , HyQvia [®] , Privilgen [®])	Established use for indications not covered by Statement of Advice
Latanoprost (Xalatan [®])	Statement of Advice is for paediatric use – established use in adults
Losartan potassium/hydrochlorothiazide (Cozaar-Comp [®])	Established use for indications not covered by Statement of Advice
Quetiapine (Seroquel [®])	Established use for indications not covered by Statement of Advice
Tadalafil 5 mg (Cialis [®])	Established use for indications not covered by Statement of Advice
Telmisartan (Micardis [®])	Established use for indications not covered by Statement of Advice
Zonisamide (Zonegran [®])	Included as an option in NICE CG137

Spend on the remaining 26 medicines, which can be monitored as non-submissions across Wales, was £1,393,313 for the financial year 2013–2014. Twenty-two of these medicines have been prescribed in primary care. Table 8 shows the primary care spend for the financial year 2013–2014 broken down by health board and weighted by population.

Table 8. Primary care spend (£) broken down by health board on medicines with an AWMSG Statement of Advice for the financial year 2013–2014

Medicine	ABMU	Aneurin Bevan	BCU	Cardiff and Vale	Cwm Taf	Hywel Dda	Powys	Wales
Amifampridine	0	0	5,082	0	0	0	0	5,082
Artemether/ lumefantrine	0	0	0	23	0	13	0	36
Azilsartan medoxomil	0	0	0	657	218	0	0	875
Azithromycin eye drops	131	23	203	210	7	119	42	735
Bilastine	0	28	0	0	0	0	0	28
Bimatoprost/timolol eye drops single use container	1,803	140	770	315	0	123	0	3,151
Bosentan	4,588	1,510	0	3,020	0	0	0	9,118
Ciprofloxacin ear drops	519	80	859	264	0	123	105	1,950
Colesevelam	14,980	6,021	15,879	18,313	3,423	20,632	8,052	87,300
Dapoxetine	396	666	127	328	15	41	0	1,573
Ethinylestradiol/ drospirenone	116	165	88	182	50	73	0	674
Hydroxycarbamide	0	6,000	500	1,133	0	3	0	7,636
Mercaptamine bitartrate	0	13,004	0	1,270	5,320	8,360	0	27,954
Paliperidone MR tablets	0	1,994	1,362	778	5,253	24	1,362	10,773
Racecadotril capsules	0	18	34	0	9	0	0	61
Sevelamer carbonate powder for oral solution	1,132	234	849	0	495	605	0	3,315
Sodium oxybate	0	0	0	10,800	0	0	0	10,800
Tadalafil (Adcirca [®])	0	0	0	491	0	0	0	491*
Tapentadol film coated tablets	4,181	2,414	2,755	6,871	442	5,170	386	22,219
Tocofersolan	0	0	3,064	0	0	218	0	3,282
Triptorelin powder for suspension for injection 22.5 mg	2,898	828	11,178	0	0	0	0	14,904
Vildagliptin/ metformin hydrochloride	14,109	34,822	2,077	32,949	4,223	23,555	476	112,211
Total (£)	44,853	67,947	44,827	77,604	19,455	59,059	10,423	324,168
Population (March 2014)	544,401	598,453	706,232	506,071	303,824	391,319	138,331	3,188,631
Spend (£) per 1,000 population	82	114	63	153	64	151	75	102

*May be an underestimate of usage as only branded product data were collected, generic prescriptions for tadalafil 20 mg would have selected Cialis[®] brand (licensed for erectile dysfunction).

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Seventeen of these medicines with a Statement of Advice have been used in secondary care. Spend on these medicines in secondary care and via WP10HP was £639,702 (secondary care spend £598,335 and WP10HP spend £41,367). Table 9 shows secondary care and WP10HP spend for the financial year 2013–2014 broken down by health board. Variation in use may reflect the configuration of particular specialties rather than different prescribing behaviours and interpretation of guidance.

Table 9. Secondary care and WP10HP spend (£) by health board on specific medicines with an AWMSG Statement of Advice for the financial year 2013–2014

Medicine	ABMU	Aneurin Bevan	BCU	Cardiff and Vale	Cwm Taf	Hywel Dda	Powys	Velindre
Aripiprazole solution for injection	0	130	0	0	20	440	0	0
Artemether/lumefantrine	0	57	0	216	0	25	0	0
Azithromycin eye drops	14	0	0	0	0	230	0	0
Bimatoprost/timolol eye drops single use container	123	158	140	0	0	140	0	0
Bosentan	14,498	9,061	27,225	14,498	0	0	0	0
Brentuximab vedotin	44,700	0	60,000	105,000	72,000	63,000	0	66,018
Cefuroxime sodium solution for intracameral injection	0	0	13,961	0	0	0	0	0
Ciprofloxacin ear drops	368	226	767	98	1,229	436	156	0
Colesevelam	625	400	2,983	2,637	472	4,613	0	0
Dapoxetine	0	104	0	0	0	0	0	0
Hydroxycarbamide	8,785	1,171	9,529	14,828	2,052	1,324	0	143
Mitotane	425	0	0	772	0	0	0	20,823
Paliperidone modified release tablets	109	0	206	49	755	0	0	0
Sodium oxybate	0	30,600	38,880	1,296	0	0	0	0
Tapentadol film coated tablets	76	303	45	1	12	82	0	0
Triptorelin powder for suspension for injection	437	0	0	0	0	0	0	0
Vildagliptin/metformin hydrochloride	0	38	0	80	0	113	0	0
Total	70,160	42,248	153,736	139,475	76,540	70,403	156	86,984

ABMU: Abertawe Bro Morgannwg University

BCU: Betsi Cadwaladr University

7.0 ANALYSIS OF MEDICINES WITHIN SPECIFIC THERAPEUTIC AREAS

Three areas have been identified for further analysis: cytokine modulators, medicines used in the prevention and treatment of osteoporosis and medicines used in the management of diabetes. These areas have been chosen for particular scrutiny because of their high cost to NHS Wales and/or because of their current therapeutic interest.

7.1 Analysis of the use of cytokine modulators

There are 10 cytokine modulators currently licensed for use in Wales. Their licensed indications include ulcerative colitis, Crohn's disease, rheumatoid arthritis and psoriasis; individual medicines have one or more specific indications. There are 11 NICE TAs and 11 AWMSG appraisals relating to this group of medicines.

Eight of the cytokine modulators have been recommended by at least one NICE/AWMSG appraisal; AWMSG has issued Statements of Advice for specific indications/sub-groups of patients for etanercept, golimumab and infliximab and NICE/AWMSG have issued negative recommendations for specific indications for etanercept and infliximab. Anakinra is not recommended for the routine treatment of rheumatoid arthritis according to NICE Clinical Guideline 79, and belimumab is awaiting a NICE TA. Anakinra and belimumab are excluded from the detailed analysis. Analysis of secondary care prescribing data identified that NHS Wales spent £84,472 on anakinra and there was no spend on belimumab.

Spend on cytokine modulators has increased steadily over the last 5 years as shown in Figure 1, and in the financial year 2013–2014 the eight cytokine modulators recommended for use in NHS Wales made up 21% of spend on all NICE/AWMSG positively appraised medicines in NHS Wales.

Figure 1. Trend in cytokine modulator spend

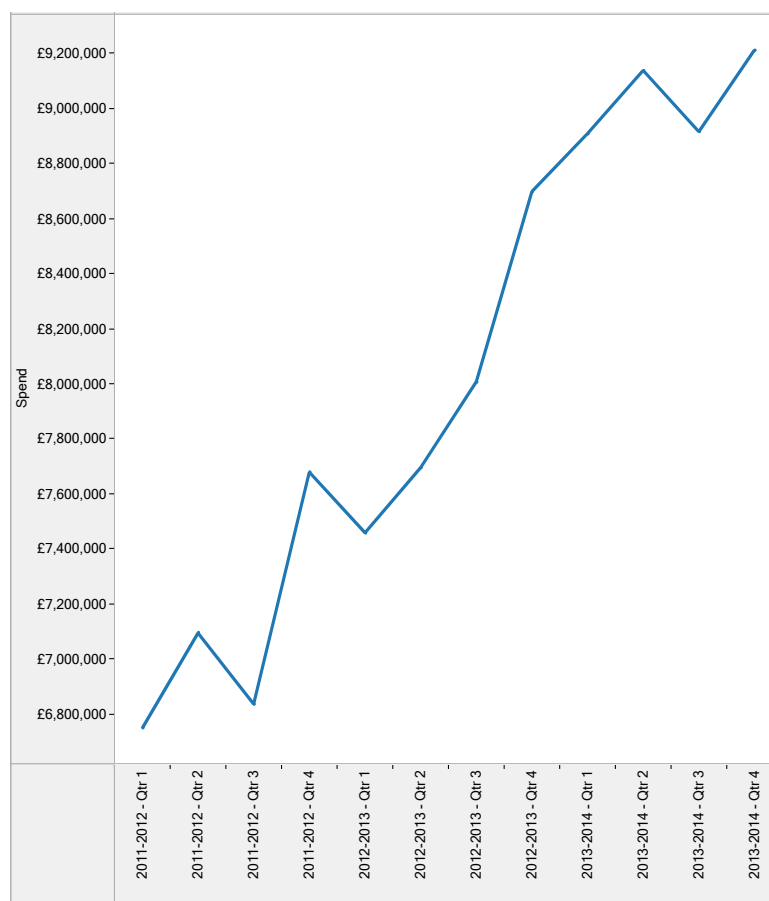


Table 10 shows spend for NHS Wales on the NICE/AWMSG recommended cytokine modulators for the financial year 2013–2014. Adalimumab, etanercept, infliximab and rituximab made up 91% of spend. The majority of adalimumab and etanercept is supplied through homecare providers i.e. specialist hospital prescribing with medicine delivery directly to the patient’s home through a homecare company. The true cost to NHS Wales is likely to be higher than that specified in the table due to factors such as prescribing in England and lack of homecare data captured via Medusa.

Table 10. Spend (£) on cytokine modulators for the financial year 2013–2014

Medicine	Primary care	Secondary care	Homecare	WP10HP	Total
Abatacept	0	243,057	264,672	0	507,729
Adalimumab	704	150,887	7,741,840	0	7,893,431
Certolizumab pegol	2,145	0	1,054,268	0	1,056,413
Etanercept	2,234	169,330	8,382,239	358	8,554,161
Golimumab	0	0	447,755	0	447,755
Infliximab	0	7,749,418	27,015	0	7,776,433
Rituximab	0	8,513,593	0	0	8,513,593
Tocilizumab	0	1,424,627	0	0	1,424,627
Total	5,083	18,250,912	17,917,789	358	36,174,142

7.2 Analysis of medicines used for the prevention and treatment of osteoporosis

TAs 160 and 161 discuss the primary and secondary prevention of osteoporosis. TA160 recommends alendronic acid, risedronate, and strontium ranelate for primary prevention, whilst TA161 recommends alendronic acid, risedronate, raloxifene, strontium ranelate and teriparatide for secondary prevention in specific circumstances. There are AWMSG Statements of Advice for strontium ranelate and teriparatide for specific indications. Teriparatide is not recommended for the treatment of osteoporosis in post-menopausal women and men at increased risk of fracture. TA204 recommends the use of denosumab in osteoporotic fractures.

Other medicines used in the treatment of osteoporosis include ibandronic acid and zoledronic acid, neither of which are covered by NICE or AWMSG guidance. Analysis of Medusa and CASPA data identified that NHS Wales spent £191,431 on ibandronic acid (150 mg tablets and 3 mg/3 ml pre-filled syringe) and £253 on zoledronic acid (5 mg infusion) in the financial year 2013–2014. Table 11 shows the spend in NHS Wales on the NICE/AWMSG recommended medicines used in the prevention and treatment of osteoporosis for the financial year 2013–2014. The majority of denosumab and teriparatide use was in secondary care, whilst that of alendronic acid, raloxifene, risedronate and strontium was in primary care.

Table 11. Spend (£) on medicines used in the prevention and treatment of osteoporosis for the financial year 2013–2014

Medicine	Primary care	Secondary care	WP10HP	Total
Alendronic acid tablets	567,939	6,839	3,598	578,376
Denosumab	75,935	474,775	1,732	552,442
Raloxifene hydrochloride	87,217	972	41	88,230
Risedronate sodium	110,999	1,725	330	113,054
Strontium ranelate	367,056	7,247	1,141	375,444
Teriparatide	1,903	553,496	0	555,399
Total	1,211,049	1,045,054	6,842	2,262,945

Table 12 shows that alendronic acid, raloxifene hydrochloride, risedronate sodium and strontium ranelate spend has reduced over the last three years. The large cost reduction for risedronate sodium is most likely due to its patent loss in December 2010. Strontium ranelate has been subject to safety concerns, with recommendations to review its use in certain patients.

Table 12. Spend in NHS Wales on NICE/AWMSG recommended medicines used in the prevention and treatment of osteoporosis

Medicine	Spend (£) 2011–2012	Spend (£) 2012–2013	Spend (£) 2013–2014	Total (£)
Alendronic acid tablets	717,085	584,114	578,376	1,879,575
Denosumab	281,015	384,120	552,442	1,217,577
Raloxifene hydrochloride	132,258	107,796	88,230	328,284
Risedronate sodium	426,960	140,988	113,054	681,002
Strontium ranelate	577,927	537,648	375,444	1,491,019
Teriparatide	519,726	547,349	555,399	1,622,474
Total	2,654,971	2,302,015	2,262,945	7,219,931

Figure 2 shows the primary care prescribing of medicines used in the prevention and treatment of osteoporosis. The graph shows a reduction in prescribing of all medicines, whilst Table 13 shows the percentage reduction in prescribed items in primary care for the financial year 2013–2014, compared to the financial year 2011–2012.

Figure 2. Primary care prescribing trend of medicines used in the prevention and treatment of osteoporosis

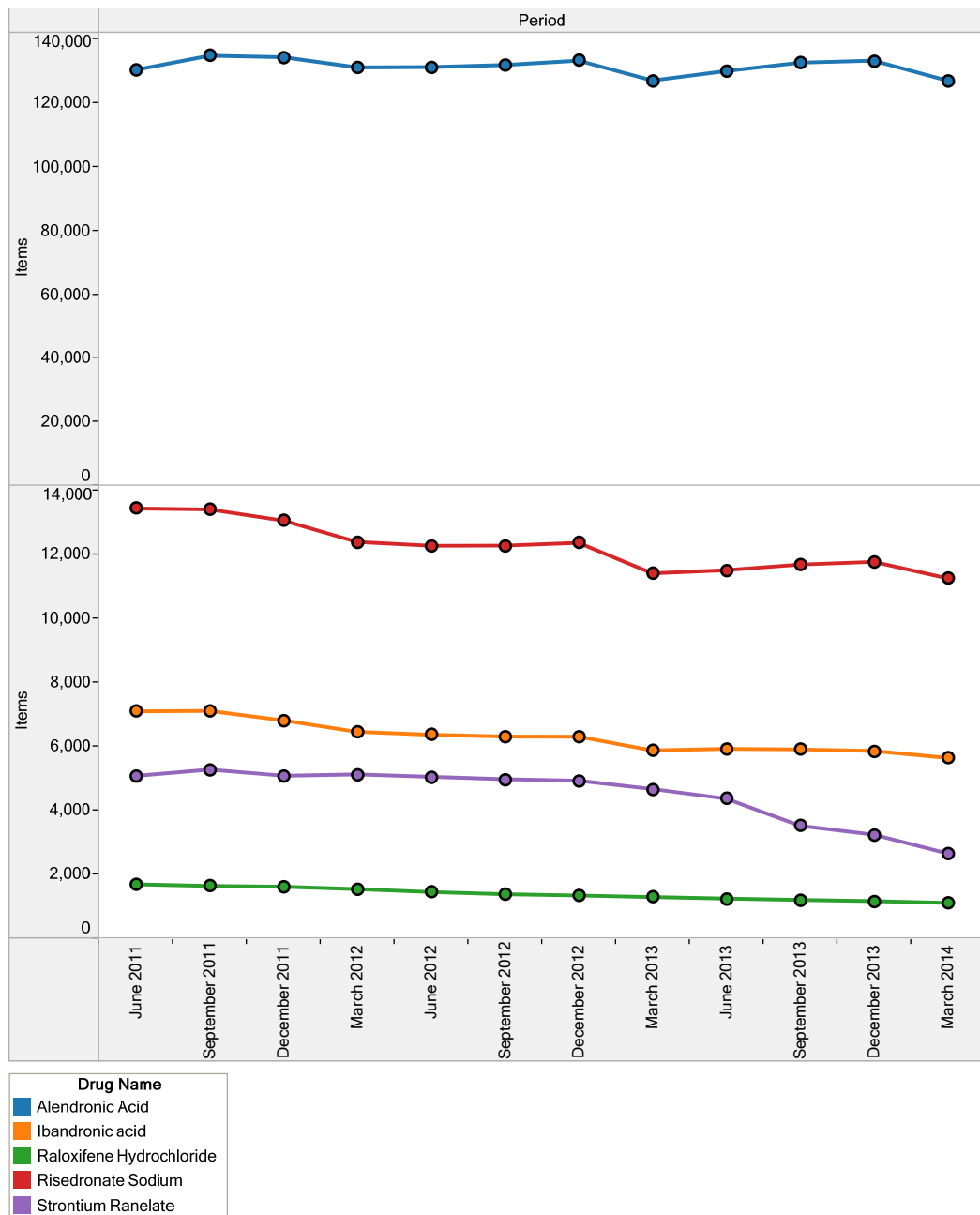


Table 13. Percentage change in primary care prescribing

Medicine	Items 2011–2012	Items 2012–2013	Items 2013–2014	Percentage reduction
Alendronic acid	530,489	523,235	522,720	1.5%
Ibandronic acid	27,432	24,809	23,281	15.1%
Raloxifene hydrochloride	6,421	5,397	4,655	27.5%
Risedronate sodium	52,272	48,294	46,191	11.6%
Strontium ranelate	20,515	19,570	13,728	33.1%

7.3 Analysis of medicines used in the management of diabetes

Four of the medicines that feature in the highest spend NICE/AWMSG recommended medicines are used in the management of diabetes. Table 14 shows the medicines used in the management of diabetes that have been subject to NICE/AWMSG appraisal or an AWMSG Statement of Advice. In all cases the appraised medicine was recommended for the indication appraised; however four Statements of Advice have also been issued by AWMSG, not recommending the medicine due to non-submission. The table also shows the spend for each of these medicines in NHS Wales for the financial year 2013–2014.

Table 14. Medicines used in the management of diabetes appraised by NICE/AWMSG or subject to an AWMSG Statement of Advice

Medicine	Spend (£) 2013–2014	NICE/AWMSG appraisal NICE publication/ministerial ratification date	Appraisal recommendation
Dapagliflozin	213,450	TA288 (June 2013)	Recommended
Exenatide	1,165,626	AWMSG reference no. 1385 (23/07/2012)	Non-submission
Exenatide modified release for injection	614,713	TA248 (February 2012)	Recommended
Insulin detemir	1,929,442	AWMSG reference no. 1427 (11/12/2012)	Recommended
Insulin glargine	6,448,050	TA53 (December 2002)	Recommended
Linagliptin	584,104	AWMSG reference no. 1667 (22/05/2013)	Recommended
Linagliptin/metformin	13,757	AWMSG reference no. 1681 (29/07/2013)	Recommended
Liraglutide	4,834,489	TA203 (October 2010)	Recommended
Lixisenatide	13,182	AWMSG reference no. 863 (06/12/2013)	Recommended
Saxagliptin	1,584,515	AWMSG reference no. 1005 (09/01/2012) AWMSG reference no. 1237 (07/08/2012) AWMSG reference no. 2229 (06/12/2013) AWMSG reference no. 1975 (06/12/2013)	Recommended Recommended Non-submission Recommended
Sitagliptin	5,050,434	AWMSG reference no. 1655 (25/10/2012)	Recommended
Vildagliptin	143,549	AWMSG reference no. 1393 (25/10/2012) AWMSG reference no. 1531 (18/03/2013) AWMSG reference no. 1529 (18/03/2013)	Recommended Recommended Non-submission
Vildagliptin/metformin hydrochloride	112,441	AWMSG reference no. 1930 (18/03/2013)	Non-submission
Total	22,707,752		

Table 15 shows the breakdown of spend on these medicines by sector: primary care, secondary care and WP10HP.

Table 15. Breakdown of spend (£) on medicines used in the management of diabetes by sector for the financial year 2013–2014

Medicine	Primary care	Secondary care	WP10HP	Total
Dapagliflozin	204,052	6,689	2,709	213,450
Exenatide	1,116,065	46,695	2,866	1,165,626
Exenatide modified release for injection	570,427	41,278	3,008	614,713
Insulin detemir	1,892,657	34,508	2,277	1,929,442
Insulin glargine	6,267,896	172,074	8,080	6,448,050
Linagliptin	559,608	23,191	1,305	584,104
Linagliptin/metformin	13,757	0	0	13,757
Liraglutide	4,611,132	203,227	20,130	4,834,489
Lixisenatide	0	13,182	0	13,182
Saxagliptin	1,551,873	29,704	2,938	1,584,515
Sitagliptin	5,030,751	16,408	3,275	5,050,434
Vildagliptin	141,534	2,000	15	143,549
Vildagliptin/metformin hydrochloride	112,211	230	0	112,441
Total	22,071,963	589,186	46,603	22,707,752

The majority of the spend is in primary care, although much of the initiation, particularly of insulin and the more specialist medicines will be undertaken in secondary care.

A more detailed analysis of primary care prescribing of medicines used in the management of diabetes has been undertaken. Total primary care spend for medicines used in the management of diabetes (excluding products used to treat hypoglycaemia and diagnostic and monitoring products) for the financial year 2013–2014 was £41,649,943. Therefore medicines subject to NICE/AWMSG appraisal or AWMSG Statement of Advice made up 53% of primary care spend. It should be noted however that in the case of exenatide (Byetta[®]), the AWMSG Statement of Advice only relates to one indication and the spend would probably be against another established indication.

Table 16 shows primary care spend for the financial year 2013–2014 on the medicines used in diabetes that have been subject to NICE/AWMSG appraisal or AWMSG Statement of Advice broken down by health board, weighted by population and also by diabetic prevalence (as per Quality Outcomes Framework [QOF] data March 2011).

Table 16. Primary care spend (£) for the financial year 2013–2014 on selected medicines used in the management of diabetes weighted by health board population

Medicine	ABMU	Aneurin Bevan	BCU	Cardiff and Vale	Cwm Taf	Hywel Dda	Powys
Dapagliflozin	30,511	26,132	18,095	54,425	7,002	65,280	2,607
Exenatide	159,682	290,975	197,350	156,815	205,266	82,639	23,338
Exenatide modified release for injection	97,608	67,578	99,403	71,783	13,278	196,403	24,374
Insulin detemir	305,789	446,128	365,583	200,340	227,784	257,939	89,094
Insulin glargine	861,675	1,258,163	1,372,556	1,211,039	431,413	840,646	292,404
Linagliptin	212,266	80,415	71,542	51,885	48,136	82,655	12,709
Linagliptin/metformin	7,695	1,696	399	2,562	133	1,239	33
Liraglutide	798,142	1,192,347	583,538	880,035	329,067	620,031	207,972
Saxagliptin	152,551	439,641	166,319	415,348	157,033	209,289	11,692
Sitagliptin	992,359	1,041,742	798,895	769,059	470,293	744,099	214,304
Vildagliptin	18,074	32,888	12,676	21,970	10,012	39,625	6,289
Vildagliptin/metformin hydrochloride	14,109	34,822	2,077	32,949	4,223	23,555	476
Total (£)	3,650,461	4,912,527	3,688,433	3,868,210	1,903,640	3,163,400	885,292
Population (March 2014)	544,401	598,453	706,232	506,071	303,824	391,319	138,331
Spend (£) per 1,000 population	6,705	8,209	5,223	7,644	6,266	8,084	6,400
QOF diabetic population (March 2013)	31,659	36,323	36,748	22,161	16,869	21,950	7,589
Spend (£) per diabetic patient	115	135	100	175	113	144	117

The table shows there is large variation in spend per 1,000 population (£5,223 to £8,209). When analysis is undertaken with weighting for the number of diabetic patients (as per QOF data March 2011), there is also a large variation (£100 to £175 per diabetic patient). The paper focuses on specific diabetes medicines which have undergone managed entry via the NICE/AWMSG appraisal process. These newer medicines used in the management of diabetes require further analysis in the context of all diabetic treatments in relation to patients' monitoring parameters and patient outcome data.

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2. NHS Wales Shared Services Partnership. Medusa prescribing system. 2013. Accessed September 2014

APPENDIX 1. USAGE OF NICE/AWMSG APPRAISED MEDICINES

Medicine	AWMSG/NICE Recommendation	2011–2012	2012–2013	2013–2014	Total
5-aminolaevulinic acid	Recommended			4,813	4,813
Abacavir/lamivudine	Recommended	266,952	405,283	451,212	1,123,447
Abarelix	Non-submission				
Abatacept	Recommended	153,016	270,898	507,729	931,643
Abciximab	Recommended	172,203	113,040	99,375	384,618
Abiraterone	Recommended	325,278	1,855,557	2,199,802	4,380,637
Aciclovir lauriad	Non-submission				
Acidinium bromide	Recommended		1,316	78,886	80,202
Adalimumab	Recommended*	5,998,503	6,781,519	7,893,431	20,673,453
Adefovir dipivoxil	Recommended	18,394	14,983	13,140	46,517
Aflibercept concentrate for infusion	Non-recommended				
Aflibercept solution for intravitreal injection	Recommended			166,165	166,165
Agalsidase alfa	Recommended	16,379	22,679	13,355	52,413
Agalsidase beta	Recommended			7,870	7,870
Alendronic acid effervescent tablets	Non-submission				
Alendronic acid tablets	Recommended	717,085	584,114	578,376	1,879,575
Alglucosidase alfa	Recommended	179,454	58,109	116,218	353,781
Alipogene tiparvec	Non-submission				
Aliskiren	Non-recommended	111,426	66,634	61,308	239,368
Alitretinoin	Recommended	261,264	301,395	314,833	877,492
Alogliptin/pioglitazone	Non-submission				
Alteplase	Recommended	304,279	410,845	573,474	1,288,598
Alteplase cathflo	Recommended		28,764	21,456	50,220
Amantadine hydrochloride	Non-recommended	47,537	50,365	44,599	142,501
Ambrisentan	Recommended		1,618		1,618
Amifampridine	Non-submission	70,839	54,960	5,082	130,881
Aminolevulinic acid	Recommended				
Amlodipine besilate orodispersible tablets	Non-submission				
Anagrelide hydrochloride	Recommended	576,566	647,612	746,402	1,970,580
Anastrozole	Recommended	1,144,473	249,325	181,867	1,575,665
Anidulafungin	Recommended	8,561	15,490	4,314	28,365
Apixaban	Recommended		21,614	100,257	121,871
Argatroban	Recommended	76,304	87,774	56,752	220,830
Aripiprazole oral	Recommended	3,914,184	4,376,366	4,919,622	13,210,172
Aripiprazole solution for injection	Non-submission	142	318	591	1,051
Artemether/lumefantrine	Non-submission	318	445	333	1,096
Atazanavir	Recommended	405,352	300,065	229,707	935,124
Atomoxetine hydrochloride	Recommended	605,179	585,498	645,000	1,835,677
Atorvastatin chewable tablets	Recommended	246	6,128	10,402	16,776
Avanafil	Non-submission				
Azacitidine	Recommended	630,080	812,080	969,518	2,411,678
Azilsartan medoxomil	Non-submission		526	876	1,402
Azithromycin eye drops	Non-submission	7	158	978	1,143
Aztreonam lysine	Recommended	12,319	5,646	86,807	104,772
Basiliximab	Recommended	134,158	109,931	100,714	344,803
Belatacept	Non-recommended				
Bendamustine	Recommended*	209,481	306,236	469,471	985,188
Bevacizumab	Non-recommended	616,883	683,867	824,331	2,125,081
Bilastine	Non-submission	15	45	28	88
Bimatoprost/timolol eye drops single use container	Non-submission			3,711	3,711
Bismuth/metronidazole/tetracycline	Non-submission				
Bivalirudin	Recommended	253,406	343,430	399,844	996,680
Boceprevir	Recommended		293,044	629,225	922,269
Bortezomib	Recommended	1,525,688	1,905,353	2,348,710	5,779,751
Bosentan	Non-submission	66,137	72,102	74,400	212,639
Bosutinib	Non-recommended				
Botulinum toxin type A	Recommended*	873,568	906,484	932,778	2,712,830
Brentuximab vedotin	Non-submission	2	243,489	410,718	654,209
Bupivacaine hydrochloride/fentanyl	Recommended	13,330	10,464	7,928	31,722

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Medicine	AWMSG/NICE Recommendation	2011–2012	2012–2013	2013–2014	Total
Buprenorphine hydrochloride	Recommended	1,620,437	1,433,065	950,756	4,004,258
Buprenorphine/naloxone	Recommended	184,989	241,435	425,410	851,834
C1-esterase inhibitor	Recommended*	7,824	10,345	19,604	37,773
Cabazitaxel	Non-recommended			17,741	17,741
Canakinumab	Non-submission				
Capecitabine	Recommended	1,667,915	1,691,285	1,325,627	4,684,827
Capsaicin cutaneous patch	Recommended	756	11,844	26,208	38,808
Carglumic acid	Non-submission	479			479
Carmustine	Recommended	14,019			14,019
Caspofungin	Non-submission	900,264	1,095,795	1,020,340	3,016,399
Catridecacog	Non-submission				
Catumaxomab	Non-submission				
Ceftaroline fosamil	Recommended				
Cefuroxime sodium solution for intracameral injection	Non-submission	15,991	15,521	13,961	45,473
Certolizumab pegol	Recommended	336,801	616,688	1,056,413	2,009,902
Cetuximab	Recommended*	851,274	692,777	778,792	2,322,843
Cholic acid	Non-submission				
Cilostazol	Non-recommended	106,875	86,564	68,942	262,381
Cinacalcet hydrochloride	Recommended*	498,234	672,743	774,197	1,945,174
Ciprofloxacin ear drops	Non-submission	1,182	1,647	5,230	8,059
Ciprofloxacin/dexamethasone ear drops	Non-submission				
Clevidipine	Non-submission				
Clofarabine	Recommended		576		576
Clopidogrel	Recommended*	777,936	877,628	909,653	2,565,217
Cobicistat	Non-submission				
Co-careldopa intestinal gel	Non-recommended				
Colecalciferol	Recommended	9,707	150,699	403,302	563,708
Colesevelam	Non-submission	67,724	76,813	99,031	243,568
Colistimethate sodium inhalation powder	Recommended				
Collagenase clostridium histolyticum	Recommended	3,900	171,600	170,040	345,540
Conestat alfa	Non-submission				
Crizotinib	Non-recommended			5,627	5,627
Dabigatran	Recommended	77,554	266,154	616,050	959,758
Dabrafenib	Non-submission				
Daclizumab	Recommended				
Dapagliflozin	Recommended		3,896	213,450	217,346
Dapoxetine	Non-submission			1,677	1,677
Darbepoetin alfa	Recommended	1,146,891	954,490	891,509	2,992,890
Darunavir	Recommended	595,465	636,360	739,280	1,971,105
Dasatinib	Non-recommended	920,058	722,964	624,444	2,267,466
Decitabine	Non-submission				
Deferasirox	Recommended*	355,408	364,875	453,123	1,173,406
Degarelix	Recommended	5,828	6,276	32,351	44,455
Denosumab	Recommended	281,015	384,120	552,442	1,217,577
Dexamethasone intravitreal implant	Recommended*	43,848	181,674	426,996	652,518
Dexamfetamine sulphate	Recommended*	197,991	242,868	249,861	690,720
Dexmedetomidine	Recommended	601	45,157	105,085	150,843
Dexrazoxane	Non-recommended			6,750	6,750
Dextromethorphan/quinidine	Non-submission				
Dihydroartemisinin/piperaquine phosphate	Recommended				
Dipyridamole modified release	Recommended	1,334,564	1,139,216	839,592	3,313,372
Docetaxel	Recommended	545,930	314,262	155,968	1,016,160
Donepezil hydrochloride	Recommended	4,341,927	1,290,172	257,690	5,889,789
Doxorubicin	Recommended*	329,669	81,000	516,703	927,372
Doxycycline periodontal gel	Non-submission				
Dronedarone	Recommended	147,296	114,519	138,821	400,636
Eculizumab	Recommended*		7,560	15,120	22,680
Efalizumab	Recommended		677	203	880
Efavirenz/emtricitabine/tenofovir disoproxil	Recommended	2,122,211	1,673,532	1,643,669	5,439,412
Eltrombopag	Recommended	15,698	61,908	128,331	205,937
Elvitegravir/cobicistat/emtricitabine/tenofovir	Recommended			3,468	3,468

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Medicine	AWMSG/NICE Recommendation	2011–2012	2012–2013	2013–2014	Total
Emtricitabine	Recommended	17,692	21,169	26,761	65,622
Emtricitabine/rilpivirine/tenofovir disoproxil	Recommended	636	113,509	300,482	414,627
Emtricitabine/tenofovir disoproxil	Recommended	1,425,887	1,004,979	1,072,386	3,503,252
Enfuvirtide	Recommended	179	86	108	373
Enoxaparin	Recommended	4,195,399	4,224,806	3,920,357	12,340,562
Entecavir	Recommended	21,866	33,409	59,884	115,159
Eplerenone	Recommended	527,267	679,093	900,943	2,107,303
Epoetin alfa	Recommended	1,223,741	1,123,180	1,047,198	3,394,119
Epoetin beta	Recommended	371,588	94,229	65,590	531,407
Epoetin theta	Recommended				
Epoetin zeta	Non-recommended*	136			136
Eptifibatide	Recommended	1,649	103	289	2,041
Eribulin	Non-recommended	5,634	58,004	72,561	136,199
Erlotinib	Recommended*	897,854	828,559	574,894	2,301,307
Esketamine hydrochloride	Non-submission				
Eslicarbazepine acetate	Recommended	143,594	157,572	286,545	587,711
Esomeprazole powder for solution for injection	Recommended			37	37
Etanercept	Recommended*	6,798,226	7,683,173	8,554,161	23,035,560
Ethinylestradiol/drospirenone	Non-submission		156	672	828
Etravirine	Recommended	90,966	71,544	80,828	243,338
Everolimus	Recommended*	161,875	124,882	73,564	360,321
Exemestane	Recommended	735,439	143,392	68,869	947,700
Exenatide	Non-submission	1,578,925	1,375,133	1,165,626	4,119,684
Exenatide modified release for injection	Recommended	20,387	363,051	614,713	998,151
Ezetimibe	Recommended	4,661,866	3,755,905	3,282,540	11,700,311
Febuxostat	Recommended	59,173	94,655	135,774	289,602
Fentanyl citrate buccal film	Non-submission				
Fentanyl nasal spray	Recommended	8,733	16,178	10,071	34,982
Ferric carboxymaltose	Recommended	222,705	362,664	384,170	969,539
Ferumoxylol	Recommended				
Fidaxomicin	Recommended		4,860	95,580	100,440
Filgrastim (all brands)	Recommended*	131,508	132,067	136,246	399,821
Fingolimod	Recommended		58,477	267,590	326,067
Fludarabine phosphate	Recommended*	181,557	114,144	158,509	454,210
Fluocinolone acetonide	Non-recommended				
Fluorouracil/salicylic acid	Recommended	4,983	13,928	25,781	44,692
Follitropin alfa	Non-submission				
Fondaparinux sodium	Recommended*	144,582	139,107	123,020	406,709
Fulvestrant	Non-recommended	327,029	187,440	185,656	700,125
Galantamine	Recommended	964,153	835,792	758,834	2,558,779
Galsulfase	Non-submission				
Gefitinib	Recommended	212,102	362,467	165,912	740,481
Gemcitabine	Recommended	159,721	151,848	157,267	468,836
Glycopyrronium inhalation powder	Recommended		1,925	65,312	67,237
Golimumab	Recommended*	25,068	233,240	447,755	706,063
Histamine dihydrochloride	Non-recommended			317	317
Human normal immunoglobulin (specific brands)	Non-submission	1,742,441	1,703,534	1,610,815	5,056,790
Hydrocortisone modified release	Non-submission				
Hydromorphone hydrochloride	Non-submission				
Hydroxycarbamide	Non-submission	29,400	39,703	45,469	114,572
Ibritumomab tiuxetan	Non-submission				
Icatibant acetate	Recommended	6,222		26,290	32,512
Idursulfase	Non-recommended				
Iloprost trometamol	Recommended				
Imatinib mesilate	Recommended*	4,222,739	4,114,566	4,226,042	12,563,347
Infliximab	Recommended*	6,427,905	7,053,927	7,776,433	21,258,265
Ingenol mebutate	Recommended			23,043	23,043
Inositol nicotinate	Non-recommended	36,110	28,335	23,649	88,094
Insulin degludec/insulin aspart	Non-submission				
Insulin detemir	Recommended	1,943,971	1,949,375	1,929,442	5,822,788
Insulin glargine	Recommended	6,367,541	6,341,431	6,448,050	19,157,022

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Medicine	AWMSG/NICE Recommendation	2011–2012	2012–2013	2013–2014	Total
Ipilimumab	Recommended		380,075	1,443,168	1,823,243
Ivabradine	Recommended*	499,620	656,689	866,628	2,022,937
Lapatinib	Recommended*	129,057	143,285	117,144	389,486
Laronidase	Recommended		128,074		128,074
Latanoprost	Non-submission	2,969,129	1,547,901	736,725	5,253,755
Lenalidomide	Recommended	2,825,191	3,472,596	3,628,184	9,925,971
Letrozole	Recommended	3,109,887	410,912	316,015	3,836,814
Levonorgestrel intrauterine device	Non-submission				
Linaclotide	Recommended			5,529	5,529
Linagliptin	Recommended	14,865	160,414	584,104	759,383
Linagliptin/metformin	Recommended		366	13,757	14,123
Liposomal cytarabine	Non-recommended	1,469	1,469		2,938
Liraglutide	Recommended	3,096,715	4,105,784	4,834,489	12,036,988
Lisdexamfetamine dimesylate	Recommended		225	43,085	43,310
Lixisenatide	Recommended		58	13,182	13,240
Lomitapide	Non-submission				
Losartan potassium/hydrochlorothiazide	Non-submission	68,991	65,811	57,409	192,211
Loxapine inhalation powder	Non-submission				
Mannitol inhalation powder	Recommended	1,478	1,144	18,654	21,276
Maraviroc	Recommended	42,275	33,017	49,451	124,743
Mecasermin	Recommended				
Memantine hydrochloride	Recommended	802,530	1,518,478	1,722,090	4,043,098
Mequitazine	Non-submission				
Mercaptamine bitartrate	Non-submission	19,964	27,802	27,954	75,720
Mercaptopurine oral suspension	Recommended	2,886	19,156	41,746	63,788
Methadone hydrochloride	Recommended	1,205,391	1,072,167	990,018	3,267,576
Methoxy polyethylene glycol-epoetin beta	Recommended	49,335		1,597	50,932
Methylphenidate hydrochloride	Recommended	2,290,584	2,410,480	2,561,213	7,262,277
Micafungin	Non-recommended		58,571		58,571
Midazolam oromucosal solution	Recommended	32,216	173,519	289,996	495,731
Mifamurtide	Recommended		103,740	21,945	125,685
Miglustat	Non-submission				
Mirabegron	Recommended		83	127,771	127,854
Mitotane	Non-submission	41,883	20,280	22,021	84,184
Mycophenolate mofetil	Recommended	1,525,820	1,195,559	1,009,860	3,731,239
Mycophenolic acid	Recommended*	294,114	388,986	405,826	1,088,926
Naftidrofuryl oxalate	Recommended	67,014	65,525	76,506	209,045
Nalmefene	Recommended			906	906
Naltrexone hydrochloride	Recommended	89,488	101,137	83,369	273,994
Natalizumab	Recommended*	284,755	531,707	725,460	1,541,922
Nelarabine	Recommended				
Nepafenac	Recommended	313	615	2,844	3,772
Nevirapine	Recommended		33,694	36,690	70,384
Nilotinib	Recommended	454,540	960,455	1,213,272	2,628,267
Nomegestrol acetate/oestradiol	Non-submission				
Ocriplasmin	Recommended			21,000	21,000
Ofatumumab	Non-recommended		36,180	7,980	44,160
Olanzapine depot injection	Non-recommended	3,987	19,053	27,170	50,210
Omaliuzumab	Recommended	840,896	1,116,540	1,112,810	3,070,246
Oseltamivir phosphate	Recommended	4,356	17,713	11,780	33,849
Oxaliplatin	Recommended	72,356	136,548	101,404	310,308
Oxycodone orodispersible tablets	Non-submission				
Paclitaxel albumin	Recommended*	12,140	62,018	76,853	151,011
Palifermin	Non-submission				
Paliperidone modified release	Non-submission	12,572	13,510	11,891	37,973
Paliperidone palmitate depot injection	Recommended	6,757	78,538	561,937	647,232
Panitumumab	Non-recommended	6,385	4,551	1,821	12,757
Parathyroid hormone	Recommended				
Paricalcitol	Non-recommended	20,234	16,807	7,590	44,631
Pasireotide	Non-submission				
Pazopanib	Recommended	616,935	1,011,562	1,372,507	3,001,004
Pegaptanib	Non-recommended				

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Medicine	AWMSG/NICE Recommendation	2011–2012	2012–2013	2013–2014	Total
Pegfilgrastim	Recommended	767,354	766,795	980,253	2,514,402
Peginterferon alfa	Recommended	631,216	842,513	844,987	2,318,716
Pegloticase	Non-recommended		8		8
Pegvisomant	Non-recommended				
Pemetrexed	Recommended*	1,437,451	1,079,570	1,481,135	3,998,156
Pentoxyfylline	Non-recommended	68,215	58,599	53,609	180,423
Perampanel	Recommended		15,625	101,080	116,705
Pharmalgen	Recommended	925	1,535	908	3,368
Phentolamine mesylate	Non-submission		17		17
Pimecrolimus	Recommended	66,793	63,619	57,196	187,608
Pirfenidone	Recommended			35,538	35,538
Pitavastatin	Non-submission				
Pixantrone	Recommended				
Plerixafor	Recommended	345,499	246,050	263,668	855,217
Pramipexole modified release	Recommended	754,549	806,533	829,895	2,390,977
Prasugrel	Recommended	164,463	277,330	338,203	779,996
Progesterone vaginal capsules	Non-submission				
Prucalopride	Recommended	109,147	228,139	297,074	634,360
Quetiapine	Non-submission	5,850,457	1,912,387	386,948	8,149,792
Quetiapine modified release	Recommended*	3,322,812	3,128,250	2,576,506	9,027,568
Rabbit anti-human thymocyte immunoglobulin	Non-submission				
Racecadotril capsules	Non-submission		30	60	90
Racecadotril granules for suspension	Non-recommended		62	31	93
Raloxifene hydrochloride	Recommended*	132,258	107,796	88,230	328,284
Raltegravir	Recommended	249,140	229,682	219,646	698,468
Ramipril oral solution	Recommended	14,821	32,471	56,954	104,246
Ranibizumab	Recommended	12,142,004	13,115,705	10,936,200	36,193,909
Ranolazine	Recommended	106,818	176,179	291,045	574,042
Regorafenib	Non-submission				
Retigabine	Recommended	3,708	22,728	19,200	45,636
Ribavirin	Recommended	347,380	245,775	331,456	924,611
Rifaximin	Recommended	46,294	107,576	165,501	319,371
Rilpivirine	Recommended		5,468	34,814	40,282
Riluzole	Recommended	406,323	387,093	91,871	885,287
Risedronate sodium	Recommended	426,960	140,988	113,054	681,002
Rituximab	Recommended	8,148,698	8,317,367	8,513,593	24,979,658
Rivaroxaban	Recommended*	205,906	217,931	658,165	1,082,002
Rivastigmine	Recommended	962,737	985,640	859,677	2,808,054
Roflumilast	Recommended	6,079	3,638	4,112	13,829
Romiplostim	Recommended	226,299	376,987	765,811	1,369,097
Ropinirole modified release	Recommended	460,719	477,817	476,944	1,415,480
Rosuvastatin	Non-recommended	5,308,253	4,032,727	3,443,123	12,784,103
Rufinamide oral suspension	Recommended		5,236	13,123	18,359
Rufinamide tablets	Recommended	82,255	103,948	120,643	306,846
Rupatadine oral solution	Non-submission				
Ruxolitinib	Non-recommended		77,237	274,860	352,097
Sapropterin	Non-submission				
Saxagliptin	Recommended*	642,231	1,152,997	1,584,515	3,379,743
Sevelamer carbonate powder	Non-submission	531	2,883	3,316	6,730
Sildenafil citrate 20 mg tablets	Recommended*	59,679	83,666	106,613	249,958
Sildenafil citrate solution for injection	Recommended			2,823	2,823
Sildenafil citrate suspension	Recommended			3,399	3,399
Silodosin	Non-submission				
Sipuleucel-T	Non-submission				
Sirolimus	Recommended	328,412	321,451	334,105	983,968
Sitagliptin	Recommended	3,533,970	4,390,306	5,050,434	12,974,710
Sodium oxybate	Non-submission	46,368	79,920	81,576	207,864
Sodium phenylbutyrate	Recommended				
Sodium valproate modified release (Episenta®)	Recommended	49,956	55,392	66,385	171,733
Somatropin	Recommended*	2,411,749	2,111,584	2,103,215	6,626,548
Sorafenib	Non-recommended	78,152	54,245	73,990	206,387

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Medicine	AWMSG/NICE Recommendation	2011–2012	2012–2013	2013–2014	Total
Stiripentol	Non-recommended**	34,303	32,654	34,526	101,483
Strontium ranelate	Recommended*	577,927	537,648	375,444	1,491,019
Sunitinib	Recommended	2,428,456	1,950,187	1,594,105	5,972,748
Tacrolimus capsules	Recommended	3,306,470	3,397,921	2,871,982	9,576,373
Tacrolimus modified release	Recommended	21,082	31,787	29,131	82,000
Tacrolimus ointment	Recommended	214,057	203,399	200,364	617,820
Tadalafil (Adcirca®)	Non-submission		35	491	526
Tadalafil 5 mg (Cialis®)	Non-submission	541,957	695,545	867,170	2,104,672
Tafamidis	Non-submission				
Tapentadol film coated tablets	Non-submission	4,371	14,049	22,737	41,157
Tapentadol modified release	Recommended	19,223	63,541	133,460	216,224
Tapentadol oral solution	Non-submission				
Tedisamil	Non-submission				
Teduglutide	Non-submission				
Tegafur uracil	Recommended	1,906	912	205	3,023
Tegafur/gimeracil/oteracil	Recommended				
Telaprevir	Recommended	32	1,063,801	899,992	1,963,825
Telavancin	Non-submission				
Telvivudine	Non-recommended				
Telmisartan	Non-submission	711,162	625,979	558,470	1,895,611
Temozolomide capsules	Recommended	212,235	128,323	149,045	489,603
Temozolomide powder for infusion	Non-submission				
Temsirolimus	Non-recommended				
Tenofovir disoproxil	Recommended	291,903	267,441	334,194	893,538
Teriflunomide	Recommended				
Teriparatide	Recommended*	519,726	547,349	555,399	1,622,474
Thalidomide	Recommended	613,425	584,142	614,947	1,812,514
Ticagrelor	Recommended	230	35,788	164,969	200,987
Tipranavir	Recommended	7			7
Tirofiban	Recommended	33,008	32,141	51,659	116,808
Tobramycin inhalation powder	Recommended				
Tocilizumab	Recommended	468,820	900,706	1,424,627	2,794,153
Tocofersolan	Non-submission	1,637	1,855	3,282	6,774
Topotecan	Recommended*	201,843	99,048	24,493	325,384
Trabectedin	Recommended	166,102	211,825	119,234	497,161
Trastuzumab	Recommended*	9,958,644	10,357,975	10,758,995	31,075,614
Triptorelin powder for injection	Non-submission	4,140	8,694	15,341	28,175
Ulipristal acetate	Recommended	10,780	20,473	62,231	93,484
Ustekinumab	Recommended	53,250	6,441	12,882	72,573
Valganciclovir	Recommended	630,156	663,398	648,674	1,942,228
Valsartan	Non-recommended	160,124	119,814	121,616	401,554
Varenicline tartrate	Recommended	1,637,552	1,464,037	1,110,341	4,211,930
Vemurafenib	Recommended		87,654	447,549	535,203
Vernakalant	Non-submission				
Vildagliptin	Recommended*	165,066	157,627	143,549	466,242
Vildagliptin/metformin hydrochloride	Non-submission	134,799	134,414	112,441	381,654
Vinflunine ditartrate	Non-recommended				
Vinorelbine	Recommended	357,178	438,608	398,568	1,194,354
Vismodegib	Non-submission				
Zaleplon	Recommended	80	458	991	1,529
Zanamivir	Recommended	118	623	1,866	2,607
Ziconitide	Non-recommended				
Zolpidem tartrate	Recommended	76,313	83,263	71,804	231,380
Zolpidem tartrate sublingual tablets	Non-submission				
Zonisamide	Non-submission**	277,070	357,883	429,441	1,064,394
Zopiclone	Recommended	538,629	507,968	454,298	1,500,895
Total (£)		181,172,208	180,127,566	187,745,248	549,045,022

*Indicates medicines that also have a NICE/AWMSG negative recommendation (“non-recommendation” or an AWMSG Statement of Advice not recommending its use for another indication) in addition to the recommendation.

**Indicates medicines that are included as an option in NICE CG137, in addition to the AWMSG negative recommendation or Statement of Advice.

APPENDIX 2. NICE TAS EXCLUDED FROM THE REPORT

The following NICE TAs involving medicines have been excluded from this report due to the broad remit of these TAs:

- TA10 – Asthma (children under 5) – Inhaler devices
- TA38 – Asthma (older children) – Inhaler devices
- TA81 – Atopic dermatitis (Eczema) – Topical steroids
- TA131 – Asthma in children – Corticosteroids
- TA138 – Asthma in adults – Corticosteroids