



Monitoring Usage in Wales of Medicines Appraised by NICE and AWMSG

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).

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This document should be cited as:

All Wales Medicines Strategy Group. Monitoring Usage in Wales of Medicines Appraised by NICE and AWMSG. November 2015.





EXECUTIVE SUMMARY

- Up to 31 March 2015, the National Institute for Health and Care Excellence (NICE) undertook 336 appraisals, of which 254 are currently active.
- Between April 2003 and 31 March 2015, the All Wales Medicines Strategy Group (AWMSG) undertook 239 appraisals:
 195 resulted in a positive recommendation for a specific indication, 44 appraisals resulted in a negative recommendation for a specific indication. During the same period, AWMSG issued 196 Statements of Advice; 140 are currently active.
- As of March 2015, 260 medicines had received a positive recommendation for use in Wales by NICE and/or AWMSG for one or more indications, costing NHS Wales £205 million for the financial year 2014–2015. This report will focus on the 135 medicines that have received a positive recommendation in the three years to March 2015.
- Of the medicines with a positive recommendation from NICE and/or AWMSG, 10 do not appear to have been used within NHS Wales in the last three years.
- As of March 2015, 63 medicines had received a negative recommendation from NICE and/or AWMSG. Spend on the 22 medicines with a negative indication for all of their indications was £3.07 million for the financial year 2014–2015: an increase of 19% compared to the previous year.
- As in previous years, two medicines make up the majority of spend on medicines with a negative recommendation:
 bevacizumab (37%) and dasatinib (22%).

- Spend on the 31 medicines with a Statement of Advice for all their indications was £937,100 for the financial year 2014–2015, a reduction of 33% compared to the previous year.
- Further analysis has been undertaken on four areas due to current therapeutic interest: analogue insulin, the direct oral anticoagulants (DOACs), inhalers for respiratory disease, and medicines supplied via homecare.
- Analogue insulin accounts for 91% of all insulin items issued in primary care. Spend in primary care for the financial year 2014– 2015 was £8.5 million.
- Total NHS Wales spend on DOACs for the financial year 2014– 2015 was £3.6 million: a 158% increase in spend over the previous year.
- Six new respiratory inhalers have been launched, and received positive recommendations from AWMSG, in the last three years for use in chronic obstructive pulmonary disease (COPD) and asthma.
- Spend on respiratory inhalers in primary care for 2014–2015 was over £80 million. Whilst the newer inhalers constitute a very small proportion of all inhalers prescribed, the increasing range of inhalers available makes this an area of potential confusion for prescribers. Appropriateness and consistency of inhaler prescribing is essential to ensure maximum patient response and safety.
- In 2014–2015, the total NHS Wales spend on all medicines supplied via homecare service providers, reported through Medusa, was £38.2 million.

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1.0 INTRODUCTION

Medicines are funded by NHS Wales following advice from two sources: NICE and AWMSG. 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 when 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.

This report monitors usage of medicines appraised between April 2003 and 31 March 2015, and also usage of medicines for which an AWMSG Statement of Advice has been issued.

Detailed analysis has also been undertaken on four specific areas due to current therapeutic interest: analogue insulin, DOACs, inhalers for respiratory disease, and medicines supplied via homecare.

The data on medicines usage are retrieved from two systems:

- The Comparative Analysis System for Prescribing Audit (CASPA) (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 dispensing.
- The Medusa data warehouse, which holds information on medicines issued by all hospitals in Wales.

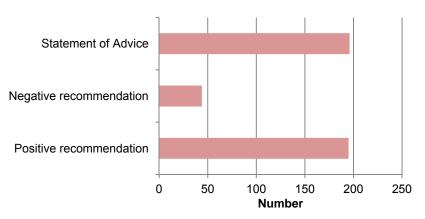
There are a number of cautions when interpreting the data. These are explained in Appendix 1.

2.0 APPRAISALS OVERVIEW

This report classifies a medicine according to its appraisal status (i.e. positive recommendation, negative recommendation, Statement of Advice) on 31 March 2015.

Between April 2003 and 31 March 2015, AWMSG undertook 239 appraisals on 185 medicines. Figure 1 shows the details of the advice issued by AWMSG.

Figure 1. Advice issued by AWMSG April 2003–31 March 2015



Twenty-six appraisals undertaken by AWMSG have subsequently been superseded by NICE Technology Appraisals (TAs) and 140 Statements of Advice are currently active.

Up to 31 March 2015, NICE had undertaken 336 TAs, including reviews and terminated appraisals, of which 254 are currently active; however, some 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.

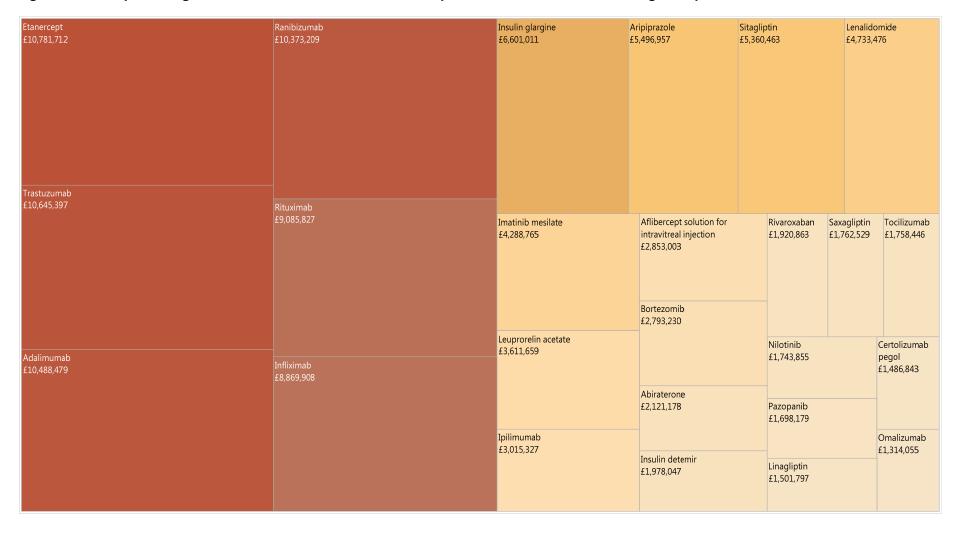
3.0 MEDICINES WITH A NICE/AWMSG POSITIVE RECOMMENDATION

As of March 2015, 260 medicines had received a positive recommendation for use in NHS Wales from NICE and/or AWMSG for one or more indication(s). Spend for the financial year 2014–2015 on these medicines by NHS Wales was £205 million. Many of the medicines that received a positive recommendation several years ago are now in established use. This report will therefore focus on those medicines that have received a positive recommendation in the three years to March 2015.

- There are 134 medicines that have received one or more positive recommendation(s) in the three years to March 2015.
- A list of the medicines with a positive recommendation that have been used within NHS Wales in the last three years, including the date of the most recent positive recommendation and the annual spend for the last three financial years, can be found in Appendix 2.
- There are ten medicines with a positive recommendation that do not appear to have been used by NHS Wales in the last three years:
 - Ceftaroline fosamil
 - Dihydroartemisinin/piperaquine phosphate
 - Epoetin theta
 - Epoetin zeta
 - Lipegfilgrastim
 - Lurasidone
 - Olodaterol hydrochloride
 - Sodium phenylbutyrate (Pheburane[®])
 - Tegafur/gimeracil/oteracil
 - Velaglucerase alfa

- Four of the six medicines with the highest spend for the financial year 2014–2015 are cytokine inhibitors: etanercept (£10,781,712), adalimumab (£10,488,479), rituximab (£9,085,827) and infliximab (£8,869,908). The other two medicines with the highest spend are the antineoplastic medicine, trastuzumab (£10,645,397), and ranibizumab intravitreal injection (£10,373,209). Figure 2 shows a pictorial representation of the 30 medicines with the highest spends.
- There are 17 medicines that have received a positive recommendation in the last three years with new spend in 2014–2015. Of these, the five with the highest spend are:
 - sofosbuvir (£377,816) and simeprevir (£248,618) for the treatment of hepatitis C, which both received their positive recommendation from NICE in February 2015;
 - dabrafenib (£201,666) for the treatment of melanoma, which received its positive recommendation from NICE in October 2014;
 - dolutegravir (£162,136) for the management of HIV, which received its positive recommendation from AWMSG in September 2014;
 - tobramycin inhaler (£151,085) for use in patients with cystic fibrosis, which received its positive recommendation from NICE in March 2013.
- The following medicines have shown some of the biggest increases in spend over the last two years (figures for 2014–2015 spend shown in brackets): dapagliflozin (£1,163,319), enzalutamide (£918,315), pirfenidone (£804,440), leuprorelin acetate (£3,611,659), aflibercept intravitreal solution (£2,853,003), paliperidone depot injection (£1,100,599), linagliptin (£1,501,797), rivaroxaban (£1,920,863), ipilimumab (£3,015,327) and golimumab (£975,244).

Figure 2. Treemap showing medicines with a NICE and/or AWMSG positive recommendation with highest spend in 2014–2015



£1,025,069 £11,000,000

4.0 MEDICINES WITH A NICE/AWMSG NEGATIVE RECOMMENDATION

As of March 2015, 63 medicines had received a negative recommendation from NICE and/or AWMSG (79 pieces of guidance) for one or more indication(s). Excluding those medicines with a positive recommendation for an alternative indication and those medicines with established use for another indication, further analysis was undertaken on 40 medicines.

- Fourteen of the medicines with a NICE/AWMSG negative recommendation do not appear to have been used by NHS Wales during the three years to March 2015.
- A further four medicines, crizotinib, dexrazoxane, liposomal cytarabine and panitumumab, which had previously been used in NHS Wales, do not appear to have been used during 2014–2015.
- Spend on the remaining 22 medicines was £3.07 million for the financial year 2014–2015, an increase of 19% compared to spend on medicines with a negative recommendation the previous year. Figure 3 shows a pictorial representation of spend on medicines with a negative recommendation.
- As in previous years, two medicines make up the majority of spend on medicines with a negative recommendation: bevacizumab (37%) and dasatinib (22%).
- 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 2014–2015 has increased by 22% compared to the previous year. Spend on bevacizumab for the year 2014–2015 was £1,128,877. Bevacizumab is being

- used mainly within Abertawe Bro Morgannwg University Health Board.
- 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 (January 2008). This positive recommendation has been superseded by a NICE TA, which did not recommend dasatinib for use for the indications appraised. Spend on dasatinib for the financial year 2014–2015 has increased by 8% compared to the previous financial year. Spend on dasatinib for the year 2014–2015 was £672,994. However, prior to this there had been a reduction in spend over the previous two years. Dasatinib is being extensively prescribed by specialists via WP10HP in some health boards.
- Ruxolitinib (£249,588) and fulvestrant (£235,212) both make up approximately 8% of spend on medicines with a negative recommendation in 2014–2015.
- Medicines which have received a negative recommendation within the last three years, which are also showing an increase in spend compared to the previous year are: insulin degludec (spend in NHS Wales for 2014–2015: £147,627), bosutinib (£44,333), aflibercept infusion (£36,896) and cabazitaxel (£31,046).
- A breakdown of spend for 2014–2015 on medicines with a NICE/AWMSG negative recommendation by health board for primary care, secondary care and WP10HP can be found in two tables in Appendix 3.

Figure 3. Medicines with a negative recommendation from NICE and/or AWMSG with spend in 2014–2015

Inositol nicotinate Bosutinib

Aflibercept concentrate for infusion

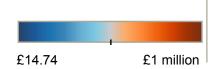
Amantadine hydrochloride Paricalcitol Ruxolitinib

Sorafenib Bevacizuma O Micafungin

Insulin degludec^{PentoxyfyllineAliskiren}
Olanzapine depot injection Cilostazol
Bromfenac

Cabazitaxel

Olanzapine depot injection Cilostazol
Bromfenac



5.0 MEDICINES WITH AN AWMSG STATEMENT OF ADVICE

As of March 2015, there were 140 active Statements of Advice, issued by AWMSG, confirming that the use of a medicine for one or more specific indications could not be endorsed due to company non-submission for appraisal. Excluding medicines with a positive or negative recommendation for an alternative indication and medicines with established use for alternative indications, further analysis was undertaken on 95 medicines.

- There are 64 medicines with one or more Statement(s) of Advice that have not been prescribed within NHS Wales during the last financial year. 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.
- Of the medicines with zero spend in 2014–2015, spend on one medicine – amifampridine – has steadily reduced over the last five years from £75,832 in 2010–2011 to zero in 2014–2015. This medicine received a Statement of Advice from AWMSG in March 2010 for the symptomatic treatment of Lambert-Eaton myasthenic syndrome.
- Spend on the 31 medicines with a Statement of Advice that can be monitored was £937,106 for the financial year 2014–2015, a reduction of 33% compared to the previous year.
- Medicines with the highest spend for 2014–2015 were rabbit anti-human thymocyte immunoglobulin (£231,487), colesevelam (£135,133), vildagliptin/metformin combination tablets (£99,202) and sodium oxybate (£89,064). However, spend on both rabbit anti-human thymocyte immunoglobulin and vildagliptin/metformin combination tablets show a reduction compared to the previous year.

- The majority of rabbit anti-human thymocyte immunoglobulin spend (94%) was in Cardiff and Vale University Health Board.
- Sodium oxybate is being used in secondary care within Betsi Cadwaladr University Health Board and Aneurin Bevan University Health Board, and in primary care within Cardiff and Vale University Health Board and Aneurin Bevan University Health Board.
- Use of colesevelam and vildagliptin/metformin combination tablets appears to be spread throughout NHS Wales, predominantly in primary care.
- There are five medicines that have received a Statement of Advice with new spend in 2014–2015. Those that make up the majority of this spend are: levonorgestrel intrauterine device 52 mg (£79,464), hydrocortisone modified release tablets (£42,134) and cefuroxime sodium solution for intracameral injection (£27,609).
- Bimatoprost/timolol eye drops presented as single use containers have seen the largest increase in use compared to the previous year; spend in 2014–2015 was £35,515. This is predominantly in Abertawe Bro Morgannwg University Health Board. Whilst this is not a large spend, it should be noted that single use eye drops generally cost more than the multiple use dropper bottles and should only be used when there is a clear indication for single use drops.
- A breakdown of spend for 2014–2015 on the 28 medicines with spend of more than £100 for the year, with an AWMSG Statement of Advice, by health board for primary care, secondary care and WP10HP can be found in Appendix 4.

6.0 ANALOGUE INSULIN

NICE Clinical Guideline 87 on the management of type 2 diabetes mellitus recommends human isophane insulin as the preferred choice, when insulin treatment is required¹. For most people with type 2 diabetes mellitus, long-acting insulin analogues offer no significant benefit over human isophane insulin, and are more expensive. Long-acting insulin analogues are recommended as the preferred treatment in type 1 diabetes². Prescribing data cannot distinguish the indication for which the insulin is being prescribed; however, disease prevalence data would suggest that a large amount of insulin analogue prescribing is for the management of type 2 diabetes.

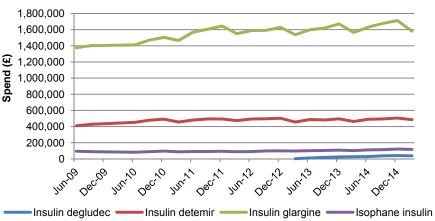
- There are three long-acting insulin analogues currently available in the UK. In addition to the NICE Clinical Guideline, all three analogue insulin preparations have been appraised by AWMSG. Insulins glargine and detemir have received positive recommendations from AWMSG for specific indications, whilst insulin degludec received a negative recommendation from AWMSG in July 2014.
- Analogue insulin spend for the financial year 2014–2015 was £8.5 million (see Table 1 for breakdown of primary care analogue insulin spend by health board) and makes up 91% of all insulin items issued in primary care (1% reduction on the previous year), 80% of all items issued on WP10HP and 77% of all issues in secondary care. Figure 4 shows the trend in NHS Wales spend on analogue insulin alongside all isophane insulin. By comparison analogue insulins make up 80% of all insulin items issued in primary care in England.
- NHS Wales spend on insulin degludec for 2014–2015 was £147.627.
- Approximately 97% of insulin spend is in primary care; however, the majority of insulin is initiated by specialists within secondary care. With GPs reluctant to make changes

to prescribing initiated by specialists, a whole health board approach is required to influence prescribing in this area.

Table 1. Primary care spend on insulin analogues by health board

	Insulin degludec	Insulin detemir	Insulin glargine	Total	List size	Spend per 100,000 population
ABMU	£32,746	£309,877	£889,565	£1,232,188	546,827	£225,334
Aneurin Bevan	£11,664	£466,174	£1,293,799	£1,771,637	600,625	£294,966
BCU	£6,840	£392,438	£1,414,562	£1,813,840	706,202	£256,844
Cardiff and Vale	£40,766	£204,821	£1,227,186	£1,472,773	509,955	£288,805
Cwm Taf	£2,995	£225,857	£461,964	£690,816	303,928	£227,296
Hywel Dda	£31,421	£247,697	£830,568	£1,109,686	391,565	£283,398
Powys	£5,098	£88,628	£287,528	£381,254	138,348	£275,576
Total	£131,530	£1,935,492	£6,405,172	£8,472,194	3,197,450	£264,967

Figure 4. Trend in insulin prescribing

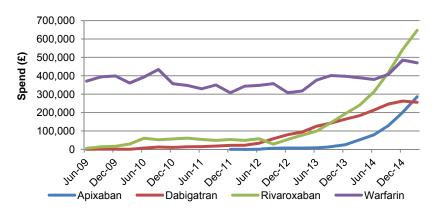


7.0 DIRECT ORAL ANTICOAGULANTS

The first of the DOACs, dabigatran etexilate, was launched in the UK in April 2008, followed by rivaroxaban (November 2008) and apixaban (September 2011). All are licensed for the prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation with one or more cardiovascular risk factor/s, the prophylaxis of venous thromboembolism following knee or hip surgery and the treatment and prevention of recurrent deep vein thrombosis and pulmonary embolism. Additionally, low-dose rivaroxaban, in combination with aspirin, or aspirin and clopidogrel, is licensed for the prevention of atherothrombotic events following an acute coronary syndrome with elevated cardiac biomarkers. There are 11 NICE TAs recommending their use within NHS Wales.

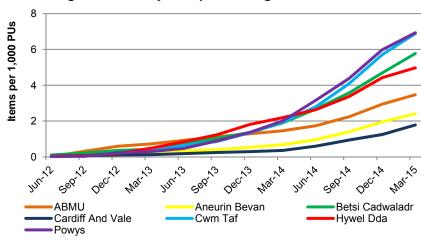
 Total spend in NHS Wales on DOACs for the financial year 2014–2015 was £3,596,309, a 158% increase on the previous year. Rivaroxaban makes up the majority (53%), perhaps because of its broader range of indications, dabigatran etexilate makes up 27% and apixaban 19% of the spend. Figure 5 shows the trend in total DOAC and warfarin spend in NHS Wales.





- Analysis of primary care prescribing for 2014–2015 shows that warfarin makes up 94.6% of anticoagulant items and 38.0% of anticoagulant cost, while the DOACs make up 5.2% of items and 61.1% of costs.
- Analysis shows uptake of DOACs in England is greater than in Wales. DOACs made up 10.5% of all anticoagulant items prescribed in primary care in England during 2014–2015.
- Figure 6 shows weighted primary care prescribing of DOACs by health board. Powys Teaching Health Board and Cwm Taf University Health Board use the most DOACs per weighted population, whilst the Welsh average is 4.21 items/1,000 prescribing units (PUs)* for the quarter to March 2015.
- By comparison, the English average is 6.01 items/1,000 PUs for the quarter to March 2015, the range across individual clinical commissioning groups being 0.86–25.2 items/1,000 PUs.

Figure 6. Primary care prescribing trend in DOACs



^{*}PUs were adopted to take account of the greater need of elderly patients for medication in reporting prescribing performance in primary care. Patients aged ≥ 65 years are counted as three PUs; patients < 65 years and temporary residents are counted as one.

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8.0 INHALERS FOR RESPIRATORY DISEASE

NICE guidance on the use of inhaled therapies in COPD recommends a stepwise approach to management, including the use of short- and long-acting beta₂ agonists, long-acting antimuscarinic antagonist (LAMA) bronchodilators and inhaled corticosteroids, dependent on symptoms and number of exacerbations³.

- Over £80 million was spent in primary care on inhaled preparations to manage respiratory disease in 2014–2015.
- Tiotropium was the first inhaled LAMA available in the UK. In the last three years, three new LAMAs have been launched and subsequently appraised by AWMSG: aclidinium bromide (Eklira Genuair®), glycopyrronium (Seebri Breezhaler®) and umeclidinium (Incruse®).
- Tiotropium spend in NHS Wales for 2014–2015 was £15.9 million, whilst total spend on the three newer LAMAs was £537,883, 3% of all LAMA spend. Figure 7 shows their trend in use within NHS Wales.
- Two new combination inhalers have also received a positive recommendation from AWMSG: umeclidinium/vilanterol (Anoro[®] Ellipta[®]) and indacaterol/glycopyrronium (Ultibro[®] Breezhaler[®]). Spend on these two products for 2014–2015 was £5,441 and £899 respectively.
- Combination inhalers containing a long-acting beta₂ agonist and a corticosteroid are established treatment in both asthma and COPD with an annual spend in primary care of £44 million. Fluticasone furoate/vilanterol (Relvar Ellipta®) received a positive recommendation from AWMSG during 2014 for use in both asthma and COPD. The majority of the £184,846 spend during 2014–2015 was in primary care (93%).

 Whilst spend on these six newer inhalers (see Table 2) is currently small, there is a rapidly increasing number and range of inhalers available. Appropriateness and consistency of inhaler prescribing is essential to ensure maximum patient response and safety.

Figure 7. Trend in the newer LAMA spend

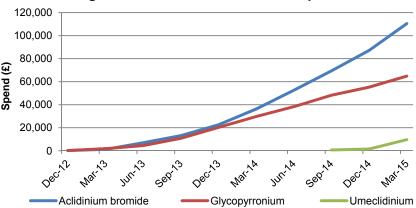


Table 2. Breakdown in spend on the six newer inhalers 2014–2015

	Spe	end		Primary care spend
	Primary care	Secondary care	List size	per 1,000 population
ABMU	£84,305	£2,267	546,827	£15,417
Aneurin Bevan	£199,879	£5,056	600,625	£33,279
BCU	£136,094	£3,863	706,202	£19,271
Cardiff and Vale	£69,204	£2,791	509,955	£13,571
Cwm Taf	£123,370	£11,628	303,928	£40,592
Hywel Dda	£48,755	£6,895	391,565	£12,451
Powys	£25,075	N/A	138,348	£18,125

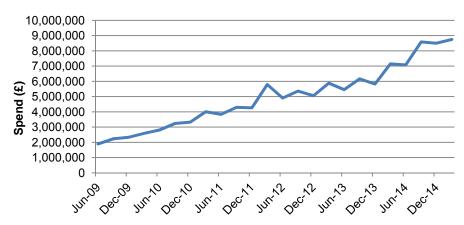
9.0 MEDICINES SUPPLIED VIA HOMECARE

Analysis of homecare spend within this report includes only medicines where supply is recorded through Medusa. Homecare medicines not recorded through Medusa are not included in this analysis, as figures for medicines not recorded cannot be accurately determined at present.

- In 2014–2015, the total spend on all medicines supplied via homecare in Wales, reported through Medusa, was £38.2 million.
- In 2014–2015, spend on medicines receiving a positive recommendation from NICE/AWMSG supplied via homecare was £32.9 million, which accounts for 86% of total homecare spend.
- Spend on this same group of medicines in secondary care was £29.5 million, and via WP10HP was £2.5 million and £5.1 million though primary care. Figure 8 shows the trend in homecare spend on medicines with a positive recommendation by NICE/AWMSG.
- No medicines with a negative recommendation from NICE/AWMSG are being supplied via homecare. Only two medicines with an AWMSG Statement of Advice are being supplied via homecare, anakinra and human immunoglobulin, at a cost of £41,000 for 2014–2015; both of which are also licensed for indications other than those for which the Statement of Advice was issued.
- The majority of the medicines supplied via homecare are cytokine modulators (£25.9 million). Other medicines supplied via homecare include: medicines used to treat

- malignant diseases (£2.3 million) and antiviral medicines to manage HIV and hepatitis C (£2.2 million).
- A small number of medicines were only supplied via the homecare route in 2014–2015: certolizumab pegol (£1,486,843), golimumab (£975,245), icatibant acetate (£57,360) and teriflunomide (£7,863).
- Spend on medicines via homecare varies across the health boards. Appendix 5 shows a breakdown by health board of homecare spend on medicines with a positive recommendation by NICE/AWMSG for 2014–2015. Several factors may contribute to these figures: the size and specialities within the secondary care facility, different supply mechanisms, and methods for recording homecare spend.

Figure 8. Trend in homecare spend on medicines with a NICE/AWMSG positive recommendation



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- 1 National Institute for Health and Care Excellence. Clinical Guideline 87. Type 2 diabetes newer agents (partial update of CG66). May 2009. Available at: http://www.nice.org.uk/CG87. Accessed Sep 2013.
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- 3 National Institute for Health and Care Excellence. Clinical Guideline 101. Chronic obstructive pulmonary disease: Management of chronic obstructive pulmonary disease in adults in primary and secondary care (partial update). 2010. Available at: https://www.nice.org.uk/quidance/cg101. Accessed Oct 2014.

APPENDIX 1. 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.
- 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.
- The figures included in this report should not be compared to previous reports monitoring usage in Wales of medicines appraised by NICE/AWMSG as there may be variations due to in year cost reconciliations within Medusa.

APPENDIX 2. USAGE OF MEDICINES THAT HAVE RECEIVED A POSITIVE RECOMMENDATION FROM NICE/AWMSG IN THE 3 YEARS TO MARCH 2015

Medicine	Date of latest NICE/AWMSG recommendation	2012–2013 spend (£)	2013–2014 spend (£)	2014–2015 spend (£)	Total (£)
5-aminolaevulinic acid	Dec-13	0	5,034	21,217	26,251
Abatacept	Feb-14	270,898	507,729	755,102	1,533,729
Abiraterone*	Jun-12	1,855,557	2,201,392	2,121,178	6,178,127
Aclidinium bromide	Jul-13	1,316	78,886	319,594	399,796
Adalimumab*	Feb-15	6,781,519	7,893,431	10,488,479	25,163,429
Afatinib	Apr-14	0	0	27,363	27,363
Aflibercept solution for intravitreal injection	Feb-14	0	166,165	2,853,003	3,019,168
Alemtuzumab	May-14	85,840	45,683	465,838	597,361
Alogliptin	Oct-14	0	27	19,292	19,319
Alogliptin/metformin	Oct-14	0	80	1,037	1,117
Alteplase	Sep-12	410,845	573,474	621,060	1,605,379
Apixaban	Feb-13	21,614	100,257	696,633	818,504
Argatroban	Jan-13	87,774	56,752	55,764	200,290
Aripiprazole	Jul-13	4,376,366	4,919,622	5,496,957	14,792,945
Aripiprazole monohydrate	Aug-14	0	1,722	132,431	134,153
Atomoxetine hydrochloride	Feb-14	585,498	645,000	680,999	1,911,497
Atorvastatin chewable tablets	Jun-12	6,128	10,402	12,714	29,244
Axitinib	Feb-15	198	29,262	215,856	245,316
Azithromycin	Aug-14	1,606	301	0	1,907
Aztreonam lysine	May-13	5,646	86,807	265,680	358,133
Boceprevir	Apr-12	293,044	629,225	185,458	1,107,727
Bortezomib	Oct-14	1,905,353	2,348,710	2,793,230	7,047,293
Botulinum toxin type A*	Dec-13	906,484	932,778	953,570	2,792,832
Bupivacaine hydrochloride/fentanyl	Nov-12	23,339	34,682	47,832	105,853
C1-esterase inhibitor*	Jul-13	10,345	19,604	20,423	50,372
Cabozantinib	Jan-15	0	0	5,760	5,760
Canagliflozin*	Jun-14	0	0	78,963	78,963
Certolizumab pegol	Oct-14	616,688	1,056,413	1,486,843	3,159,944
Colecalciferol	Nov-12	150,699	403,518	608,635	1,162,852
Colistimethate sodium inhalation powder	Mar-13	0	0	54,886	54,886
Dabigatran	Dec-14	266,154	616,050	978,813	1,861,017
Dabrafenib	Oct-14	0	0	201,666	201,666
Dapagliflozin	Jun-13	3,896	213,450	1,163,319	1,380,665
Darbepoetin alfa	Nov-14	954,490	892,385	900,837	2,747,712
Darunavir*	May-14	636,360	739,280	968,845	2,344,485
Degarelix	Dec-12	6,276	32,351	82,194	120,821
Delta-9- tetrahydrocannabinol/cannabidiol	Aug-14	57,775	60,625	61,125	179,525
Denosumab*	Oct-12	384,120	552,442	728,658	1,665,220
Dexmedetomidine	Aug-12	45,157	105,085	90,145	240,387
Dimethyl fumarate	Aug-14	86,303	207,799	351,656	645,758

Medicine	Date of latest NICE/AWMSG recommendation	2012–2013 spend (£)	2013–2014 spend (£)	2014–2015 spend (£)	Total (£)
Dolutegravir	Sep-14	0	0	162,136	162,136
Eltrombopag	Jul-14	61,908	128,331	205,421	395,660
Elvitegravir/cobicistat/emtricitabine/tenofovir	Dec-13	0	3,468	82,163	85,631
Empagliflozin	Mar-15	0	0	1,894	1,894
Emtricitabine/rilpivirine/tenofovir disoproxil	Jul-14	113,509	300,482	546,426	960,417
Enzalutamide	Jul-14	0	35,441	918,315	953,756
Eplerenone	Jan-13	679,093	901,051	1,108,415	2,688,559
Epoetin alfa	Nov-14	1,123,180	1,047,309	1,173,926	3,344,415
Epoetin beta	Nov-14	94,229	66,532	55,554	216,315
Erlotinib*	Jun-12	828,559	574,894	521,894	1,925,347
Eslicarbazepine acetate	Nov-12	157,572	286,545	345,398	789,515
Esomeprazole powder for solution for injection	April-12	0	37	15	52
Etanercept*	Dec-13	7,683,173	8,554,333	10,781,712	27,019,218
Etravirine	Dec-13	71,544	80,828	69,707	222,079
Everolimus*	Aug-12	124,882	73,564	99,943	298,389
Fidaxomicin	Dec-12	4,860	95,580	181,116	281,556
Fingolimod	Apr-12	58,477	267,590	460,552	786,619
Fluocinolone acetonide	Nov-13	0	0	10,200	10,200
Fluorouracil/salicylic acid	Jun-12	13,928	25,781	26,046	65,755
Fluticasone furoate/vilanterol	Aug-14	0	1,978	184,846	186,824
Follitropin alfa	Jan-15	36,036	32,917	24,409	93,362
Glycopyrronium inhalation powder	May-13	1,925	65,312	206,548	273,785
Golimumab	Feb-15	233,240	447,755	975,244	1,656,239
Imatinib mesilate*	Nov-14	4,114,566	4,244,665	4,288,765	12,647,996
Indacaterol/glycopyrronium	May-14	0	0	899	899
Infliximab*	Mar-15	7,053,927	8,271,512	8,869,908	24,195,347
Ingenol mebutate	Jul-13	0	23,043	45,202	68,245
Insulin detemir	Dec-12	1,949,375	1,929,441	1,978,047	5,856,863
Insulin glargine*	Mar-13	6,343,562	6,450,808	6,601,011	19,395,381
Ipilimumab	Jul-14	380,075	1,443,168	3,015,327	4,838,570
Ivabradine*	Nov-12	656,689	869,094	1,025,069	2,550,852
Lapatinib*	Aug-13	143,285	117,144	88,230	348,659
Lenalidomide	Sep-14	3,472,596	3,504,038	4,733,476	11,710,110
Leuprorelin acetate	Jan-15	167,157	166,285	3,611,659	3,945,101
Linaclotide	Feb-14	0	5,529	29,674	35,203
Linagliptin	May-13	160,414	584,104	1,501,797	2,246,315
Linagliptin/metformin	Aug-14	366	13,795	49,481	63,642
Lisdexamfetamine dimesylate	Dec-13	225	43,085	160,338	203,648
Lixisenatide	Dec-13	58	16,625	290,202	306,885
Lubiprostone*	Jul-14	0	0	12,979	12,979
Mannitol inhalation powder	Nov-12	2,631	20,812	20,389	43,832
Mercaptopurine oral suspension	Oct-12	19,156	41,746	56,410	117,312
Midazolam oromucosal solution	Jun-12	173,519	290,193	373,307	837,019
Mirabegron	Jun-13	83	127,771	579,490	707,344
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Monitoring Usage in Wales of Medicines Appraised by NICE and AWMSG

Medicine	Date of latest NICE/AWMSG recommendation	2012–2013 spend (£)	2013–2014 spend (£)	2014–2015 spend (£)	Total (£)
Nalmefene	Nov-14	0	906	14,465	15,371
Nepafenac	Aug-13	615	2,844	7,848	11,307
Nevirapine	Jul-12	33,694	94,249	63,853	191,796
Nilotinib	Apr-12	960,455	1,213,272	1,743,855	3,917,582
Ocriplasmin	Oct-13	0	21,000	18,000	39,000
Omalizumab*	Apr-13	1,116,540	1,112,810	1,314,055	3,543,405
Paclitaxel albumin-bound nanoparticles*	Sep-14	88,549	150,469	213,782	452,800
Paliperidone palmitate depot injection	Nov-12	78,538	561,937	1,100,599	1,741,074
Pazopanib	Dec-13	1,011,562	1,372,507	1,698,179	4,082,248
Peginterferon alfa	Nov-13	842,513	844,987	522,023	2,209,523
Perampanel	Jul-13	15,625	101,080	259,119	375,824
Pirfenidone	Apr-13	0	32,376	804,440	836,816
Pixantrone	Feb-14	0	0	90,392	90,392
Ponatinib	Jan-15	0	6,060	65,355	71,415
Prasugrel	Jul-14	277,330	338,203	363,698	979,231
Raltegravir	Dec-13	229,682	220,275	265,773	715,730
Ramipril oral solution	Nov-12	32,471	57,470	88,614	178,555
Ranibizumab	Nov-13	13,115,705	11,070,502	10,373,209	34,559,416
Ribavirin	Nov-13	221,270	248,416	191,709	661,395
Rifaximin	Mar-15	107,576	165,501	305,517	578,594
Rilpivirine	Jul-12	5,468	34,814	41,454	81,736
Rituximab	Mar-14	8,317,367	8,895,255	9,085,827	26,298,449
Rivaroxaban	Mar-15	217,931	678,197	1,920,863	2,816,991
Rufinamide	Oct-12	109,185	133,871	155,229	398,285
Saxagliptin*	Dec-13	1,152,997	1,584,514	1,762,529	4,500,040
Sildenafil citrate suspension	Jan-13	0	3,399	13,185	16,584
Simeprevir	Feb-15	0	0	248,618	248,618
Sitagliptin	Oct-12	4,453,873	5,111,310	5,360,463	14,925,646
Sofosbuvir	Feb-15	0	0	377,816	377,816
Telaprevir	Apr-12	1,063,801	899,992	317,221	2,281,014
Tenofovir disoproxil	May-14	267,441	334,194	367,755	969,390
Teriflunomide	Jan-14	0	0	7,863	7,863
Tobramycin inhalation powder	Mar-13	0	0	151,085	151,085
Tocilizumab*	May-14	900,706	1,424,627	1,758,446	4,083,779
Trastuzumab*	Oct-12	10,357,975	10,776,117	10,645,397	31,779,489
Ulipristal acetate	Aug-13	20,473	62,231	167,279	249,983
Umeclidinium	Jan-15	0	0	11,741	11,741
Umeclidinium/vilanterol	Mar-15	0	0	5,441	5,441
Vemurafenib	Dec-12	87,654	447,550	791,091	1,326,295
Vildagliptin*	Mar-13	157,627	143,550	127,130	428,307

^{*}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.

APPENDIX 3. USAGE OF MEDICINES THAT HAVE RECEIVED A NEGATIVE RECOMMENDATION FROM NICE/AWMSG

Primary care spend for the financial year 2014–2015 on medicines with a negative recommendation from NICE/AWMSG

	A	NBMU	Aneu	ırin Bevan		вси	Cardit	ff and Vale	Cv	vm Taf	Hyv	vel Dda	Р	owys	Total
Medicine	Spend (£)	Spend (£) per 100,000 population	Spend (£)												
Aliskiren	6,701	1,225	10,631	1,770	5,985	848	10,412	2,042	5,402	1,777	9,867	2,520	2,331	1,685	51,329
Amantadine hydrochloride	15,054	2,753	9,118	1,518	27,700	3,922	5,929	1,163	4,350	1,431	10,536	2,691	5,860	4,235	78,547
Bromfenac	9	2	17	3	595	84	17	3	26	8	17	4	0	0	681
Cilostazol	5,223	955	7,224	1,203	14,753	2,089	490	96	4,895	1,611	15,562	3,974	1,476	1,067	49,623
Fampridine	0	0	0	0	0	0	0	0	0	0	0	0	3,982	2,878	3,982
Fulvestrant	0	0	0	0	0	0	0	0	0	0	1,045	267	0	0	1,045
Inositol nicotinate	2,241	410	4,458	742	3,948	559	3,143	616	1,199	395	2,200	562	1,470	1,063	18,659
Insulin degludec	32,746	5,988	11,664	1,942	6,840	969	40,766	7,994	2,995	985	31,421	8,024	5,098	3,685	131,530
Pentoxyfylline	6,771	1,238	8,418	1,402	11,916	1,687	3,018	592	9,120	3,001	9,731	2,485	1,024	740	49,998
Racecadotril granules for suspension	0	0	6	1	8	1	0	0	0	0	0	0	0	0	14
Total	68,745	12,571	51,536	8,581	71,745	10,159	63,775	12,506	27,987	9,208	80,379	20,527	21,241	15,353	385,408

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Secondary care and WP10HP spend (£) for the financial year 2014–2015 on medicines with a negative recommendation from NICE/AWMSG

	ABM	U	Aneurin l	Bevan	вси		Cardiff ar	nd Vale	Cwm T	af	Hywel	Dda	Powys	Velindre	
Medicine	Secondary care	WP10- HP	WP10- HP	Secondary care	Total										
Aflibercept concentrate for infusion	0	0	1,419	0	12,772	0	0	0	1,419	0	4,257	0	0	17,029	36,896
Aliskiren	53	0	0	0	32	0	60	0	0	0	111	0	0	0	256
Amantadine hydrochloride	354	128	366	332	517	18	354	1	36	32	173	1	15	0	2,327
Bevacizumab	605,602	0	30,301	0	113,066	0	24,900	0	19,487	0	110,516	0	0	225,005	1,128,877
Bosutinib	8,248	0	0	0	7,217	0	28,868	0	0	0	0	0	0	0	44,333
Bromfenac	0	0	0	0	0	850	0	0	0	43	0	17	0	0	910
Cabazitaxel	0	0	0	0	0	0	0	0	0	0	0	0	0	31,046	31,046
Cilostazol	217	0	36	0	0	0	0	0	71	24	295	5	0	0	648
Dasatinib	50,500	85,503	0	213,423	47,886	82,691	56,512	117,441	0	0	19,038	0	0	0	672,994
Eribulin	0	0	3,466	0	7,930	0	0	0	0	0	7,798	0	0	3,466	22,660
Fulvestrant	50,778	0	8,776	0	100,303	0	0	0	0	0	57,676	0	0	16,634	234,167
Inositol nicotinate	54	0	32	51	0	0	54	0	36	0	18	0	0	0	245
Insulin degludec	10,714	331	86	835	1,642	0	674	0	605	0	1,210	0	0	0	16,097
Micafungin	0	0	42,537	0	65,256	0	0	0	0	0	0	0	0	0	107,793
Ofatumumab	0	0	0	0	0	0	7,464	0	0	0	1,200	0	0	0	8,664
Olanzapine depot injection	1,925	0	2,480	0	2,535	0	11,639	0	0	0	16,332	0	0	0	34,911
Paricalcitol	0	0	0	0	5,869	0	1,163	0	0	0	0	0	0	0	7,032
Pentoxyfylline	1,972	309	0	150	1,267	0	1,204	92	831	253	454	0	0	0	6,532
Ruxolitinib	0	0	0	0	105,876	0	0	0	0	0	143,712	0	0	0	249,588
Sorafenib	2,682	0	0	0	42,919	0	28,613	0	0	0	0	0	0	0	74,214
Total	733,099	86,271	89,499	214,791	515,087	83,559	161,505	117,534	22,485	352	362,790	23	15	293,180	2,680,190

APPENDIX 4. USAGE OF MEDICINES THAT HAVE RECEIVED A STATEMENT OF ADVICE FROM AWMSG

Primary care, secondary care and WP10HP spend (£) for the financial year 2014–2015 on medicines with an AWMSG Statement of Advice (Figures in brackets show the amount of the secondary care spend issued on WP10HP.)

	Al	вми	Aneur	in Bevan	Е	CU	Cardiff	and Vale	Cw	m Taf	Hyw	el Dda	Po	owys	Velindre
Medicine	Primary care	Secondary care/ WP10HP	Secondary care/ WP10HP												
Aripiprazole solution for injection	0	0	0	621	17	4	0	0	0	4	0	1,047	0	0	0
Artemether/ lumefantrine	0	49	23	50	0	25	0	273	11	29	0	50	0	0	0
Azilsartan medoxomil	0	0	0	0	0	0	689	0	218	0	0	0	0	0	0
Azithromycin eye drops	126	35 (35)	7	63 (63)	7	19 (19)	35	0	21	17	119	199 (35)	0	0	0
Bilastine	42	0	28	0	45	178 (178)	15	0	0	0	14	0	0	0	0
Bimatoprost/ timolol eye drops single use container	16,636	826 (826)	2,231	479 (479)	8,543	321 (321)	2,858	0	0	0	2,911	196 (196)	514	0	0
Bosentan	0	18,123	0	356	0	12,686	1,510	5,400	0	10,572 (10,572)	0	0	0	0	0
Busulfan	0	0	0	0	0	0	0	29,666	0	0	0	0	0	0	0
Cefuroxime sodium solution for intracameral injection	0	16,971	0	10,638	0	0	0	0	0	0	0	0	0	0	0
Ciprofloxacin ear drops	460	341 (341)	103	260	568	828 (828)	158	0	123	1,085 (1,085)	0	35 (35)	135	380 (380)	0
Colesevelam	20,702	1,793 (923)	11,549	1,348 (1,348)	17,470	3,517 (3,517)	32,681	4,618	3,743	144 (105)	25,828	3,713 (22)	8,027	0	0
Dapoxetine	533	0	277	53 (53)	496	196	911	0	109	0	513	0	0	0	0
Dulaglutide	0	91 (91)	0	0	0	0	0	0	0	0	182	0	0	0	0
Ethinylestradiol/ drospirenone	551	0	893	0	465	0	295	0	40	0	17	0	0	0	0
Hydrocortisone modified release	9,729	1,376 (1,376)	12,655	224 (224)	650	0	14,357	0	815	0	2,328	0	0	0	0
Hydromorphone hydrochloride	0	8,293	0	0	0	0	0	2,506	0	0	0	0	0	0	1,240
Hydroxycarbamide	0	3,367	4,017	4	0	0	6,700	1,600	0	0	0	0	500	0	0

Monitoring Usage in Wales of Medicines Appraised by NICE and AWMSG

	AE	зми	Aneuri	in Bevan	E	CU	Cardiff a	and Vale	Cw	m Taf	Hyw	el Dda	Po	owys	Velindre
Medicine	Primary care	Secondary care/ WP10HP	Primary care	Secondary care/WP10 HP	Secondary care/WP10 HP										
Levonorgestrel intrauterine device 52mg	12,496	0	23,584	0	15,136	0	10,648	0	4,840	0	7,216	0	5,544	0	0
Mercaptamine bitartrate	0	0	70	0	0	0	3,300	0	6,080	0	7,600	0	0	0	0
Mitotane	0	0	0	0	0	0	0	0		0	0	0	0	0	5,834
Paliperidone	3,064	0	1,216	0	292	1,638	1,167	0	2,432	0	0	0	292	0	0
Progesterone vaginal capsules	0	0	378	36 (36)	84	0	560	0	504	0	168	0	0	0	0
Rabbit anti-human thymocyte immunoglobulin	0	14,480	0	0	0	0	0	217,007	0	0	0	0	0	0	0
Sevelamer carbonate powder for oral solution	1,659	1,383	668	0	2,004	601	167	4,087 (156)	0	0	334	401	0	0	0
Sodium oxybate	0	0	1,080	35,280 (35,280)	0	41,904	10,800	0	0	0	0	0	0	0	0
Tapentadol film coated tablets	3,026	0	3,795	644 (644)	3,006	5	3,331	14	922	0	8,360	45	361	0	0
Tocofersolan	0	0	491	0	6,565	196	0	0	0	0	0	0	0	0	0
Vildagliptin/ metformin hydrochloride	14,522	0	28,818	0	2,209	0	26,896	38	3,350	0	22,780	113	476	0	0
Total	83,546	67,128	91,883	50,056	57,557	62,118	117,078	265,209	23,208	11,851	78,370	5,799	15,849	380	7,074
Spend per 100,000 population	15,278		15,298		8,150		22,958		7,636		20,015		11,456		

APPENDIX 5. SPEND ON MEDICINES SUPPLIED VIA HOMECARE THAT HAVE RECEIVED A POSITIVE RECOMMENDATION FROM NICE/AWMSG

	ABMU	Aneurin Bevan	BCU	Cardiff and Vale	Cwm Taf	Hywel Dda	Velindre
Abacavir/lamivudine	£222,450	0	£33,103	0	0	0	0
Abatacept	£242,495	0	£100,249	£18,966	£33,191	£128,588	0
Adalimumab*	£2,752,681	£2,474,136	£2,336,099	0	£1,414,238	£1,408,560	0
Atazanavir	£40,549	0	£21,215	0	0	0	0
Axitinib	0	0	0	0	0	0	£3,712
Certolizumab pegol	£176,605	£617,403	£148,005	0	£219,505	£325,325	0
Darbepoetin alfa	£168,431	0	£93,956	£185,890	0	0	0
Darunavir*	£293,781	0	£13,728	0	0	0	0
Deferasirox*	0	0	£21,168	0	0	0	0
Dimethyl fumarate	£5,338	£131,014	0	0	0	0	0
Dolutegravir	£47,731	0	0	0	0	0	0
Efavirenz/emtricitabine/ tenofovir disoproxil	£633,856	0	£112,680	0	0	0	0
Elvitegravir/cobicistat/ emtricitabine/tenofovir	£10,735	0	0	0	0	0	0
Emtricitabine	£17,920	0	0	0	0	0	0
Emtricitabine/rilpivirine/ tenofovir disoproxil	£99,528	0	£26,312	0	0	0	0
Emtricitabine/tenofovir disoproxil	£383,475	0	£57,365	0	0	0	0
Entecavir	£5,086	0	0	0	0	0	0
Epoetin alfa	£59,086	£5,441	£49,277	£394,015	0	0	0
Etanercept*	£4,088,370	£1,285,391	£2,865,386	0	£1,093,414	£1,412,161	0
Etravirine	£26,511	0	£1,068	0	0	0	0
Ezetimibe	£603	0	0	0	0	0	0
Fingolimod	£188,234	£83,129	0	£22,932	0	0	0
Golimumab	£241,335	£190,564	£123,782	0	£165,701	£253,863	0
Icatibant acetate*	0	0	0	£57,360	0	0	0
Infliximab*	0	0	0	£78,850	0	£37,997	0
Maraviroc	3,530	0	0	0	0	0	0
Paliperidone palmitate depot injection	0	0	0	£61,283	£36,033	£142,806	0
Pazopanib	£16,675	0	0	0	0	0	0
Pirfenidone	£155,389	0	0	£244,881	0	0	0
Raltegravir	£73,162	0	0	0	0	0	0
Rilpivirine	£28,439	0	0	0	0	0	0
Simeprevir	0	0	0	£44,796	0	0	0
Somatropin*	£1,718	0	£24,042	0	0	0	0
Sunitinib*	£1,569	0	0	0	0	0	0
Tenofovir disoproxil	£45,759	0	£1,539	0	0	0	0
Teriflunomide	£7,863	0	0	0	0	0	0
Teriparatide*	£30,451	£816	£141,106	£315,235	£26,372	£69,384	0
Tocilizumab	£6,451	0	£17,203	0	£21,504	£58,777	0
Trastuzumab*	£665,688	0	£28,908	0	0	0	£1,294,625
Ustekinumab*	£648,394	£367,137	£458,385	0	£6,441	£111,644	0
Total	£11,389,888	£5,155,031	£6,674,576	£1,424,208	£3,016,399	£3,949,105	£1,298,337

^{*}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.