Monitoring Usage in Wales of Medicines Appraised by NICE and AWMSG

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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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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 dispensing.
- The Medusa data warehouse, which holds information on medicines issued by all hospitals in Wales.

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

<table>
<thead>
<tr>
<th>Medicine</th>
<th>NICE/AWMSG positive recommendations NICE publication/ministerial ratification date</th>
<th>Spend (£) 2013–2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin glargine</td>
<td>TA53 (December 2002) AWMSG reference no. 1673 (18/03/2013)</td>
<td>6,448,050</td>
</tr>
<tr>
<td>Sitagliptin</td>
<td>AWMSG reference no. 1655 (25/10/2012)</td>
<td>5,050,434</td>
</tr>
<tr>
<td>Aripiprazole oral</td>
<td>AWMSG reference no. 27 (22/07/2009) TA213 (January 2011) TA292 (July 2013)</td>
<td>4,919,622</td>
</tr>
<tr>
<td>Liraglutide</td>
<td>TA203 (October 2010)</td>
<td>4,834,489</td>
</tr>
<tr>
<td>Imatinib*</td>
<td>TA70 (October 2003) TA86 (October 2004) TA251 (April 2012)</td>
<td>4,226,042</td>
</tr>
<tr>
<td>Enoxaparin</td>
<td>AWMSG reference no. 125 (28/05/2010)</td>
<td>3,920,357</td>
</tr>
<tr>
<td>Lenalidomide</td>
<td>TA171 (June 2009)</td>
<td>3,628,184</td>
</tr>
<tr>
<td>Ezetimibe</td>
<td>TA132 (November 2007)</td>
<td>3,282,540</td>
</tr>
<tr>
<td>Tacrolimus capsules</td>
<td>TA85 (September 2004) TA99 (April 2006)</td>
<td>2,871,982</td>
</tr>
</tbody>
</table>

*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

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

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

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Ministerial ratification date</th>
<th>Company estimated spend</th>
<th>Actual spend (percent of estimate)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Year 1</td>
<td>Year 2</td>
</tr>
<tr>
<td>Tacrolimus modified release tablets</td>
<td>01/09/2011</td>
<td>£376,096</td>
<td>£714,582</td>
</tr>
<tr>
<td>Ferric carboxymaltose</td>
<td>01/09/2011</td>
<td>£196,539</td>
<td>£271,602</td>
</tr>
<tr>
<td>Collagenase Clostridium histolyticum (Xiapex®)</td>
<td>20/12/2011</td>
<td>£71,136</td>
<td>£141,024</td>
</tr>
<tr>
<td>Tapentadol modified release tablets</td>
<td>09/01/2012</td>
<td>£32,940</td>
<td>£161,040</td>
</tr>
<tr>
<td>Esomeprazole IV solution</td>
<td>25/04/2012</td>
<td>£1,565</td>
<td>£1,565</td>
</tr>
<tr>
<td>Fluorouracil/salicylic acid</td>
<td>19/06/2012</td>
<td>£37,741</td>
<td>£72,662</td>
</tr>
<tr>
<td>Rilpivirine</td>
<td>23/07/2012</td>
<td>£56,074</td>
<td>£126,776</td>
</tr>
<tr>
<td>Rifaximin 200 mg tablet</td>
<td>23/07/2012</td>
<td>£7,520</td>
<td>£7,520</td>
</tr>
<tr>
<td>Dexametadomine</td>
<td>07/08/2012</td>
<td>£124,108</td>
<td>£186,304</td>
</tr>
<tr>
<td>Dihydroartemisinin/piperaquine phosphate</td>
<td>07/08/2012</td>
<td>£1,200</td>
<td>£1,200</td>
</tr>
<tr>
<td>Rufinamide oral suspension</td>
<td>25/10/2012</td>
<td>£18,612</td>
<td>£18,612</td>
</tr>
<tr>
<td>Eslicarbazepine acetate</td>
<td>09/11/2012</td>
<td>£116,510</td>
<td>£136,089</td>
</tr>
<tr>
<td>Paliperidone palmitate depot injection</td>
<td>09/11/2012</td>
<td>£167,523</td>
<td>£1,875,082</td>
</tr>
<tr>
<td>Ramipril oral solution</td>
<td>09/11/2012</td>
<td>£14,400</td>
<td>£14,400</td>
</tr>
<tr>
<td>Fidaxomicin</td>
<td>11/12/2012</td>
<td>£157,400</td>
<td>£243,874</td>
</tr>
<tr>
<td>Argatroban</td>
<td>16/01/2013</td>
<td>£379,115</td>
<td>£379,115</td>
</tr>
</tbody>
</table>

The actual spend on tacrolimus modified release tablets, esomeprazole IV solution, fluorouracil/salicylic acid, rilpivirine, dexametadomine, 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®), rilpivirine 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

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

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.

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

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

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

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/subgroup 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/subgroup 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

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

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

<table>
<thead>
<tr>
<th>Medicine</th>
<th>ABMU</th>
<th>Aneurin Bevan</th>
<th>BCU</th>
<th>Cardiff and Vale</th>
<th>Cwm Taf</th>
<th>Powys</th>
<th>Wales</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amifampridine</td>
<td>0</td>
<td>0</td>
<td>5,082</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Artemether/ lumefantrine</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>23</td>
<td>0</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td>Azilsartan medoxomil</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>657</td>
<td>218</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Azithromycin eye drops</td>
<td>131</td>
<td>23</td>
<td>203</td>
<td>210</td>
<td>7</td>
<td>119</td>
<td>42</td>
</tr>
<tr>
<td>Bilastine</td>
<td>0</td>
<td>28</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Bimatprost/timolol eye drops</td>
<td>1,803</td>
<td>140</td>
<td>770</td>
<td>315</td>
<td>0</td>
<td>123</td>
<td>0</td>
</tr>
<tr>
<td>Bosantan</td>
<td>4,588</td>
<td>1,510</td>
<td>0</td>
<td>3,020</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Ciprofloxacin ear drops</td>
<td>519</td>
<td>80</td>
<td>859</td>
<td>264</td>
<td>0</td>
<td>123</td>
<td>105</td>
</tr>
<tr>
<td>Colesevelam</td>
<td>14,980</td>
<td>6,021</td>
<td>15,879</td>
<td>18,313</td>
<td>3,423</td>
<td>20,632</td>
<td>8,052</td>
</tr>
<tr>
<td>Dapoxetine</td>
<td>396</td>
<td>666</td>
<td>127</td>
<td>328</td>
<td>15</td>
<td>41</td>
<td>0</td>
</tr>
<tr>
<td>Ethinylestradiol/drospirenone</td>
<td>116</td>
<td>165</td>
<td>88</td>
<td>182</td>
<td>50</td>
<td>73</td>
<td>0</td>
</tr>
<tr>
<td>Hydroxyccarbamide</td>
<td>0</td>
<td>6,000</td>
<td>500</td>
<td>1,133</td>
<td>0</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Mercaptamine bitartrate</td>
<td>0</td>
<td>13,004</td>
<td>0</td>
<td>1,270</td>
<td>5,320</td>
<td>8,360</td>
<td>0</td>
</tr>
<tr>
<td>Paliperidone MR tablets</td>
<td>0</td>
<td>1,994</td>
<td>1,362</td>
<td>778</td>
<td>5,253</td>
<td>24</td>
<td>1,362</td>
</tr>
<tr>
<td>Racacodotril capsules</td>
<td>0</td>
<td>18</td>
<td>34</td>
<td>0</td>
<td>9</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sevelamer carbonate powder</td>
<td>1,132</td>
<td>234</td>
<td>849</td>
<td>0</td>
<td>495</td>
<td>605</td>
<td>0</td>
</tr>
<tr>
<td>Sodium oxybate</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>10,800</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Tadalafil (Adcirca®)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>491</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Tapentadol film coated tablets</td>
<td>4,181</td>
<td>2,414</td>
<td>2,755</td>
<td>6,871</td>
<td>442</td>
<td>5,170</td>
<td>386</td>
</tr>
<tr>
<td>Tocofersolan</td>
<td>0</td>
<td>0</td>
<td>3,064</td>
<td>0</td>
<td>0</td>
<td>218</td>
<td>0</td>
</tr>
<tr>
<td>Triptorelin powder for suspension</td>
<td>2,898</td>
<td>828</td>
<td>11,178</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Vildagliptin/metformin hydrochloride</td>
<td>14,109</td>
<td>34,822</td>
<td>2,077</td>
<td>32,949</td>
<td>4,223</td>
<td>23,555</td>
<td>476</td>
</tr>
<tr>
<td>Total (£)</td>
<td>44,853</td>
<td>67,947</td>
<td>44,827</td>
<td>77,604</td>
<td>19,455</td>
<td>59,059</td>
<td>10,423</td>
</tr>
</tbody>
</table>


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).
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

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

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

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

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

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

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

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Alendronic acid tablets</td>
<td>717,085</td>
<td>584,114</td>
<td>578,376</td>
<td>1,879,575</td>
</tr>
<tr>
<td>Denosumab</td>
<td>281,015</td>
<td>384,120</td>
<td>552,442</td>
<td>1,217,577</td>
</tr>
<tr>
<td>Raloxifene hydrochloride</td>
<td>132,256</td>
<td>107,796</td>
<td>88,230</td>
<td>328,284</td>
</tr>
<tr>
<td>Risedronate sodium</td>
<td>426,960</td>
<td>140,988</td>
<td>113,054</td>
<td>681,002</td>
</tr>
<tr>
<td>Strontium ranelate</td>
<td>577,927</td>
<td>537,648</td>
<td>375,444</td>
<td>1,491,019</td>
</tr>
<tr>
<td>Teriparatide</td>
<td>519,726</td>
<td>547,349</td>
<td>555,399</td>
<td>1,622,474</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>2,654,971</strong></td>
<td><strong>2,302,015</strong></td>
<td><strong>2,262,945</strong></td>
<td><strong>7,219,931</strong></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Alendronic acid</td>
<td>530,489</td>
<td>523,235</td>
<td>522,720</td>
<td>1.5%</td>
</tr>
<tr>
<td>Ibandronic acid</td>
<td>27,432</td>
<td>24,809</td>
<td>23,281</td>
<td>15.1%</td>
</tr>
<tr>
<td>Raloxifene hydrochloride</td>
<td>6,421</td>
<td>5,397</td>
<td>4,655</td>
<td>27.5%</td>
</tr>
<tr>
<td>Risedronate sodium</td>
<td>52,272</td>
<td>48,294</td>
<td>46,191</td>
<td>11.6%</td>
</tr>
<tr>
<td>Strontium ranelate</td>
<td>20,515</td>
<td>19,570</td>
<td>13,728</td>
<td>33.1%</td>
</tr>
</tbody>
</table>
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

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

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

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>
<thead>
<tr>
<th>Medicine</th>
<th>ABMU</th>
<th>Aneurin Bevan</th>
<th>BCU</th>
<th>Cardiff and Vale</th>
<th>Cwm Taf</th>
<th>Hywel Dda</th>
<th>Powys</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dapagliflozin</td>
<td>30,511</td>
<td>26,132</td>
<td>18,095</td>
<td>54,425</td>
<td>7,002</td>
<td>65,280</td>
<td>2,607</td>
</tr>
<tr>
<td>Exenatide</td>
<td>159,682</td>
<td>290,975</td>
<td>197,350</td>
<td>156,815</td>
<td>205,266</td>
<td>82,639</td>
<td>23,338</td>
</tr>
<tr>
<td>Exenatide modified release for injection</td>
<td>97,608</td>
<td>67,578</td>
<td>99,403</td>
<td>71,783</td>
<td>13,278</td>
<td>196,403</td>
<td>24,374</td>
</tr>
<tr>
<td>Insulin detemir</td>
<td>305,789</td>
<td>446,128</td>
<td>365,583</td>
<td>200,340</td>
<td>227,784</td>
<td>257,939</td>
<td>89,094</td>
</tr>
<tr>
<td>Insulin glargine</td>
<td>861,675</td>
<td>1,258,163</td>
<td>1,372,556</td>
<td>1,211,039</td>
<td>431,413</td>
<td>840,646</td>
<td>292,404</td>
</tr>
<tr>
<td>Linagliptin</td>
<td>212,266</td>
<td>80,415</td>
<td>71,542</td>
<td>51,885</td>
<td>48,136</td>
<td>82,655</td>
<td>12,709</td>
</tr>
<tr>
<td>Linagliptin/metformin</td>
<td>7,695</td>
<td>1,696</td>
<td>399</td>
<td>2,562</td>
<td>133</td>
<td>1,239</td>
<td>33</td>
</tr>
<tr>
<td>Liraglutide</td>
<td>798,142</td>
<td>1,192,347</td>
<td>563,538</td>
<td>880,035</td>
<td>329,067</td>
<td>620,031</td>
<td>207,972</td>
</tr>
<tr>
<td>Saxagliptin</td>
<td>152,551</td>
<td>439,641</td>
<td>166,319</td>
<td>415,348</td>
<td>157,033</td>
<td>209,289</td>
<td>11,692</td>
</tr>
<tr>
<td>Sitagliptin</td>
<td>992,359</td>
<td>1,041,742</td>
<td>798,895</td>
<td>769,059</td>
<td>470,293</td>
<td>744,099</td>
<td>214,304</td>
</tr>
<tr>
<td>Vildagliptin</td>
<td>18,074</td>
<td>32,888</td>
<td>12,676</td>
<td>21,970</td>
<td>10,012</td>
<td>39,625</td>
<td>6,289</td>
</tr>
<tr>
<td>Vildagliptin/metformin hydrochloride</td>
<td>14,109</td>
<td>34,822</td>
<td>2,077</td>
<td>32,949</td>
<td>4,223</td>
<td>23,555</td>
<td>476</td>
</tr>
<tr>
<td><strong>Total (£)</strong></td>
<td><strong>3,650,461</strong></td>
<td><strong>4,912,527</strong></td>
<td><strong>3,688,433</strong></td>
<td><strong>3,868,210</strong></td>
<td><strong>1,903,640</strong></td>
<td><strong>3,163,400</strong></td>
<td><strong>885,292</strong></td>
</tr>
</tbody>
</table>

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 | 6,084 |

QOF diabetic population (March 2013) | 31,659 | 36,323 | 36,748 | 22,161 | 16,869 | 21,950 | 7,589 | 7,589 |

Spend (£) per diabetic patient | 115 | 135 | 100 | 175 | 113 | 144 | 117 | 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.
REFERENCES

## Appendix 1. Usage of NICE/AWMSG Appraised Medicines

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### Medicine Recommendation Report

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**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