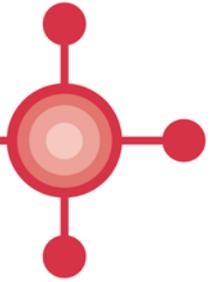


All Wales Medicines Strategy Group

Grŵp Strategaeth Meddyginiaethau Cymru Gyfan



Medicines Identified as Low Priority for Funding in NHS Wales – Paper 2

December 2018

This document has been prepared by the All Wales Prescribing Advisory Group (AWPAG) with support from 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, Medicines Identified as Low Priority for Funding in NHS Wales – Paper 2. December 2018.



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1.0 INTRODUCTION

The purpose of this document is to encourage clinically effective and cost-effective use of resources at a time when there are real financial pressures on the NHS. This document provides prescribing advice to clinicians and health boards in Wales, with the aim of reducing unwarranted variation in the use of medicines that should not routinely be prescribed.

It will be for health boards to interpret the advice and determine how it is best implemented; this will include determining the circumstances in which these medicines should or should not be used.

Prescribers are expected to have due regard for this advice when deciding whether or not to prescribe these medicines. However, the guidance contained herein does not remove the clinical discretion of the prescriber in accordance with their professional duties.

2.0 BACKGROUND

In 2015–2016, prescribing expenditure in NHS Wales totalled £0.85 billion¹. This represented 5.7% of total Welsh Government expenditure. It is therefore vital that a prudent approach is taken to review medicines that offer a limited clinical benefit to patients and are therefore considered a low priority for funding.

Welsh Government, NHS Wales Chairs and Chief Executives and Medical Directors have agreed a National Improvement Programme, which includes a commitment to identify opportunities to improve prescribing and develop a list of medicines for restricted use. This work has been progressed via the Chief Pharmacists Group/Chief Pharmacists (peer) Group, via the All Wales Prescribing Advisory Group (AWPAG), and has been based on priority areas identified by NHS Clinical Commissioners.

The advice contained within this document aims to reduce inappropriate variation in prescribing of medicines identified as low priority for funding across NHS Wales. This will ensure that health boards/trusts and clinicians are able to make the most efficient use of the resources available to them.

This document is the second of a series aimed at decreasing the prescribing of medicines identified as a low priority for funding in NHS Wales. The first [Low Priority for Funding](#) document was published in October 2017.

¹ This figure is a combined calculation of primary care and secondary care spends taken from CASPA (NHS Wales Shared Services Partnership) and Medusa (NHS Wales Informatics Service) systems respectively.

3.0 RECOMMENDATIONS

The aim of this document is to minimise the prescribing of medicines that offer low clinical effectiveness to patients or where more cost-effective treatments are available. Four medicines/medicine groups have been identified for the purposes of this document. These are:

- omega-3 fatty acid compounds
- oxycodone and naloxone combination product
- paracetamol and tramadol combination product
- perindopril arginine.

The first of these, omega-3 fatty acid compounds, are considered to be items of low clinical effectiveness due to a lack of robust evidence. For the others, they are considered to be items which are clinically effective but more cost-effective alternatives are available. In Table 1, a specific recommendation has been provided for each of these medicine groups, as well as the rationale for the recommendation, and any guidance on patient exemptions. As with the first paper, the recommendations are based on the NHS England document: ['Items which should not routinely be prescribed in primary care: Guidance for CCGs'](#).

The 2017–2018 NHS Wales expenditure for each identified medicine group is also provided within Table 1. However, this does not necessarily represent the potential savings available as alternative products may need to be substituted. Appendix 1 provides a primary and secondary care breakdown of this expenditure.

Appendix 2 provides a list of the products used to populate the primary care spend calculations.

Appendix 3 provides maps showing expenditure data for each health board. These data have been provided by PrescQIPP, which is an NHS funded, not-for-profit organisation supporting quality, optimised prescribing for patients.

Appendix 4 provides the primary care spend per 1,000 patients for each health board in 2017–2018. Appendix 5 provides primary care spend per 1,000 patients trend data for each health board from December 2013 to March 2018.

All health boards and Velindre Trust will be expected to action this advice and put mechanisms in place to ensure these areas are reviewed, with direction given by Medical Directors working with their Chief Pharmacists. Where necessary, medicines management teams should work closely together with relevant specialist teams to ensure patients identified as part of these recommendations are supported appropriately.

As part of this process it is recommended that the formulary status of each of these medicines is reviewed and that the medicines are incorporated into the local Interventions Not Normally Used (INNU) policies. These medicines should not be routinely prescribed or initiated for any new patients unless this is specified in the recommendations or associated patient exemptions listed herein. Patients currently prescribed these medicines should be reviewed and switched to an alternative product where appropriate. Access to these medicines outside of these recommendations should only be via the Individual Patient Funding Request (IPFR) process.

Some resources to help support the implementation of these recommendations are detailed in Appendix 6.

Appendix 7 provides an overview of the progress made with the medicines contained within the first Low Priority for Funding paper.

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A dashboard hosted within the [Server for Prescribing Information Reporting and Analysis \(SPIRA\)](#), accessible to all users who are on the NHS Wales Network, provides more detailed analysis for the usage of medicines identified within the Low Priority for Funding papers.

Table 1. Medicines identified as low priority for funding within NHS Wales and not recommended for routine prescribing

Recommendation rationale	NHS Wales expenditure 2017–2018
Omega-3 fatty acid compounds	
<p>Explanation: Omega-3 fatty acid compounds are essential fatty acids which can be obtained from the diet. They are licensed for adjunct to diet and statin therapy in type IIb or type III hypertriglyceridemia; adjunct to diet in type IV hypertriglyceridemia; adjunct in secondary prevention in those who have had a myocardial infarction (MI) in the preceding three months. NICE have reviewed the evidence and advised they are not suitable for routine prescribing by making the following “Do not do” recommendations:</p> <ul style="list-style-type: none"> • Do not offer or advise people to use omega-3 fatty acid capsules or supplemented foods to prevent another MI. If people choose to take omega-3 fatty acid capsules or eat supplemented foods, be aware that there is no evidence of harm. • Do not offer omega-3 fatty acid compounds for the prevention of cardiovascular disease (CVD) to any of the following: <ul style="list-style-type: none"> ○ people who are being treated for primary prevention ○ people who are being treated for secondary prevention ○ people with chronic kidney disease ○ people with type 1 diabetes ○ people with type 2 diabetes. • Do not offer the combination of a bile acid sequestrant (anion exchange resin), fibrate, nicotinic acid or omega-3 fatty acid compound with a statin for primary/secondary CVD prevention. • Do not offer omega-3 fatty acids to adults with non-alcoholic fatty liver disease because there is not enough evidence to recommend their use. • Do not use omega-3 fatty acids to manage sleep problems in children and young people with autism. • People with familial hypercholesterolemia should not routinely be recommended to take omega-3 fatty acid supplements. • Do not offer omega-3 or omega-6 fatty acid compounds to treat multiple sclerosis. <p>A recent Cochrane review found moderate- and high-quality evidence to suggest that increasing eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) has little or no effect on mortality or cardiovascular health. Previous suggestions of benefits from EPA and DHA supplements appear to originate from trials with higher risk of bias.</p> <p>Recommendation: Within NHS Wales it is recommended that omega-3 fatty acids should not be routinely prescribed. Patients currently prescribed omega-3 fatty acids should be reviewed and switched to an alternative product where appropriate. However, where omega-3 fatty acid compounds are being used in the management of disorders of triglyceride metabolism, acute pancreatitis can be precipitated on withdrawal. Therefore, any review in these patients should be made in close collaboration with relevant specialist teams.</p> <p>Patient exemptions: Patients using omega-3 fatty acid compounds who have severe hypertriglyceridaemia. Patients in class II-IV chronic heart failure ('off-label' use).</p>	<p style="text-align: center;">£502,816 (This figure is the combined 2017–2018 expenditure in primary and secondary care. See Appendix 2 for specific basket of medicines measured.)</p>
<p>The guidance contained herein does not remove the clinical discretion of the prescriber in accordance with their professional duties.</p>	

Recommendation rationale	NHS Wales expenditure 2017–2018
Oxycodone and naloxone combination product	
<p>Explanation: Oxycodone and naloxone combination product is used to treat severe pain and can also be used second line in restless legs syndrome. The opioid antagonist naloxone is added to counteract opioid-induced constipation by blocking the action of oxycodone at opioid receptors locally in the gut.</p> <p>A PrescQIPP bulletin did not identify a benefit of oxycodone and naloxone combination product over other analgesia (with laxatives if necessary). Due to the significant cost of the oxycodone and naloxone combination product and the unclear role of the combination product in therapy compared with individual products, routine use is not appropriate.</p> <p>Recommendation: Within NHS Wales it is recommended that oxycodone and naloxone combination product should not be routinely prescribed. Patients currently prescribed oxycodone and naloxone combination product should be reviewed and switched to an alternative product where appropriate.</p> <p>Patient exemptions: No specific patient exemptions identified. However, in exceptional circumstances, if there is a need for the oxycodone and naloxone combination product to be prescribed, this should be in a cooperation arrangement with a multi-disciplinary team and/or healthcare professional.</p>	<p>£319,067 (This figure is the combined 2017–2018 expenditure in primary and secondary care. See Appendix 2 for specific basket of medicines measured.)</p>
<p>The guidance contained herein does not remove the clinical discretion of the prescriber in accordance with their professional duties.</p>	
Paracetamol and tramadol combination product	
<p>Explanation: The paracetamol and tramadol combination product is more expensive than purchasing the individual components as separate products (Drug Tariff).</p> <p>A PrescQIPP bulletin did not identify any significant advantages over individual products, however it does recognise that some people may prefer to take one product instead of two. There are also different strengths of tramadol (37.5 mg) and paracetamol (325 mg) in the combination product compared to commonly available individual preparations of tramadol (50 mg) and paracetamol (500 mg), although PrescQIPP found no evidence that a combination product is more effective or safer than the individual preparations.</p> <p>Due to the extra cost of a combination product, paracetamol and tramadol combination product should not be routinely prescribed.</p> <p>Recommendation: Within NHS Wales it is recommended that paracetamol and tramadol combination product should not be routinely prescribed. Patients currently prescribed paracetamol and tramadol combination product should be reviewed and switched to an alternative product where appropriate.</p> <p>Patient exemptions: No specific patient exemptions identified.</p>	<p>£86,926 (This figure is the combined 2017–2018 expenditure in primary and secondary care. See Appendix 2 for specific basket of medicines measured.)</p>
<p>The guidance contained herein does not remove the clinical discretion of the prescriber in accordance with their professional duties.</p>	

Recommendation rationale	NHS Wales expenditure 2017–2018
Perindopril arginine	
<p>Explanation: Perindopril is an angiotensin-converting-enzyme (ACE) inhibitor used in heart failure, hypertension, diabetic nephropathy and prophylaxis of cardiovascular events. The perindopril arginine salt version was developed as it is more stable in extremes of climate than the perindopril erbumine salt, which results in a longer shelf-life. Perindopril arginine is significantly more expensive than perindopril erbumine and a PrescQIPP bulletin stated there was no clinical advantage of the arginine salt.</p> <p>NICE CG127 <i>Hypertension in adults: diagnosis and management</i> recommends that prescribing costs are minimised.</p> <p>Due to the significant extra costs associated with the perindopril arginine, and perindopril erbumine being readily available, perindopril arginine should not be routinely prescribed. A 2.5 mg dose of perindopril arginine is equivalent to a 2 mg dose of perindopril tert-butylamine (erbumine).</p> <p>Recommendation: Within NHS Wales it is recommended that perindopril arginine should not be routinely prescribed in primary care. Patients currently prescribed perindopril arginine should be reviewed and switched to an alternative product where appropriate.</p> <p>Patient exemptions: No specific patient exemptions identified.</p>	<p style="text-align: center;">£82,790</p> <p>(This figure is the combined 2017–2018 expenditure in primary and secondary care. See Appendix 2 for specific basket of medicines measured.)</p>
<p>The guidance contained herein does not remove the clinical discretion of the prescriber in accordance with their professional duties.</p>	

APPENDIX 1. PRIMARY AND SECONDARY CARE EXPENDITURE IN 2017–2018 ON THE FOUR MEDICINES/MEDICINE GROUPS IDENTIFIED AS LOW PRIORITY FOR FUNDING WITHIN NHS WALES

Table 2. Primary and secondary care 2017–2018 expenditure on four low priority medicines/medicine groups

Low priority item	Primary care expenditure (£)	Secondary care expenditure (£)	Total NHS Wales expenditure (£)
Omega-3 fatty acid compounds	485,678	17,138	502,816
Oxycodone and naloxone combination product	306,300	12,768	319,067
Paracetamol and tramadol combination product	86,903	23	86,926
Perindopril arginine	82,584	206	82,790

APPENDIX 2. BASKETS OF MEDICINES USED FOR THE EXPENDITURE CALCULATIONS

Table 3. Basket of medicines used for the ‘Omega-3 fatty acid compounds’ expenditure calculation

Omega-3 fatty acid compounds
Teromeg_Cap 1g
Prestylon_Cap 1g
Omega 3-Acid-Ethyl Esters_Cap 1g
Omega 3_Cap 1000mg
Dualtis_Cap 1000mg
Omega-3 Marine Triglycerides
Gppe Cap_Omacor 1g
Omacor_Cap 1g
Omega-H3_Geriatric Cap
Omega-3 Fish Oil_Cap

Table 4. Basket of medicines used for the ‘Oxycodone and naloxone combination product’ expenditure calculation

Oxycodone and naloxone combination product
Oxycodone Hcl/naloxone Hcl_Tab 10/5mgm/r
Oxycodone Hcl/naloxonehcl_Tab 20/10mgm/r
Oxycodone Hcl/naloxonehcl_Tab 5/2.5mgm/r
Oxycodone Hcl/naloxonehcl_Tab 40/20mgm/r
Targinat_Tab 10mg/5mg M/r
Targinat_Tab 20mg/10mg M/r
Targinact_Tab 5mg/2.5mg M/r
Targinact_Tab 40mg/20mg M/r

Table 5. Basket of medicines used for the ‘Paracetamol and tramadol combination product’ expenditure calculation

Paracetamol and tramadol combination product
Tramadol Hcl/paracet_Tab 37.5mg/325mg
Tramadol/paracet_Tab Eff 37.5/325mg S/f
Tramacet_Tab 37.5mg/325mg
Tramacet_Tab Eff 37.5mg/325mg

Table 6. Basket of medicines used for the ‘Perindopril arginine’ expenditure calculation

Perindopril arginine
Perindopril Arginine_Tab 2.5mg
Perindopril Arginine_Tab 5mg
Perindopril Arginine_Tab 10mg
Coversyl Arginine_Tab 2.5mg
Coversyl Arginine_Tab 5mg
Coversyl Arginine_Tab 10mg
Perindopril Argin/indapam_Tab 5mg/1.25mg
Coversyl Arginine Plus_Tab

APPENDIX 3. PRESCQIPP DATA MAPS FOR APRIL 2017 TO MARCH 2018

Figure 1. Omega-3 fatty acid compounds usage in Welsh health boards

Due to notable differences between medicine baskets used to populate PrescQIPP and NHS Wales data this map is currently omitted.

Figure 2. Oxycodone and naloxone combination product usage in Welsh health boards

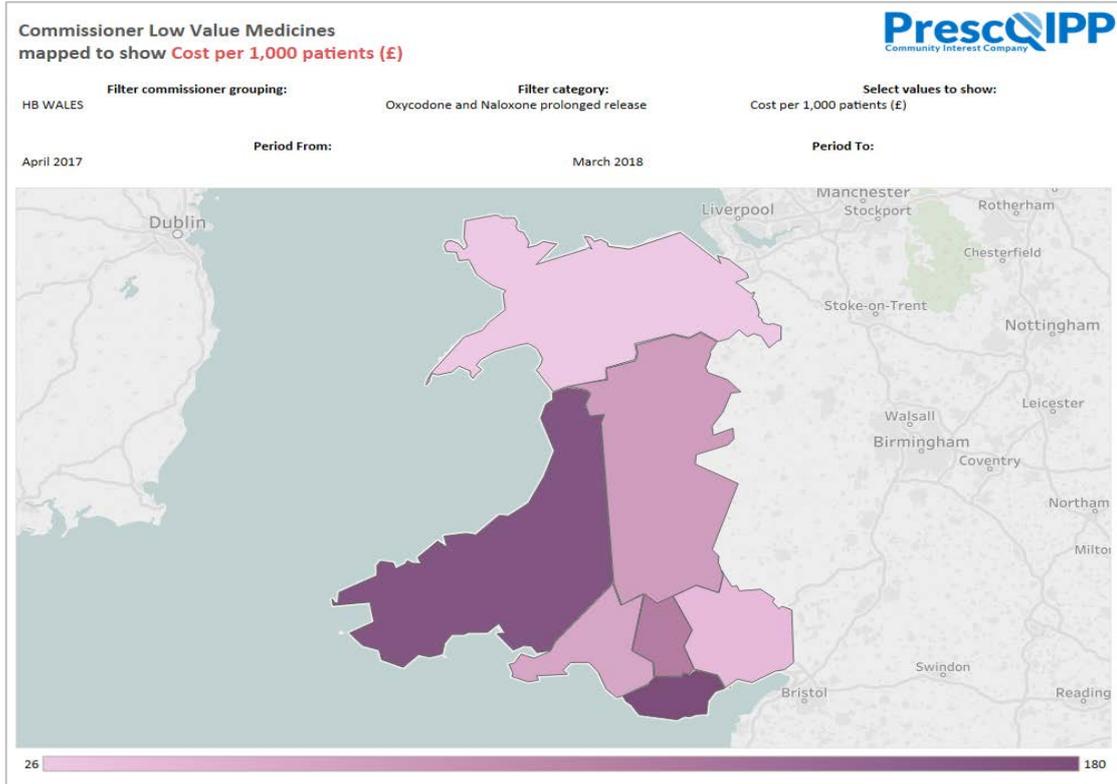


Figure 3. Paracetamol and tramadol combination product usage in Welsh health boards

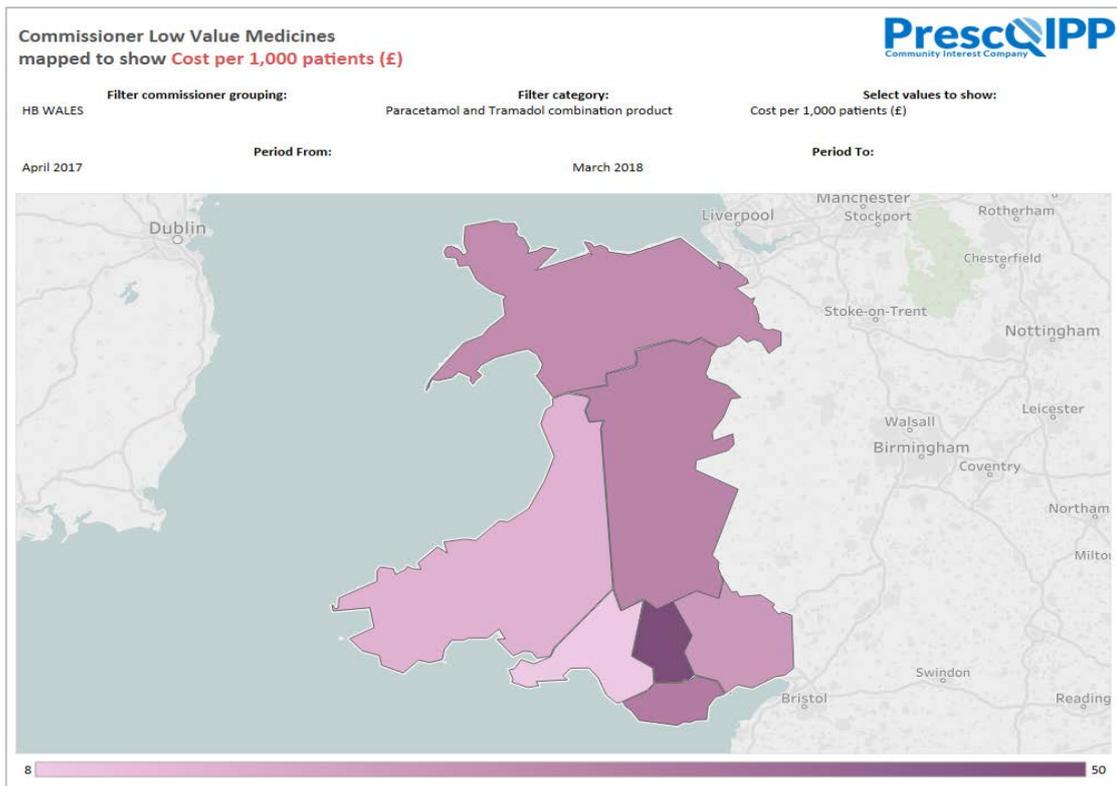
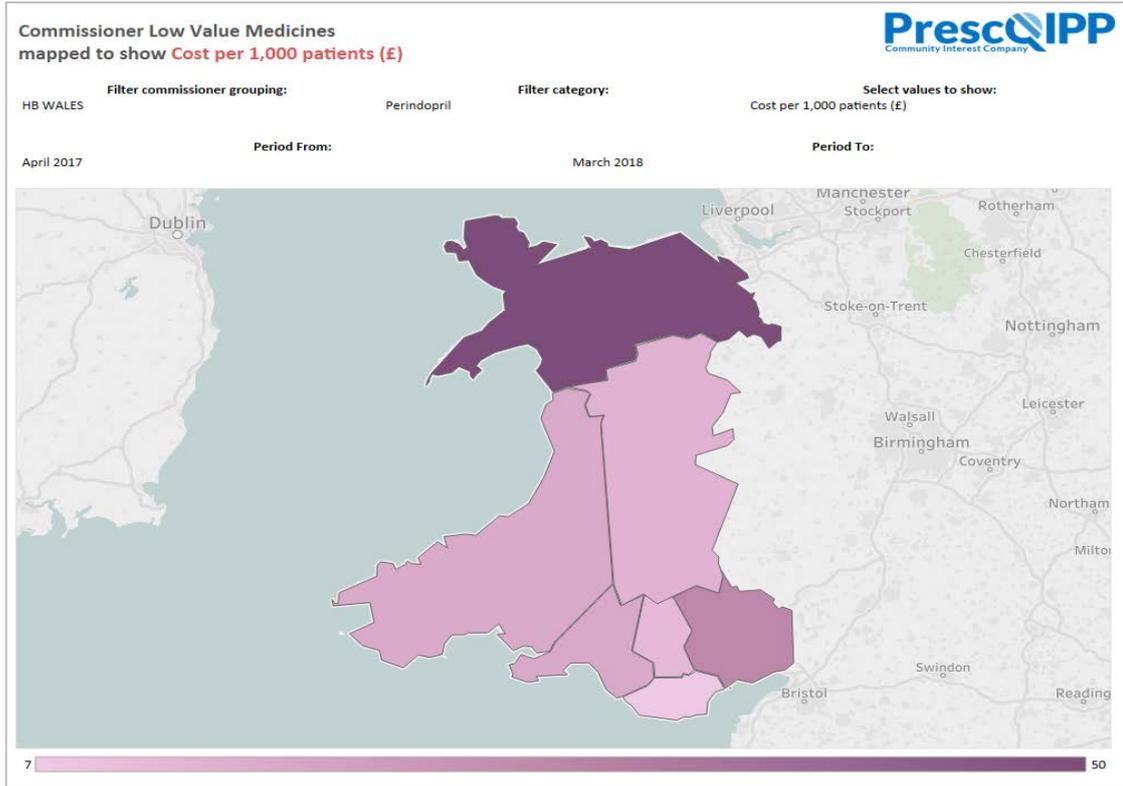


Figure 4. Perindopril arginine usage in Welsh health boards



APPENDIX 4. COST PER 1,000 PATIENTS DATA**Table 7. Primary care cost per 1,000 patients (£) in 2017–2018 for the four medicines/medicine groups identified as low priority for funding per health board in Wales**

	ABMU	Aneurin Bevan	BCU	Cardiff and Vale	Cwm Taf	Hywel Dda	Powys	Wales
Omega-3 fatty acid compounds	33.24	40.14	42.56	27.92	50.29	43.10	14.02	35.90
Oxycodone and naloxone combination product	17.54	11.31	6.96	48.50	30.87	45.72	20.41	25.90
Paracetamol and tramadol combination product	2.26	6.26	7.39	8.84	13.60	4.12	8.15	7.23
Perindopril arginine	4.50	7.44	13.42	1.80	3.14	4.44	3.68	5.49

Data is for National-GP in CASPA and calculated as an average of four quarters in 2017–2018

APPENDIX 5. PRIMARY CARE SPEND PER 1,000 PATIENTS TREND DATA

Figure 5. Omega-3 fatty acid compounds cost per 1,000 patients (£) trend data

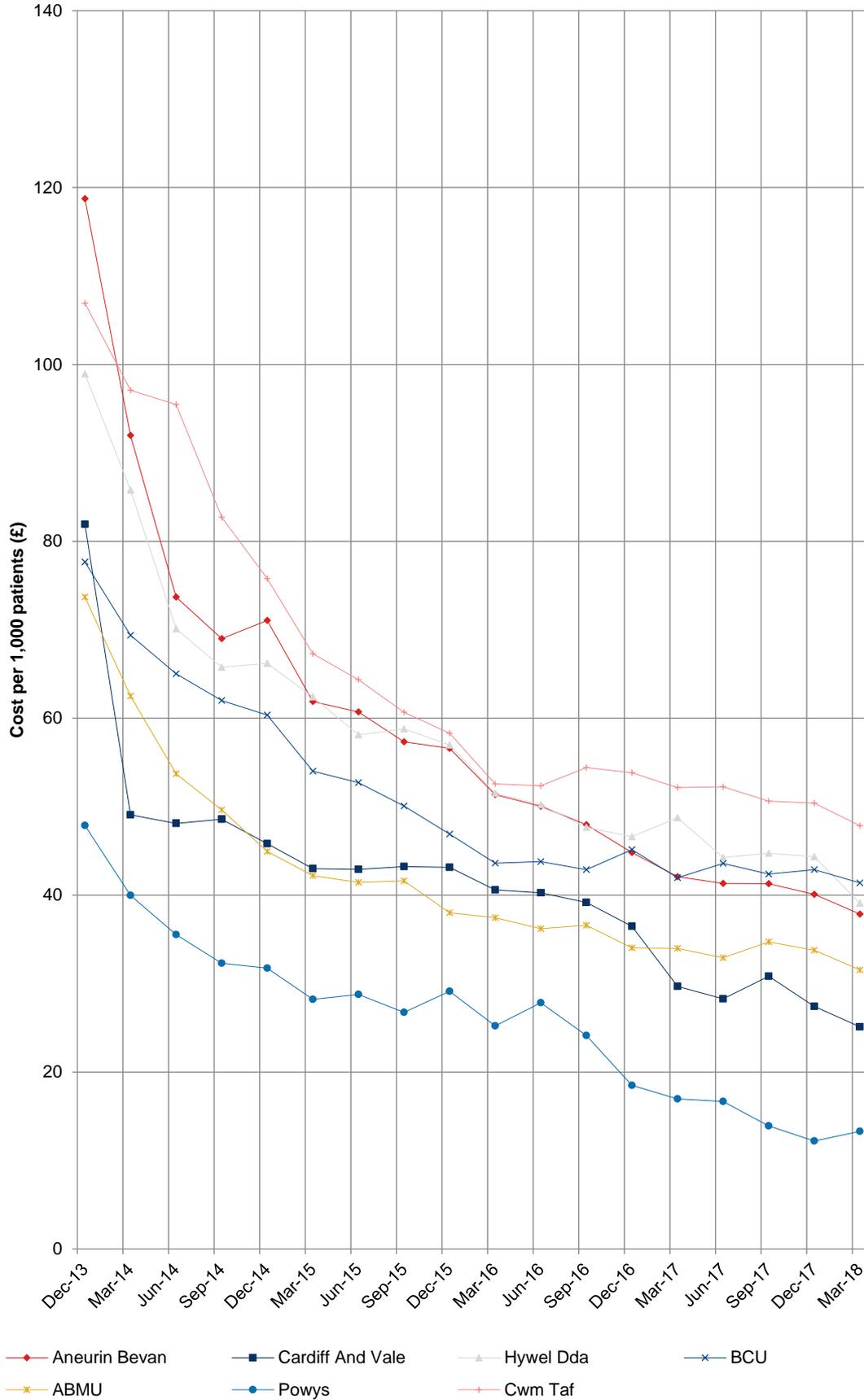


Figure 6. Oxycodone and naloxone combination product cost per 1,000 patients (£) trend data

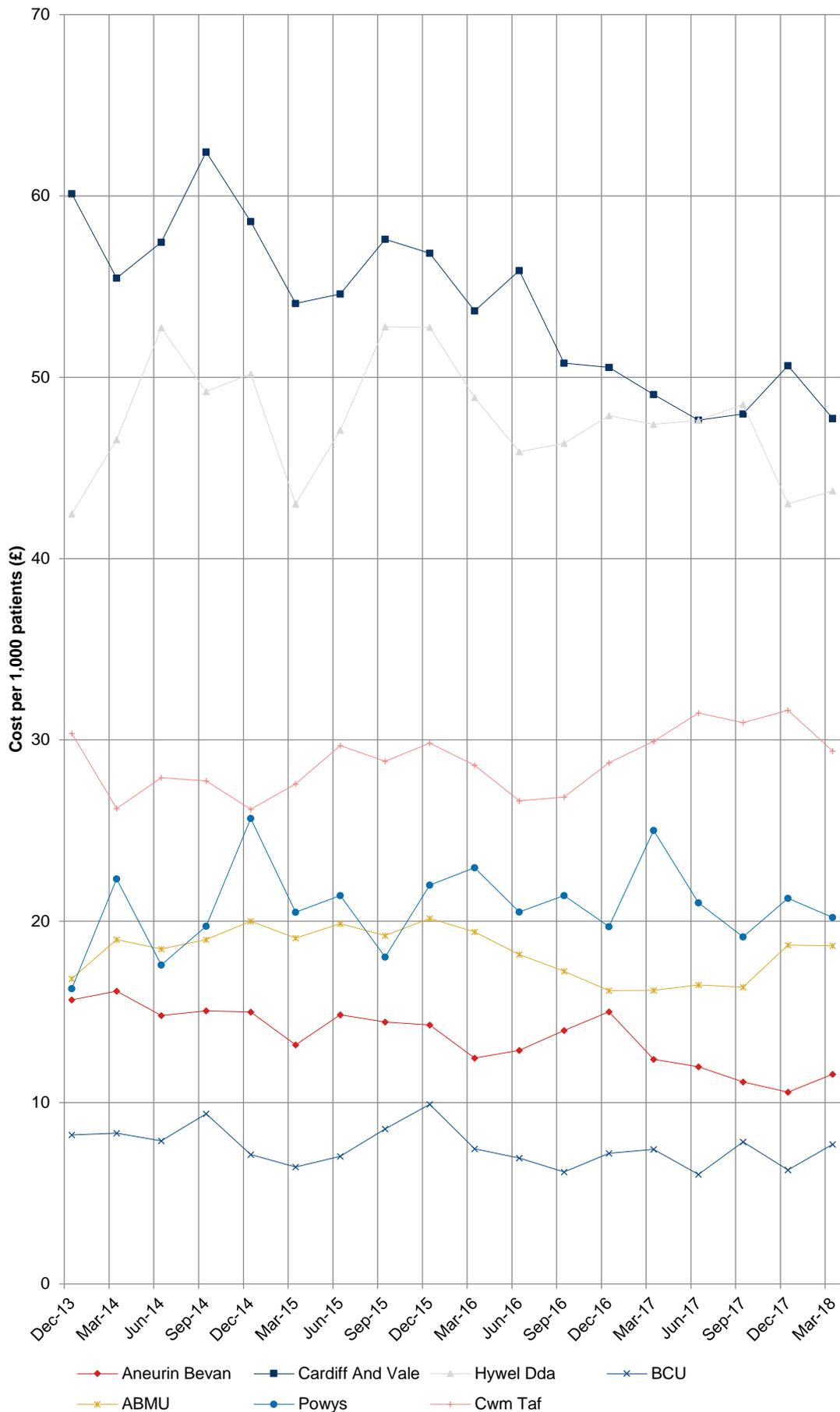


Figure 7. Paracetamol and tramadol combination product cost per 1,000 patients (£) trend data

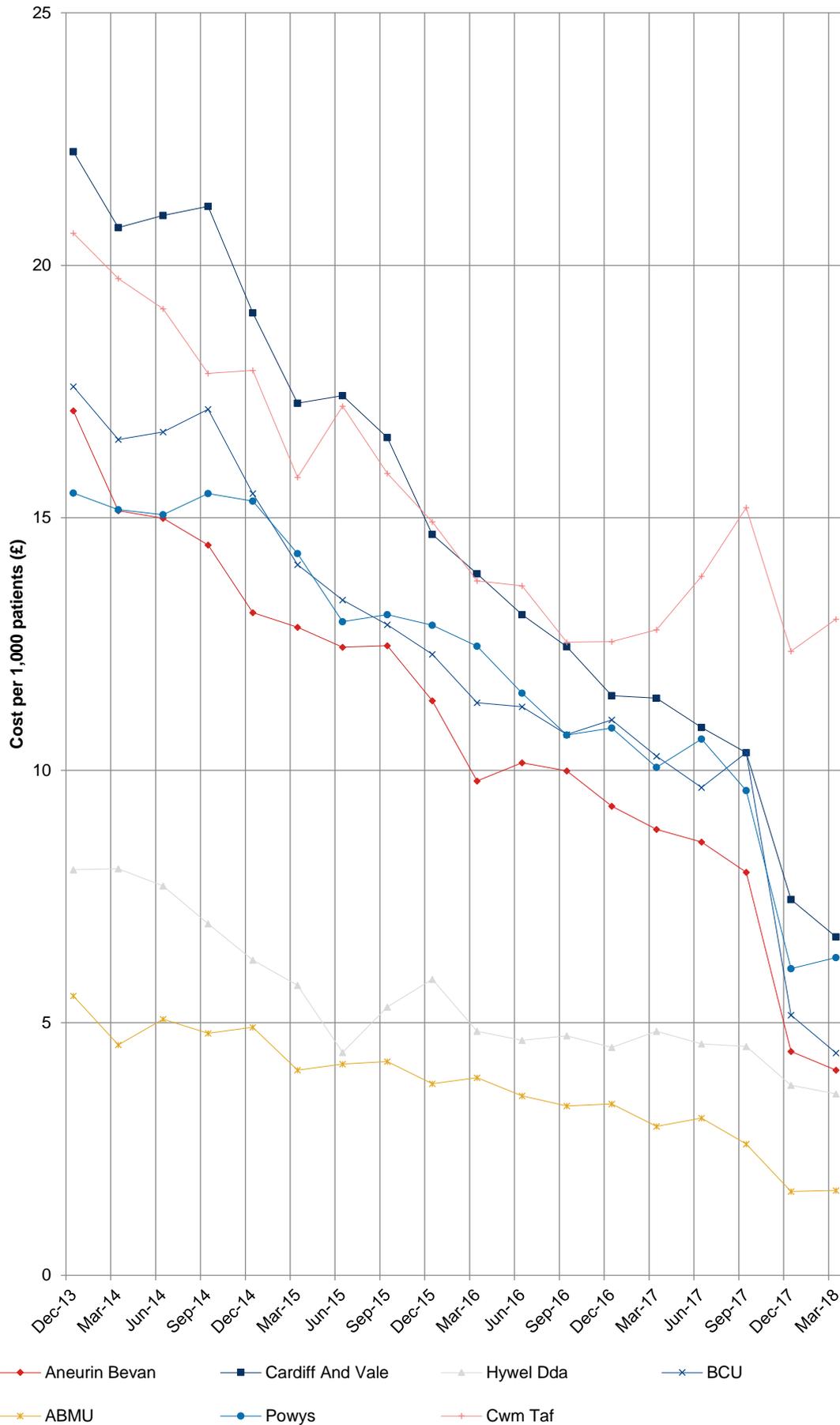
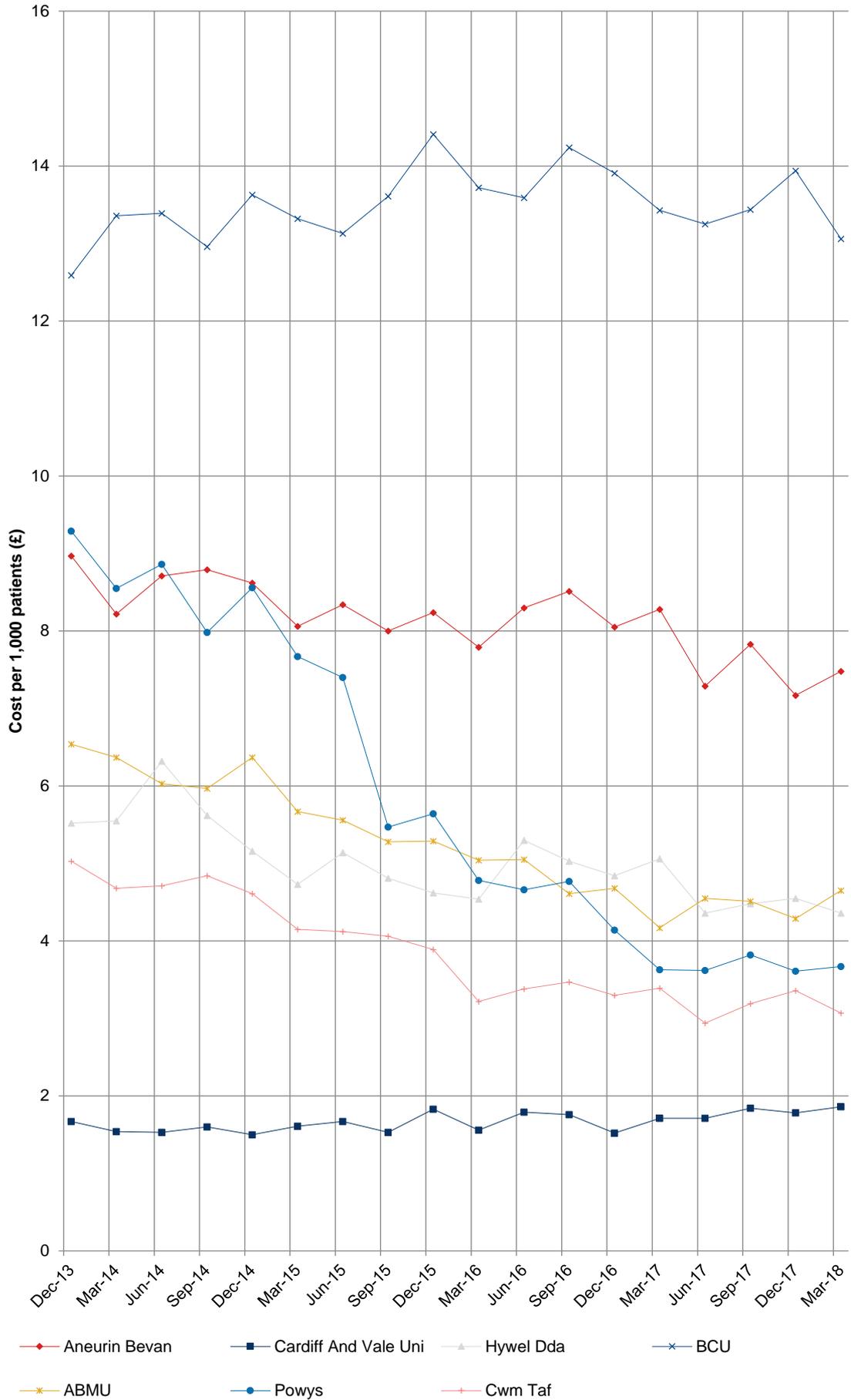


Figure 8. Perindopril arginine cost per 1,000 patients (£) trend data



APPENDIX 6. SUPPORTING INFORMATION FOR IMPLEMENTATION OF THE RECOMMENDATIONS

1. Omega-3 fatty acid compounds – NICE ‘Do not do’ recommendations

- [Do not offer or advise people to use omega-3 fatty acid capsules or supplemented foods to prevent another MI. If people choose to take omega-3 fatty acid capsules or eat supplemented foods, be aware that there is no evidence of harm.](#)
- [Do not offer omega-3 fatty acid compounds for the prevention of cardiovascular disease \(CVD\) to any of the following:](#)
 - [people who are being treated for primary prevention](#)
 - [people who are being treated for secondary prevention](#)
 - [people with chronic kidney disease](#)
 - [people with type 1 diabetes](#)
 - [people with type 2 diabetes.](#)
- [Do not offer the combination of a bile acid sequestrant \(anion exchange resin\), fibrate, nicotinic acid or omega-3 fatty acid compound with a statin for primary/secondary CVD prevention.](#)
- [Do not offer omega-3 fatty acids to adults with non-alcoholic fatty liver disease because there is not enough evidence to recommend their use.](#)
- [Do not use omega-3 fatty acids to manage sleep problems in children and young people with autism.](#)
- [People with familial hypercholesterolemia should not routinely be recommended to take omega-3 fatty acid supplements.](#)
- [Do not offer omega-3 or omega-6 fatty acid compounds to treat multiple sclerosis.](#)

2. Omega-3 fatty acid compounds – Further resources

- [NICE resources for 'Omega-3 fatty acids'](#)
- [PrescQIPP bulletin 210. 2018. Omega-3 fatty acid compounds and other fish oils](#)
- [PrescQIPP. Items which should not routinely be prescribed – patient leaflets](#)

3. Oxycodone and naloxone combination product

- [PrescQIPP bulletin 56. 2014. Oxycodone/naloxone prolonged release \(Targinact®\) tablets](#)
- [PrescQIPP. Items which should not routinely be prescribed – patient leaflets](#)

4. Paracetamol and tramadol combination product

- [PrescQIPP bulletin 62. 2014. Switching Tramacet® to paracetamol alone or paracetamol and codeine](#)
- [PrescQIPP. Items which should not routinely be prescribed – patient leaflets](#)

5. Perindopril arginine

- [PrescQIPP bulletin 59. 2014. Perindopril arginine](#)
- [PrescQIPP. Items which should not routinely be prescribed – patient leaflets](#)

APPENDIX 7. PRIMARY AND SECONDARY CARE EXPENDITURE IN 2016–2017 AND 2017–2018 ON THE FIVE MEDICINES IDENTIFIED AS LOW PRIORITY FOR FUNDING IN NHS WALES (PAPER 1)

Table 8. Primary and secondary care expenditure in 2016–2017

Low priority item	Primary care expenditure (£)	Secondary care expenditure (£)	Total NHS Wales expenditure (£)
Co-proxamol	238,179	22,749	260,928
Lidocaine 5% plasters	1,954,746	220,658	2,175,404
Tadalafil once daily (2.5 mg and 5 mg tablets)	1,450,728	24,089	1,474,817
Liothyronine oral preparations	1,195,847	308,198	1,504,045
Doxazosin modified release tablets	234,932	1,645	236,577

Table 9. Primary and secondary care expenditure in 2017–2018

Low priority item	Primary care expenditure (£)	Secondary care expenditure (£)	Total NHS Wales expenditure (£)
Co-proxamol	115,850	15,154	131,004
Lidocaine 5% plasters	1,954,230	173,906	2,128,136
Tadalafil once daily (2.5 mg and 5 mg tablets)	1,606,582	21,290	1,627,872
Liothyronine oral preparations	1,162,328	335,374	1,497,702
Doxazosin modified release tablets	225,495	1,546	227,041

Table 10. Primary and secondary care expenditure percentage change between 2016–2017 and 2017–2018

Low priority item	Primary care expenditure percentage change (%)	Secondary care expenditure percentage change (%)	Total NHS Wales expenditure percentage change (%)
Co-proxamol	-51.4	-33.4	-44.8
Lidocaine 5% plasters	-0.03	-21.2	-2.17
Tadalafil once daily (2.5 mg and 5 mg tablets)	10.7	-11.6	10.4
Liothyronine oral preparations	-2.80	8.82	-0.42
Doxazosin modified release tablets	-4.02	-6.02	-4.03

It should be noted that the Low Priority for Funding (Paper 1) was published in October 2017 and therefore only spending within quarters 3 and 4 of 2017–2018 have the potential to have been influenced by it.