All Wales Medicines Strategy Group

Grŵp Strategaeth Meddyginiaethau Cymru Gyfan

Medicines Identified as Low Priority for Funding in NHS Wales

October 2017

(Section on liothyronine updated and addendum added in November 2019)

This document has been prepared by the NHS Wales Pharmacy Directors with support from the All Wales Therapeutics and Toxicology Centre (AWTTC), and has been endorsed by the All Wales Medicines Strategy Group (AWMSG).

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CONTENTS

1.0 INTRODUCTION

The purpose of the document is to encourage clinically effective and cost effective use of resources at a time when there are real financial pressures on the NHS. The document provides prescribing advice to clinicians and health boards in Wales, with the aim of reducing unwarranted variation in 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 billion. This represents 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 primary care prescribing and develop a list of medicines for restricted use. This work has been progressed via the Pharmacy Directors peer group 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 and clinicians are able to make the most efficient use of the resources available to them.

3.0 RECOMMENDATIONS

The aim of this document is to minimise the prescribing of medicines that offer a limited clinical benefit to patients and where more cost effective treatments *may be* available. Five medicines have been identified for the purposes of this document.

The first of these five medicines is co-proxamol, which was withdrawn from the UK market in 2005. Any co-proxamol prescriptions currently issued are for an unlicensed product. Within NHS Wales it is recommended that co-proxamol is not prescribed. Further rationale for this recommendation is provided in Table 1.

The remaining four medicines identified are:

- lidocaine plasters
- tadalafil once daily preparations
- liothyronine
- doxazosin modified release tablets

For each of these four medicines Table 2 provides a specific recommendation, as well as the rationale for the recommendation, and any guidance on patient exemptions.

The 2016–2017 NHS Wales expenditure for each identified medicine is also provided within Tables 1 and 2. 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 maps showing expenditure data for Welsh health boards and English clinical commissioning groups (CCGs). Also included are tables illustrating the ranking of Welsh health boards in relation to all health boards and CCGs. These data have been provided by PrescQIPP, which is an NHS funded not-for-profit organisation supporting quality, optimised prescribing for patients.

All health boards and Velindre Trust will be expected to action this advice, with direction given by Medical Directors working with their Chief Pharmacists, to put in place mechanisms to ensure these areas are reviewed.

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 initiated for any new patients unless this is specified in the recommendations or patient exemptions listed below. Access to these medicines outside of these recommendations should only be via the Individual Patient Funding Request (IPFR) process.

Resources to support implementation of these recommendations are detailed in Appendix 3.

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

Recommendation rationale	NHS Wales expenditure 2016–2017
Co-proxamol	
Co-proxamol was withdrawn in 2005 on the advice of the Medicines and Healthcare products Regulatory Agency (MHRA) Committee on Safety of Medicines. This withdrawal was phased over a two-year period to allow alternative regimens to be prescribed. This advice has been recently highlighted again in a joint Health Professional Letter by the Chief Medical Officer and Chief Pharmaceutical Officer[1] in Welsh Government: • There is no robust evidence that co-proxamol is more effective than paracetamol alone in either chronic or acute use. • No patient group has been identified in which the risk/benefit ratio favours using co-proxamol. • The fatal dose of co-proxamol is relatively low and can be potentiated by alcohol and other CNS depressants. • Death from co-proxamol overdose occurs rapidly; the risk of dying after co-proxamol overdose is 2.3 times that for tricyclic antidepressants, 10 times that for co-codamol or co-dydramol, and 28.1 times that for paracetamol. • Co-proxamol is an unlicensed medicine[1]. ***Recommendation:*** **Within NHS Wales it is recommended that co-proxamol is not prescribed.** • All patients currently receiving prescriptions for co-proxamol should be urgently reviewed with the intention of switching patients to alternative, safer treatments. ***Patient exemptions:*** No specific patient exemptions identified.	£260,928

Table 2. Medicines identified as low priority for funding within NHS Wales and not recommended for routine prescribing

Recommendation rationale	NHS Wales expenditure 2016–2017
Lidocaine plasters	
Lidocaine 5% plasters are licensed for post herpetic neuralgia only. However, evidence for this and other unlicensed indications is limited and their place in therapy is unclear. With regards to their use in neuropathic pain NICE has recently stated there is no convincing evidence of effectiveness[2]. Therefore any potential benefit of treatment needs to be balanced against its high cost compared to other treatment options available. Significant savings are available by reviewing treatment and discontinuing if ineffective or being used for an unlicensed indication[3]. ***Recommendation*: Within NHS Wales it is recommended that the prescribing of lidocaine plasters in primary care should be restricted to the licensed indication of post herpetic neuralgia in patients for whom alternative treatments have proved ineffective or where alternative treatments are contra-indicated.** • Patients on long-term therapy with lidocaine plasters should be assessed for continued need, with the view to discontinuing treatment or having a longer plaster free period between applications. • Off label use should only be initiated by pain specialists in secondary care and should be in line with MHRA guidance on the use of off label and unlicensed medicines. • Patients being prescribed lidocaine plasters for an unlicensed indication should be reviewed with the intention of discontinuing treatment or switching to a licensed alternative wherever possible. ***Patient exemptions:*** No specific patient exemptions identified.	£2,175,404
Tadalafil – once daily preparations	
Update (January 2018) – Generic versions of once daily tadalafil are now available; this is likely to lead to a reduction in the Drug Tariff price for these preparations. Therefore health boards may wish to consider prioritising other medicines within this guidance.	
Tadalafil once daily (2.5 mg and 5 mg) is licensed for erectile dysfunction (ED) in men who anticipate a frequent use of tadalafil (i.e. at least twice weekly). This gives a potential advantage in that ED therapy could be taken without regard to timing of sexual activity. However, there is no current evidence to support a benefit in taking tadalafil on a daily basis over on demand treatment in the general ED population. This should also be considered in the context of treatment costs, with tadalafil once daily costing up to 30 times more than treatment with generic sildenafil on demand[4]. Tadalafil once daily 5 mg is also licensed for the signs and symptoms of benign prostatic hyperplasia (BPH) in adult males. An AWMSG Statement of Advice has been issued stating that in the absence of a submission from the holder of the marketing authorisation, tadalafil once daily 5 mg (Cialis®) cannot be endorsed for use within NHS Wales for the treatment of the signs and symptoms of BPH in adult males[5]. A once daily preparation of tadalafil 20 mg is licensed for the treatment of pulmonary hypertension (Adcirca®). An AWMSG Statement of Advice has been issued stating that tadalafil (Adcirca®) has not been endorsed for use within NHS Wales for the treatment of pulmonary arterial hypertension[6]. ***Recommendation*: Within NHS Wales it is recommended that tadalafil once daily preparations are not routinely prescribed.** • Patients currently being prescribed tadalafil once daily for ED should be reviewed and switched to an alternative on demand phosphodiesterase type 5 (PDE5) inhibitor. • Patients currently being prescribed tadalafil once daily for BPH should be referred for specialist review where appropriate. • Clinical evidence for the use of PDE5 inhibitors for penile rehabilitation is limited and conflicting. In the absence of robust evidence favouring a particular treatment regimen, local policy makers may advocate choosing the medicine with the lowest acquisition cost, where clinically appropriate[4]. ***Patient exemptions:*** No specific patient exemptions identified.	£1,474,817

<table>
<tr><th>Recommendation rationale</th><th>NHS Wales expenditure 2016–2017</th></tr>
<tr><td colspan="2">Liothyronine</td></tr>
<tr><td colspan="2">Update (November 2019) – Information contained within this section has been updated in light of recently published Regional Medicines Optimisation Committee (RMOC) guidance.</td></tr>
<tr><td>
Levothyroxine is the oral thyroid hormone of choice as it is cost effective, suitable for once daily dosing due to its long half-life and provides stable and physiological quantities of thyroid hormones for patients requiring replacement[7].

Liothyronine is not recommended for prescribing as it has a much shorter half-life and steady-state levels cannot be maintained with once daily dosing[7]. There is currently insufficient evidence of clinical effectiveness and cost effectiveness to support the use of liothyronine (either alone or in combination) for the treatment of hypothyroidism[7]. These recommendations also apply to patients prescribed unlicensed dried thyroid extracts (such as Armour Thyroid®, NP Thyroid® and Nature-Throid®). In 2016–2017 over £50,000 was spent on unlicensed dried thyroid extracts within NHS Wales.

Recommendation*: Within NHS Wales it is recommended that liothyronine is not routinely prescribed for treating primary hypothyroidism in patients who are not under the care of an endocrinologist. After initiation and a period of oversight by the endocrinologist, it may be appropriate for ongoing prescribing of liothyronine to be continued in primary care. The following table summarises recommendations on the use of liothyronine in specific patient populations[8]:
<table>
<tr><th>Indication and treatment regimen</th><th>Action for General Practitioners and NHS Consultants</th></tr>
<tr><td>Hypothyroidism
Patients currently receiving liothyronine monotherapy, or liothyronine and levothyroxine combination therapy</td><td>Patients currently prescribed liothyronine, or levothyroxine and liothyronine combination therapy, for hypothyroidism should be reviewed to consider switching to levothyroxine monotherapy where clinically appropriate. In some cases a retrospective review of the basis for the original diagnosis of hypothyroidism may be necessary. Arrangements should be made for switching to be undertaken by a consultant NHS endocrinologist, or by a General Practitioner with consultant NHS endocrinologist support. Patients who are currently obtaining supplies via private prescription or self-funding should not be offered NHS prescribing unless they meet the criteria in this guidance.
The consultant endocrinologist must specifically define the reason if any patient currently taking liothyronine should not undergo a trial titration to levothyroxine monotherapy, and this must be communicated to the General Practitioner.</td></tr>
<tr><td>Hypothyroidism
Levothyroxine and liothyronine combination therapy for new patients</td><td>In rare situations where patients experience continuing symptoms whilst on levothyroxine (that have a material impact upon normal day to day function), and other potential causes have been investigated and eliminated, a 3 month trial with additional liothyronine may occasionally be appropriate. This is only to be initiated by a consultant NHS endocrinologist. Following this trial the consultant NHS endocrinologist will advise on the need for ongoing liothyronine. Many endocrinologists may not agree that a trial of levothyroxine/liothyronine combination therapy is warranted in these circumstances and their clinical judgement is valid given the current understanding of the science and evidence of the treatments.</td></tr>
<tr><td>Oncology – Thyroid disease</td><td>Prescribing liothyronine in thyroid cancer, where it is used as an adjuvant to radioactive iodine treatment, should only be addressed by specialists in secondary/tertiary care. Thyroid cancer patients who have completed their treatment usually need to take levothyroxine for life and should be managed in the same way as patients with hypothyroidism.</td></tr>
<tr><td>Resistant depression
Liothyronine monotherapy, or liothyronine and levothyroxine combination therapy</td><td>All patients currently receiving liothyronine for a psychiatric indication should be reviewed by a consultant NHS psychiatrist, who should consider switching to an alternative treatment where clinically appropriate, or levothyroxine monotherapy where hypothyroidism is diagnosed. Patients continuing to receive liothyronine should be overseen by a consultant NHS psychiatrist.</td></tr>
</table>
Continued on page 7

* These recommendations have been updated following the publication of the Regional Medicines Optimisation Committee (RMOC) publication: ‘Guidance – Prescribing of Liothyronine’[8]
</td><td>£1,504,045</td></tr>
</table>

<table>
<tr><th>Recommendation rationale</th><th>NHS Wales expenditure 2016–2017</th></tr>
<tr><td colspan="2">Liothyronine – continued</td></tr>
<tr><td>
<table>
<tr><th>Indication and treatment regimen</th><th>Action for General Practitioners and NHS Consultants</th></tr>
<tr><td>Use of unlicensed thyroid extracts (e.g. Armour thyroid, ERFA Thyroid), plus compound thyroid hormones, iodine containing preparations, dietary supplementation.</td><td>The prescribing of unlicensed liothyronine and thyroid extract products is not supported.</td></tr>
</table>
Patient exemptions:
This recommendation does not apply to the use of liothyronine post thyroidectomy in thyroid cancer patients. Prescribing in thyroid and parathyroid cancer should only be addressed by specialists in secondary / tertiary care.
</td><td></td></tr>
<tr><td colspan="2">Doxazosin modified release tablets</td></tr>
<tr><td>Doxazosin is licensed for the treatment of hypertension and BPH. It has a long half-life of 22 hours making it suitable for once daily dosing. Immediate release and modified release forms of doxazosin are available. Both are administered once daily and so a modified release version of doxazosin offers no advantage in terms of patient adherence[9]. Modified release doxazosin is more than six times the cost of immediate release doxazosin[10].

Recommendation: Within NHS Wales it is recommended that doxazosin modified release tablets are not routinely prescribed.
Patients currently prescribed doxazosin modified release tablets should be reviewed and switched to an immediate release preparation.
For patients prescribed doxazosin tablets for the treatment of hypertension, review may be an opportunity to take into account NICE CG127 recommendations, which place alpha-blockers at step 4 (for consideration in resistant hypertension)[11].
Patient exemptions:
No specific patient exemptions identified.</td><td>£236,574</td></tr>
</table>

REFERENCES

1. Welsh Government. WHC (2017) 026 Health Professional Letter – Prescribing of co-proxamol. 2017. Available at: http://gov.wales/docs/dhss/publications/170619whc026en.pdf. Accessed December 2018.
2. National Institute for Health and Care Excellence. Clinical Guideline 173. Neuropathic pain: pharmacological management - 4-year surveillance 2017. Available at: https://www.nice.org.uk/guidance/cg173/evidence/appendix-a-summary-of-evidence-from-surveillance-pdf-4604023118 Accessed December 2018.
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4. PrescQIPP. Tadalafil once daily (Cialis® once-a-day). Bulletin 144. 2016. Available at: https://www.prescqipp.info/our-resources/bulletins/bulletin-144-tadalafil-once-daily-drop-list/. Accessed December 2018.
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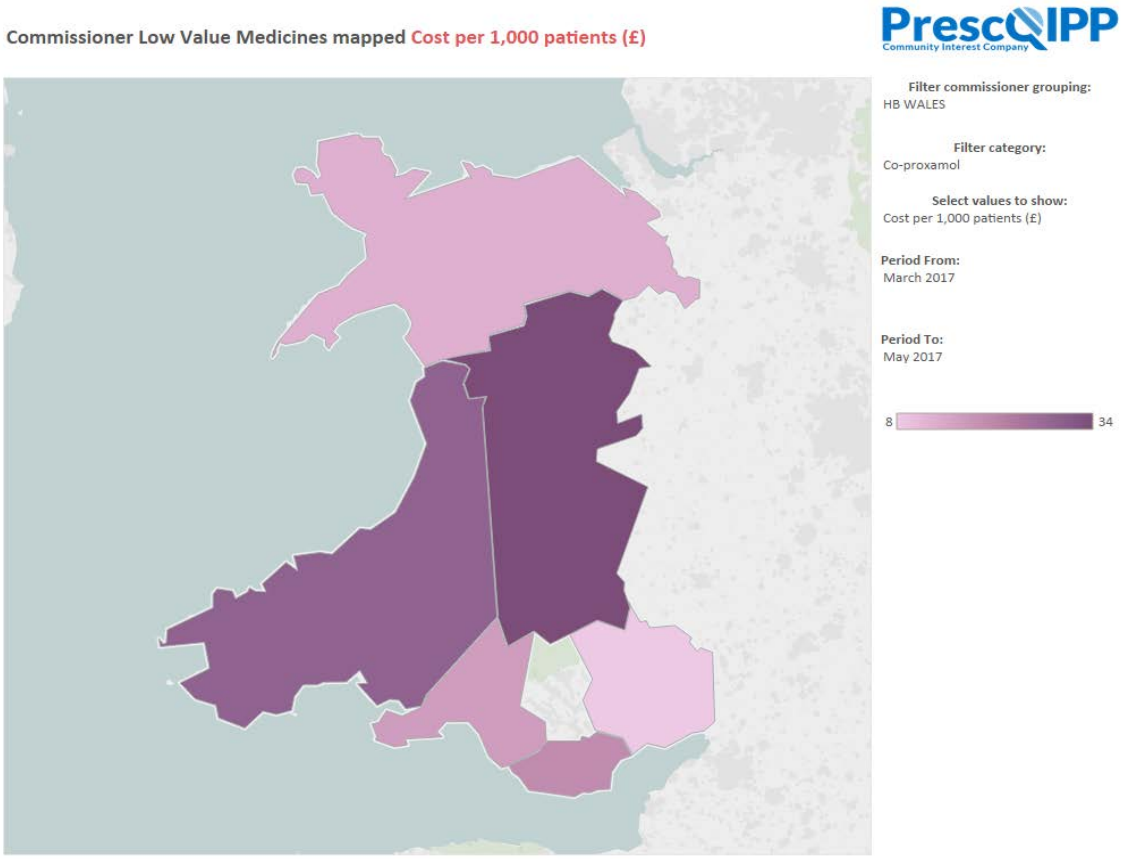
7. PrescQIPP. Switching liothyronine (L-T3) to levothyroxine (L-T4) in the management of primary hypothyroidism. Bulletin 121. 2016. Available at: https://www.prescqipp.info/our-resources/bulletins/bulletin-121-liothyronine/. Accessed December 2018.
8. Regional Medicines Optimisation Committee (RMOC). Guidance - prescribing of liothyronine. 2019. Available at: https://www.sps.nhs.uk/wp-content/uploads/2019/07/RMOC-Liothyronine-guidance-V2.6-final-1.pdf. Accessed September 2019.
9. PrescQIPP. Doxazosin modified release tablets. Bulletin 195. 2018. Available at: https://www.prescqipp.info/our-resources/bulletins/bulletin-195-doxazosin-mr/. Accessed December 2018.
10. NHS Business Services Authority. Drug Tariff. 2017. Available at: https://www.nhsbsa.nhs.uk/pharmacies-gp-practices-and-appliance-contractors/drug-tariff. Accessed December 2018.
11. National Institute for Health and Care Excellence. Clinical Guideline 127. Hypertension in adults: diagnosis and management (CG127). 2016. Available at: https://www.nice.org.uk/guidance/cg127. Accessed July 2019.

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

Low priority item	Primary care expenditure (£)	Secondary care expenditure (£)	Total NHS Wales expenditure (£)
Co-proxamol	238,179	22,749	260,928
Lidocaine 5% plasters	1,987,866	187,538	2,175,404
Tadalafil once daily (2.5 mg and 5 mg tablets)	1,466,663	8,154	1,474,817
Liothyronine oral preparations	1,250,752	253,293	1,504,045
Doxazosin modified release tablets	235,089	1,485	236,574

APPENDIX 2. PRESCQIPP DATA FOR MARCH TO MAY 2017

Figure 1. Co-proxamol usage in Welsh health boards and English CCGs



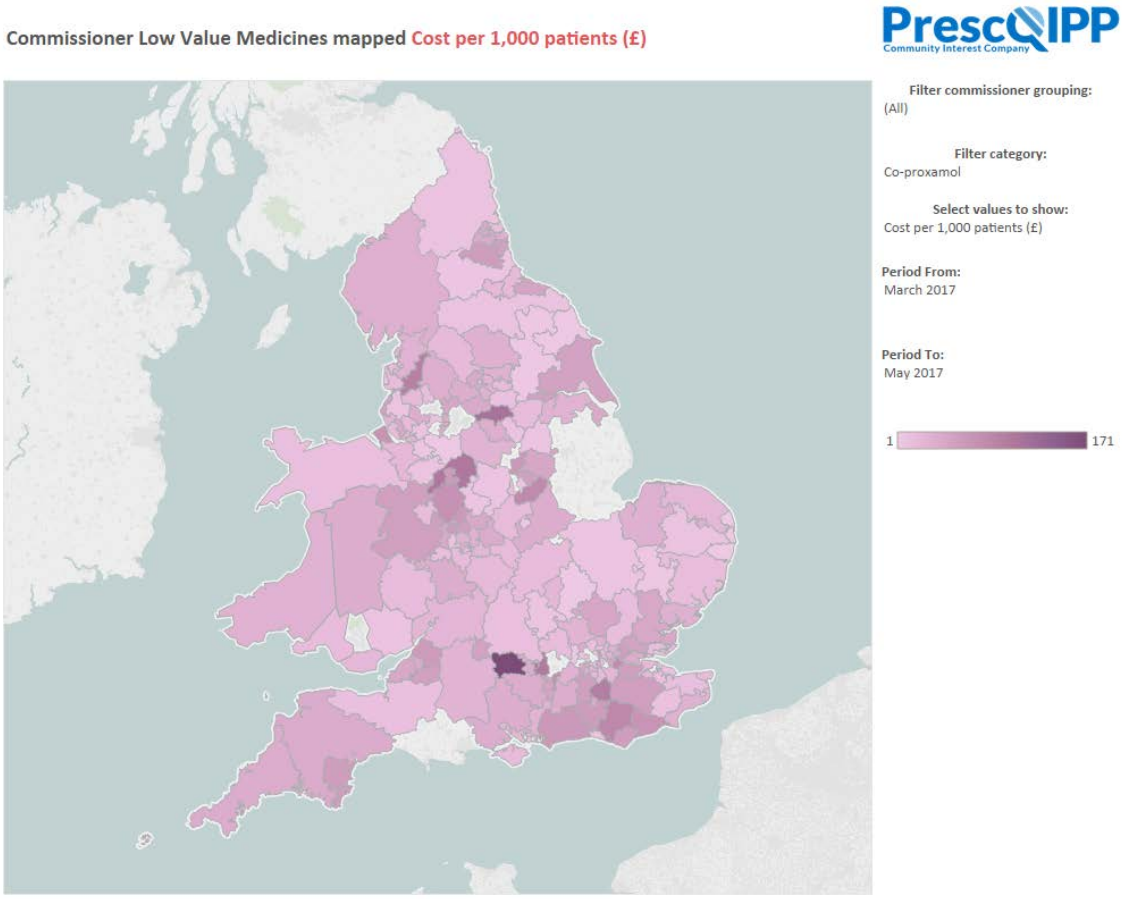


Figure 2. Lidocaine plaster usage in Welsh health boards and English CCGs

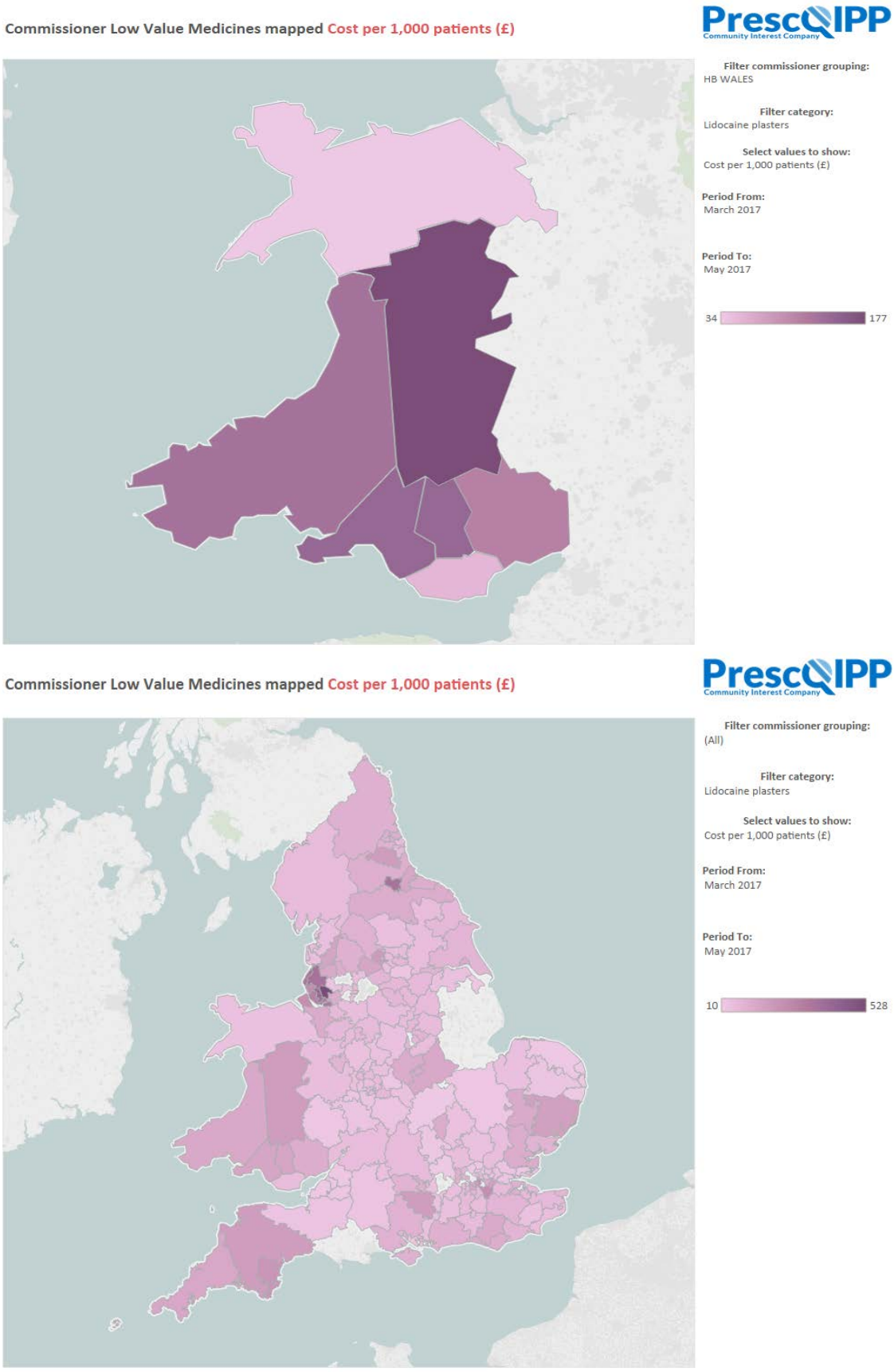


Figure 3. Tadalafil once daily usage in Welsh health boards and English CCGs

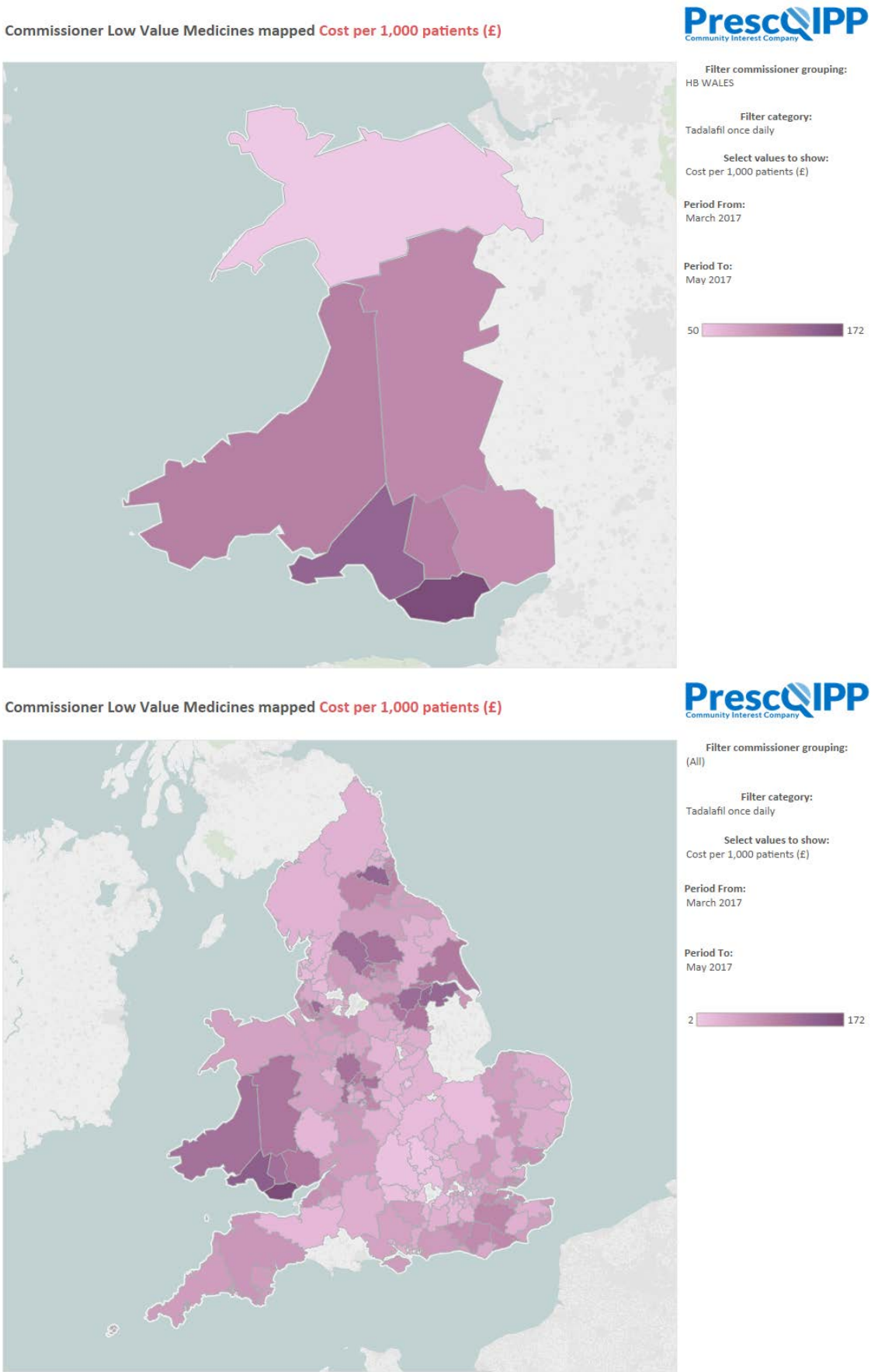


Figure 4. Liothyronine usage in Welsh health boards and English CCGs

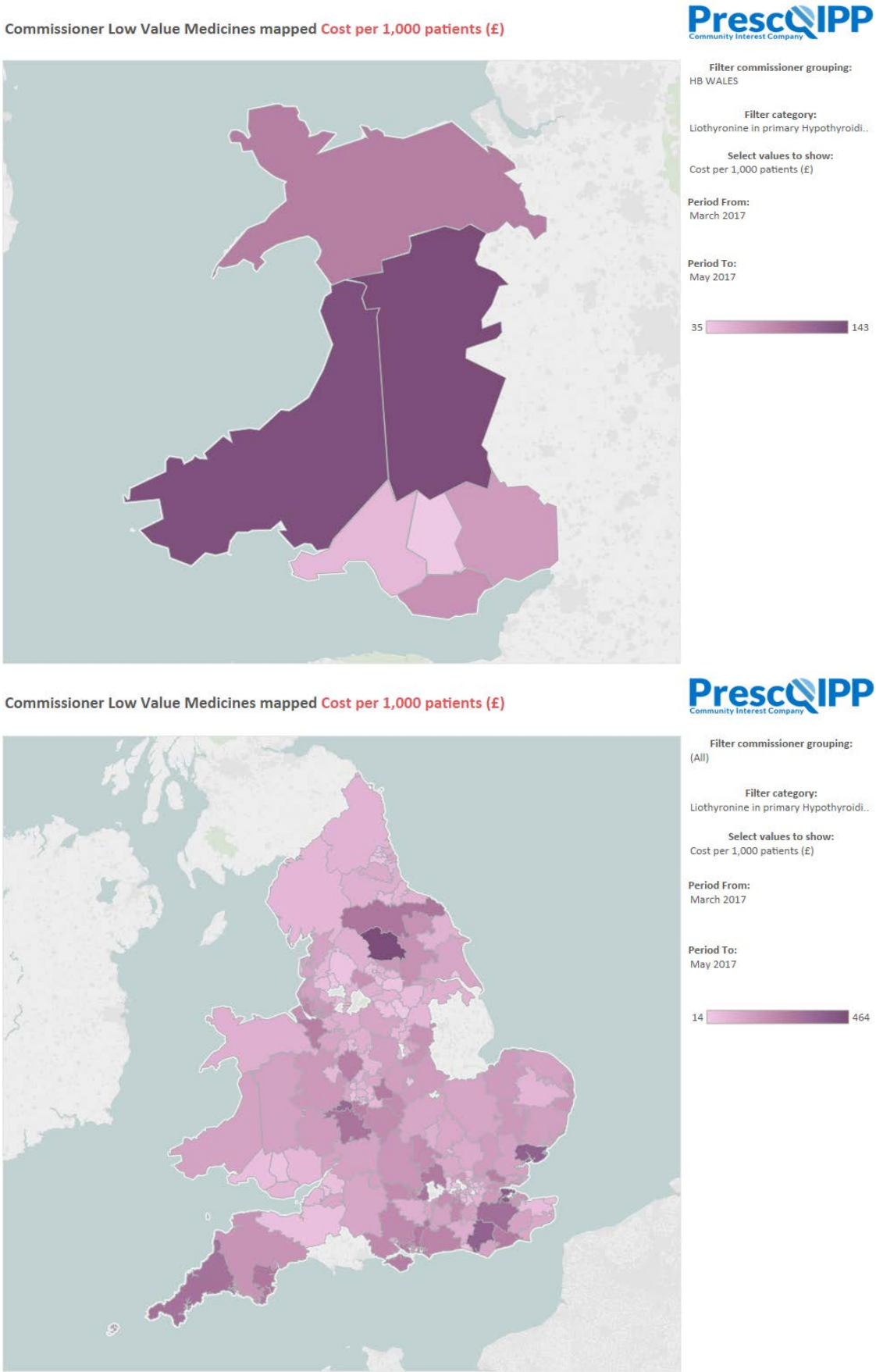
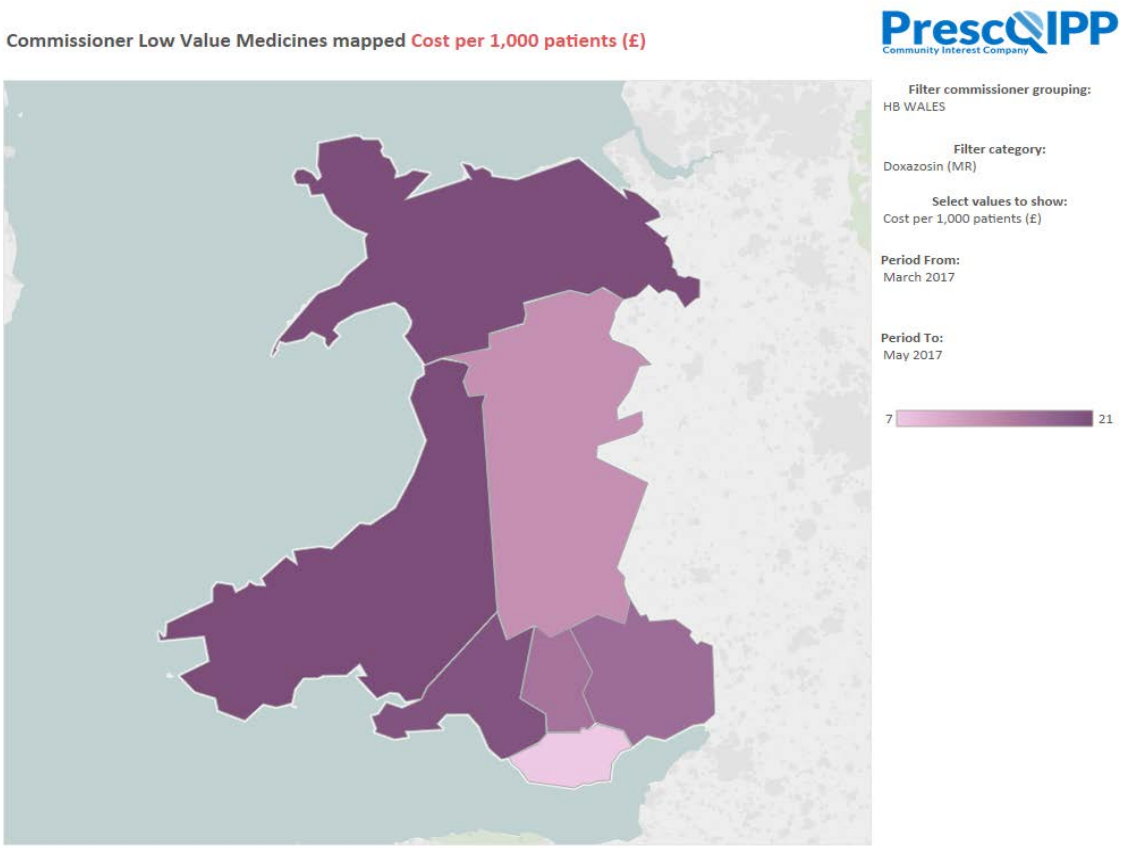


Figure 5. Doxazosin modified release usage in Welsh health boards and English CCGs



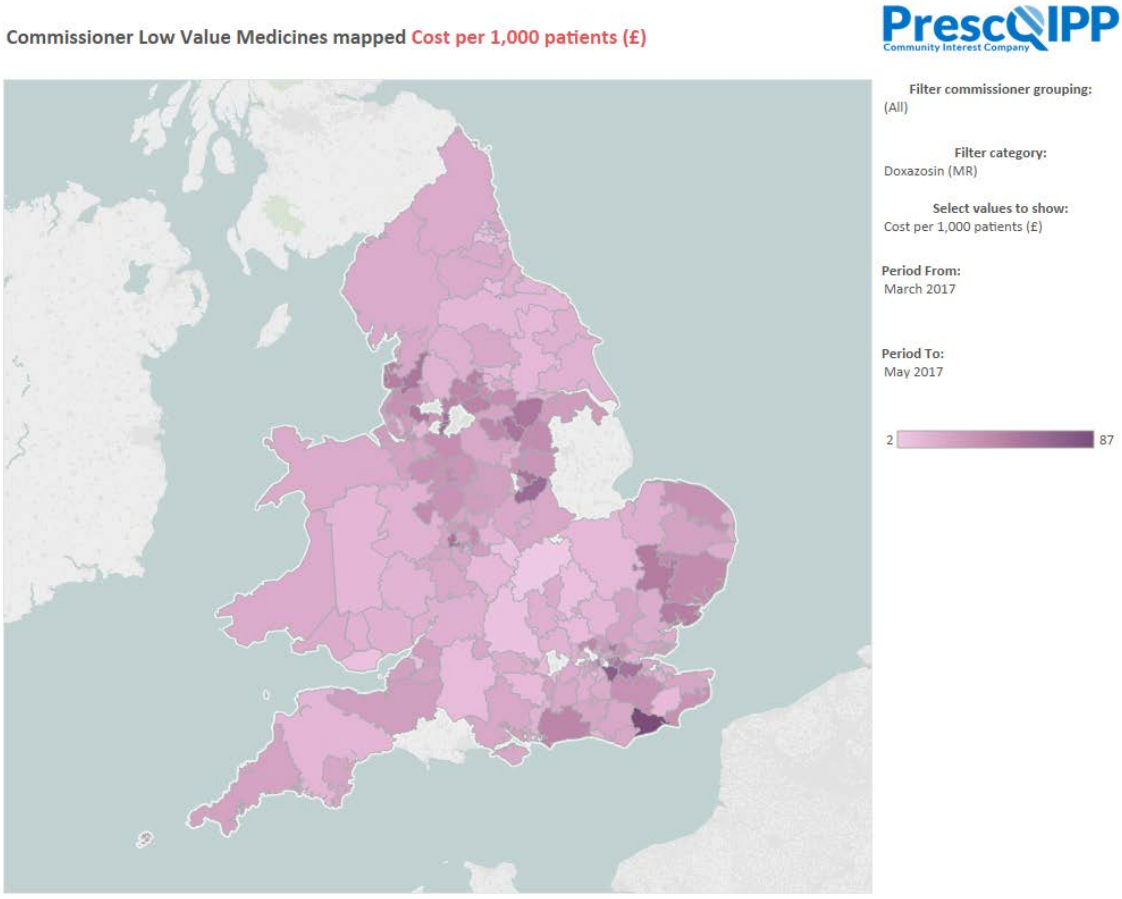


Table 3. Cost per 1,000 patients for the five medicines identified as low priority for funding per health board in Wales*

	ABM (£)	Aneurin Bevan (£)	BCU (£)	Cardiff and Vale (£)	Cwm Taf (£)	Hywel Dda (£)	Powys (£)
Co-proxamol	3.82	2.79	3.82	6.44	0	8.57	9.08
Lidocaine patch	66.57	53.19	15.32	21.98	60.89	75.14	67.25
Tadalafil once daily	46.01	32.71	15.81	54.56	37.58	37.73	35.65
Liothyronine	16.7	26.3	31.13	23.45	12.26	47.23	47.6
Doxazosin modified release	6.35	5.55	6.74	2.24	5.23	6.86	4.23

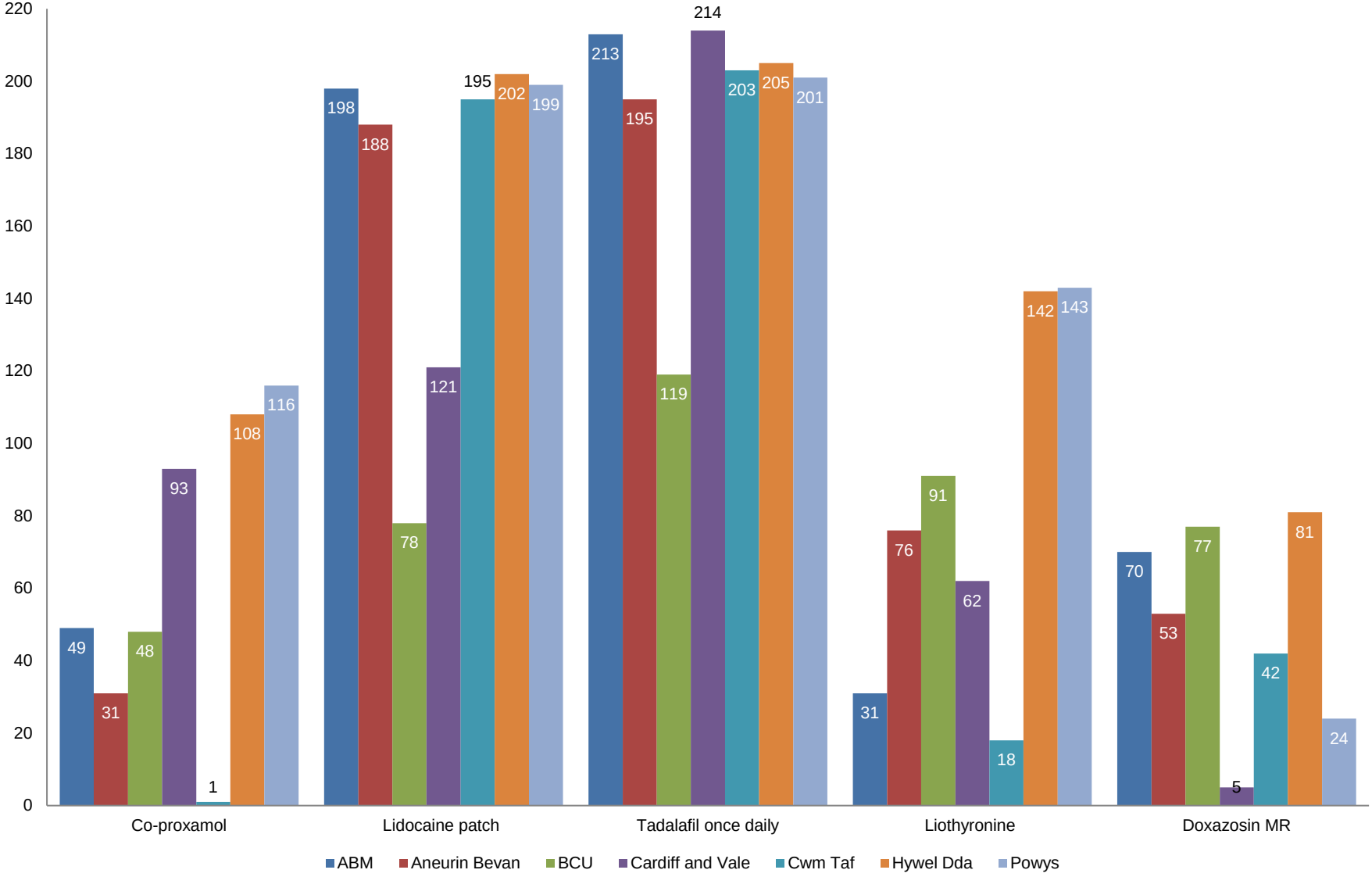
*Average cost over the three-month period of March to May 2017

Table 4. Ranking† of health boards in Wales within all health boards/CCGs in Wales and England for the five medicines identified as low priority for funding (n = 214)§

	ABM	Aneurin Bevan	BCU	Cardiff and Vale	Cwm Taf	Hywel Dda	Powys
Co-proxamol	49	31	48	93	1	108	116
Lidocaine patch	198	188	78	121	195	202	199
Tadalafil once daily	213	195	119	214	203	205	201
Liothyronine	31	76	91	62	18	142	143
Doxazosin modified release	70	53	77	5	42	81	24

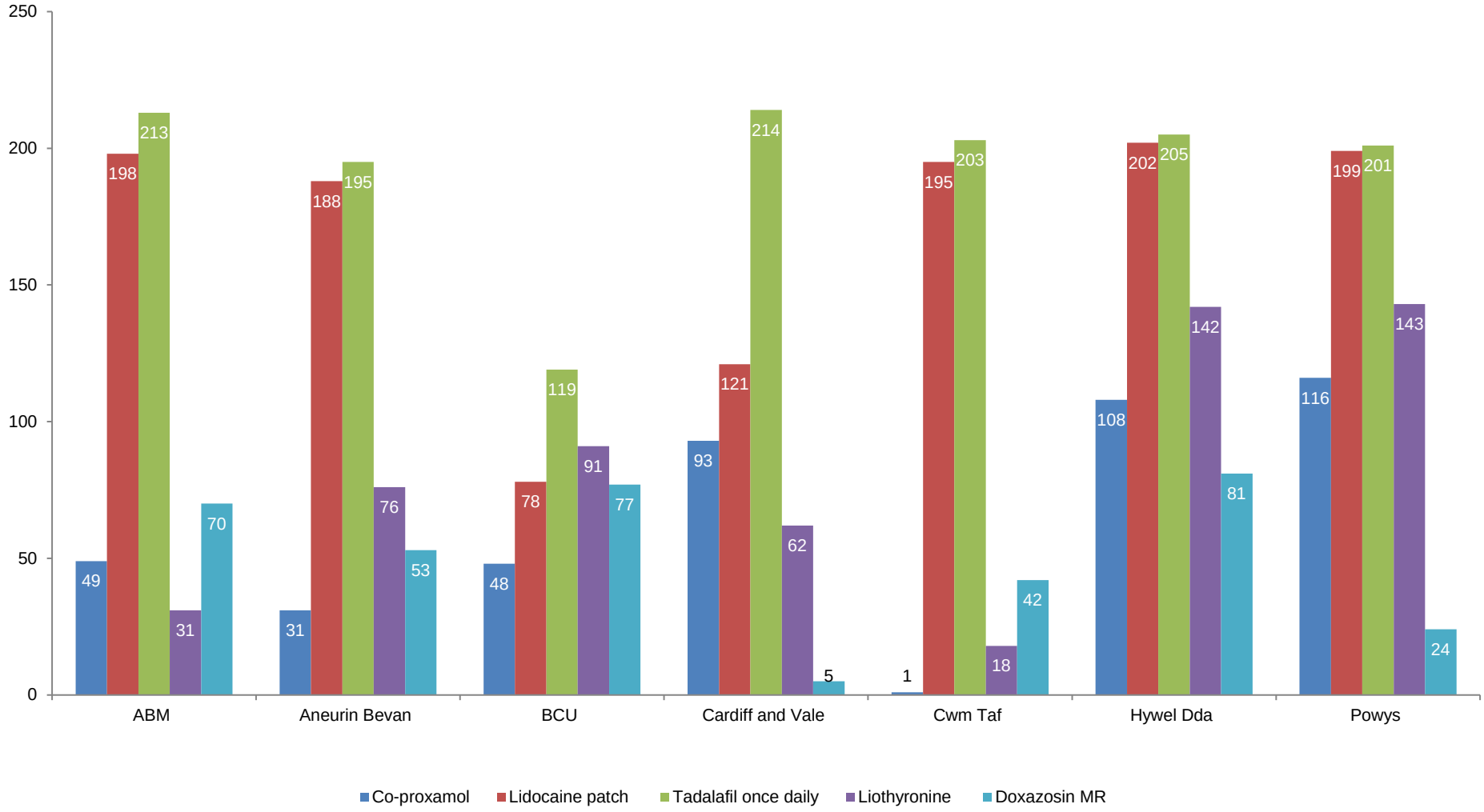
†1 is the best performing, 214 is the worst performing
§Average over the three-month period of March to May 2017

Figure 6. Ranking† of health boards within all Welsh health boards and English CCGs for medicines identified as low priority for funding by medicine§



†1 is the best performing, 214 is the worst performing
§Average over the three-month period of March to May 2017

Figure 7. Ranking† of health boards within all Welsh health boards and English CCGs for medicines identified as low priority for funding by health board§



†1 is the best performing, 214 is the worst performing
§Average over the three-month period of March to May 2017

APPENDIX 3. SUPPORTING INFORMATION FOR IMPLEMENTATION OF THE RECOMMENDATIONS

1. Co-proxamol
Welsh Government: Health Professional Letter: Prescribing of co-proxamol

2. Lidocaine plasters
NICE CG173 Neuropathic pain in adults: pharmacological management in non-specialist settings
NICE CG173 4-year surveillance: neurophathic pain - pharmacological management
PrescQIPP bulletin: Lidocaine plasters (DROP-List)
Off-label or unlicensed use of medicines: prescribers' responsibilities

3. Tadalafil – once daily preparations
NICE CG97 Lower urinary tract symptoms in men: management
PrescQIPP bulletin: Tadalafil

4. Liothyronine
British Thyroid Association: Management of primary hypothyroidism: statement by the British Thyroid Association Executive Committee
PrescQIPP bulletin: Switching liothyronine (L-T3) to levothyroxine (L-T4) in the management of primary hypothyroidism
Specialist Pharmacy Service: What clinical evidence is there to support the use of desiccated thyroid extract products?
Specialist Pharmacy Service: What factors need to be considered when prescribing for lactose intolerant adults?

5. Doxazosin modified release tablets
NICE CG127 Hypertension in adults: diagnosis and management
NICE CG97 Lower urinary tract symptoms in men: management
Specialist Pharmacy Service: Switching from modified release doxazosin to standard release doxazosin in patients with hypertension

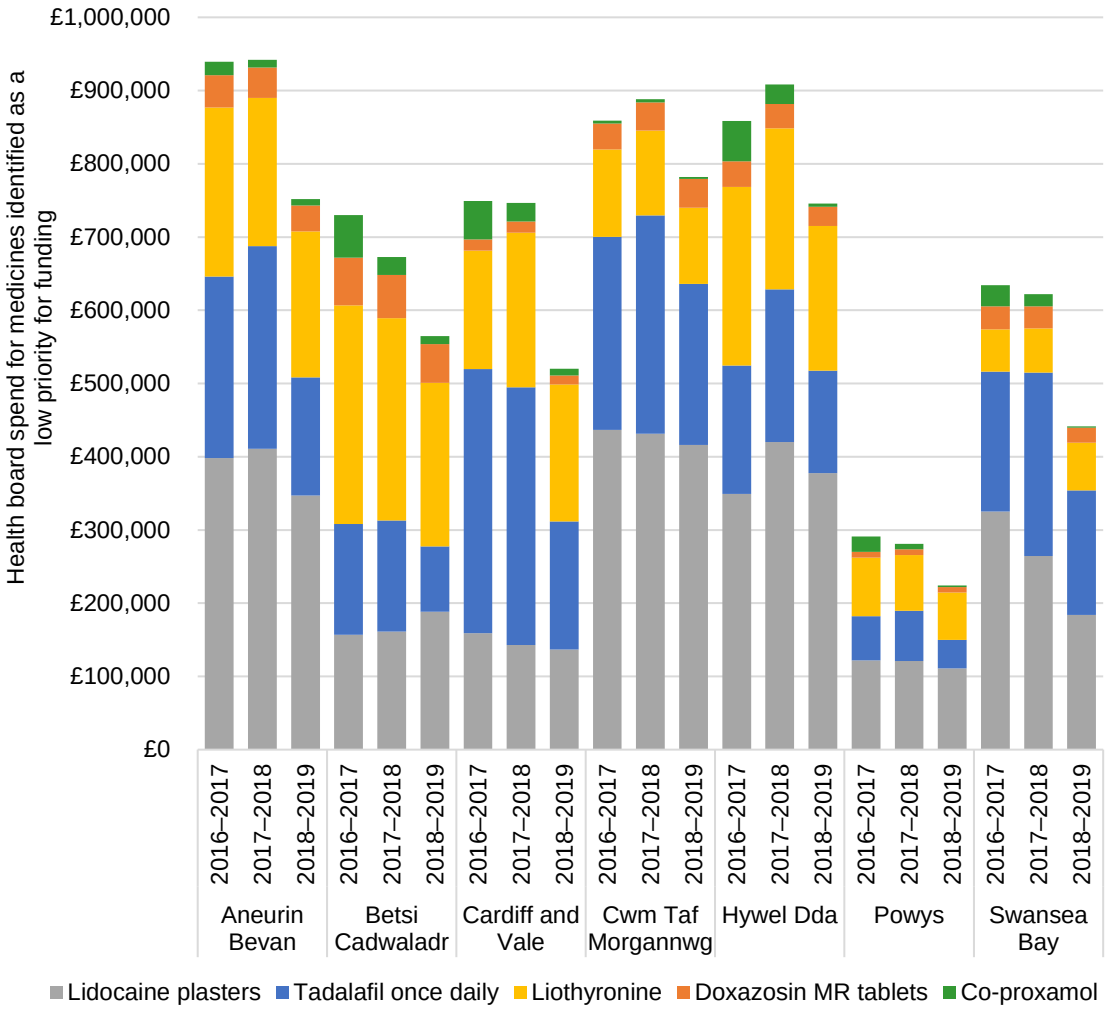
ADDENDUM 1. UPDATE ON MEDICINES EXPENDITURE 2016–2019

(Added in November 2019)

Table 1. NHS Wales spend from financial year 2016–2017 to 2018–2019 for medicines identified as a low priority for funding

	NHS Wales spend (£)			Percentage change between 2016–2017 and 2018–2019
	2016–2017	2017–2018	2018–2019	
Co-proxamol	238,179	115,506	40,212	-83.1%
Doxazosin MR tablets	234,197	225,277	193,802	-17.2%
Lidocaine plasters	1,946,925	1,951,561	1,760,272	-9.59%
Liothyronine	1,192,119	1,162,227	1,041,384	-12.6%
Tadalafil once daily	1,449,738	1,606,224	994,397	-31.4%

Figure 1. Health board spend from financial year 2016–2017 to 2018–2019 for medicines identified as low priority for funding



This data is available to view on the Server for Prescribing Information Reporting and Analysis (SPIRA), where it is updated on a monthly basis. Users who are on the NHS Wales network can access SPIRA via the AWTTC website.