Secondary Care National Prescribing Indicators 2016–2017
This report has been prepared by a multiprofessional collaborative group, with support from the All Wales Prescribing Advisory Group (AWPAG) and 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:
## CONTENTS

1.0 INSULIN.......................................................................................................................... 3
  1.1 Background and evidence.............................................................................................. 3
  1.2 Costs and cost savings.................................................................................................. 4
  1.3 Examples of programmes undertaken ........................................................................ 4
2.0 BIOSIMILARS ..................................................................................................................... 6
  2.1 Background and evidence.............................................................................................. 6
  2.2 Costs and cost savings.................................................................................................. 7
  2.3 Examples of programmes undertaken ........................................................................ 7
3.0 ANTIBIOTICS .................................................................................................................... 8
  3.1 Background and evidence.............................................................................................. 8
  3.2 Useful resources and good practice.............................................................................. 9
REFERENCES.......................................................................................................................... 10
APPENDIX 1. DIABETES PRESCRIBING DATA................................................................. 12
APPENDIX 2. BIOSIMILAR DATA ......................................................................................... 13
APPENDIX 3. DATA COLLECTION PRO-FORMA: ANTIBIOTIC SURGICAL PROPHYLAXIS.................................................................................................................. 14
APPENDIX 4: ANTIBIOTIC DATA......................................................................................... 15
SUMMARY

The aim of National Prescribing Indicators (NPIs) is to highlight therapeutic priorities for NHS Wales. Although historically NPIs have only measured prescribing in primary care, the principles apply to all care settings. AWPAG has previously endorsed the principle to develop NPIs for use in secondary care.

In December 2014, AWPAG discussed a proposal to develop two secondary care NPIs focusing on antibiotic prescribing: surgical prophylaxis over 24 hours and treatment for respiratory tract infections over one week. Although AWPAG supported the use of a measure around antibiotic prescribing, using the point prevalence survey (PPS) to collect data was not suitable, as data can only be collected once a year.

Other areas where it may be appropriate to develop NPIs were also discussed, e.g. pain, diabetes, ophthalmology and overactive bladder diagnoses. A Task and Finish Group of AWPAG was convened and met in March 2015. Following extensive discussion, three areas were proposed for further development:

1. Insulin prescribing
2. Prescribing of biosimilars
3. Antibiotic surgical prophylaxis
1.0 INSULIN

**Purpose:** Ensure long-acting analogue insulin prescribing in type 2 diabetes mellitus is in line with NICE guidance to maximise cost-effective prescribing within Wales.

**Unit of measure:** Items/number of long-acting insulin analogues expressed as a percentage of total insulin prescribed within primary and secondary care.

**Aim for 2016–2017:** To reduce prescribing of long-acting insulin analogues and to achieve prescribing levels below the Welsh average for prescribing within secondary care.

1.1 Background and evidence

The National Institute for Health and Care Excellence (NICE) Clinical Guideline (CG) 87 (2009) on the management of type 2 diabetes mellitus (T2DM) recommends that when control of blood glucose remains or becomes inadequate on oral anti-diabetic therapy, then insulin should be considered as the next treatment option. Human isophane (neutral protamine Hagedorn [NPH]) insulin is recommended as the first choice regimen\(^1\). For most people with T2DM, long-acting insulin analogues offer no significant benefit over human NPH insulin, and are more expensive. Indeed, NICE considered the available evidence and concluded that, while there is support for insulin glargine and insulin detemir to lower the incidence of hypoglycaemic events, the use of these insulins as first-line insulins in T2DM could not be justified on health economic grounds\(^2,3\).

In 2011, the UK Cochrane Centre and NICE published an analysis of the available long-term trials considering the use of long-acting insulin analogues versus NPH insulin in T2DM, and concluded that insulin glargine and insulin detemir were almost identically effective compared to NPH insulin in long-term metabolic control (measured by glycated haemoglobin [HbA\(_1c\)])\(^4\). The report acknowledges that fewer patients experienced symptomatic or nocturnal hypoglycaemic episodes with either of the two analogues; however, no conclusive information on late complications or on possible differences in the number of fatalities exists. The report concludes that, in the absence of evidence to suggest the superiority of the long-acting insulin analogues over NPH insulin in terms of improved safety, glycaemic control or reduction of long-term diabetic complications, a cautious approach to prescribing the long-acting insulin analogues is advised\(^4\).

NICE Guideline (NG) 17 (2015), on the diagnosis and management of type 1 diabetes mellitus (T1DM), recommends twice-daily insulin detemir as basal insulin therapy for adults with T1DM\(^5\). Prescribing data cannot differentiate between long-acting insulin analogues prescribed for T1DM and T2DM; therefore, monitoring of all long-acting insulin analogues is undertaken. In light of the fact that prevalence data suggest that only 10% of patients with diabetes have T1DM\(^6\), the prescribing data indicate that long-acting insulin analogues are being widely used to manage T2DM.

Despite the recommendations outlined in NICE CG87, the prescribing cost for long-acting insulin analogues was £8.5 million in primary care and £243,315 in secondary care for the 2014–2015 financial year. The majority of insulin prescribing is initiated by a specialist clinician within secondary care and therefore review of hospital prescribing practice will affect the primary care prescribing trend. Prescribing will often continue in the primary care setting and it is therefore important to consider data for primary and secondary care.
In Wales, the proportion of insulin prescribed as long-acting insulin analogues in primary care for 2014–2015 was 90.6%; this is a slight decrease from the previous year (91.5%). By comparison, the average for England was 79% (range across clinical commission groups [CCGs]: 38–97%) for the quarter to March 2015\(^7\). For NHS Wales secondary care, the average quantity of long-acting insulin analogues prescribed as a percentage of total long- and intermediate-acting insulin was 77% (April 2014–March 2015). See Appendix 1 for more information.

1.2 Costs and cost savings
As diabetes accounts for 10% of the NHS costs, and the number of diabetic patients continues to increase, any potential cost saving to NHS Wales is likely to be significant. A UK study, published by the British Medical Journal, concluded that the rise of insulin analogues has had a substantial financial impact on the NHS, yet there has been no observable clinical benefit to justify the increased use of these medicines\(^10\).

A report highlighting the cost of diabetes medicines suggests that £725 million was spent on diabetes medicines in the UK in 2010–2011 and, of this, £269 million was on basal analogue insulins\(^4\). A study by Holden and colleagues states that if guidelines for insulin prescribing had been followed between 2000 and 2009, the UK NHS would have saved £625 million\(^11\). Extra money spent on long-acting insulin analogues may be considered better spent on diabetes specialist nurses or dieticians to help educate and manage the growing population of diabetic patients\(^3\).

Calculations indicate that if the prescribing of long-acting insulin analogues can be reduced by 10–30% across all health boards in Wales, the potential cost savings would be an estimated £700,000 to £1 million in one year. It is important to note that the biosimilar insulin glargine (Abasaglar\(^®\)) is now licensed and currently undergoing appraisal by AWMSG. This medicine is cheaper than the original insulin glargine (Lantus\(^®\)) and therefore, although biosimilar insulin analogues are more expensive than the standard NPH insulin, cost savings may not be as great as those estimated above.

1.3 Examples of programmes undertaken
A number of CCGs have developed programmes to reduce the prescribing of long-acting insulin analogues. The aim of these programmes has been to ensure diabetes is managed in line with the recommendations outlined in NICE CG87\(^3\) and to improve diabetes services by using the money saved to establish appropriate facilities to support diabetic nurses, patients and carers\(^12\).

In 2010, Nene and Corby CCGs embarked on a project to redesign the diabetes services within Northamptonshire. Local prescribing data showed that in September 2010, NPH insulin accounted for only 15% of all long- and intermediate-acting insulin prescribed within Northamptonshire. In line with the national Quality, Innovation, Productivity and Prevention (QIPP) programme, developed by the Department of Health, Northamptonshire was keen to reverse the trend of NPH insulin prescribing and use the savings to fund the development of a multi-disciplinary team (MDT) for diabetes patients within the community\(^13\). By July 2012, NPH insulin accounted for 25% of all long- and intermediate-acting insulin, and savings of over £600,000 had been achieved\(^13\). This money was used to fund the MDT, which has since achieved a 48% reduction in admissions, saving £301,000 as well as providing a number of additional benefits, including consistent training and support to primary care clinicians and practice nurses, patient education and improved quality of service for patients. Current prescribing figures (March 2015) for Nene CCG (of which Northamptonshire is a part) show that the percentage of insulin prescribed as long-acting insulin analogues is 72%, which is below the average for England and Wales.
A similar initiative was set up in Newham CCG to ensure appropriate insulin prescribing in line with NICE CG87; reduce unnecessary spending on long-acting insulin analogues; improve patient outcomes without the risk of hypoglycaemic episodes; and increase the capability and confidence of health care professionals to prescribe and manage human insulin and patients within the current pathway, in order to avoid increased utilisation of secondary care. The initiative had impressive results and the proportion of long-acting insulin analogues decreased from 94% to 87% (2012–2013). This change was accompanied by an improvement in glycaemic control and, although it was not possible to determine the contribution of this change, it was evidence of an overall improvement in diabetes care\textsuperscript{14}. Current prescribing figures (March 2015) for Newham CCG show that the percentage of insulin prescribed as long-acting insulin analogues is 80%.

In June 2014, Cumbria CCG addressed the need to reduce prescribing of basal analogue insulin and suggested that any savings were re-invested into developing the capacity of primary care to deliver high quality diabetic care, including the initiation and review of insulin for T2DM patients. It was estimated that a 10% reduction in analogue insulin prescribing would result in a cost saving of £85,000. No data have been reported to date; however, the report highlights that Cumbria has historically been a high prescriber of basal analogue insulin and has one of the highest levels of prescribing in the North of England\textsuperscript{15}. Recent prescribing data (March 2015) show that the percentage of insulin prescribed as long-acting insulin analogues in Cumbria is 66%, which is well below the average for England and Wales.
2.0 BIOSIMILARS

**Purpose:** Ensure prescribing of biosimilar medicines is in line with AWMSG guidance to support cost-effective prescribing within Wales.

**Unit of measure:** Quantity of biosimilar medicines prescribed as a percentage of total ‘reference’ product plus biosimilar.

**Aim for 2016–2017:** Increase the appropriate use of biosimilar medicines in line with guidance and increase commercial competition.

2.1 Background and evidence

Biological medicines are medicines that are made or derived from a biological source and, as such, are complex, with inherent variability in their structure. A biosimilar medicine is a biological medicine that is developed to be highly similar and clinically equivalent to an existing biological medicine (i.e. ‘reference medicine’ or ‘originator medicine’). The regulatory authority applies stringent criteria in their evaluation of the studies comparing the quality, safety and efficacy of the ‘reference’ product and the biosimilar to show that there are no clinically meaningful differences.

It is the responsibility of the clinician, in consultation with the patient, to make the decision about whether to prescribe a biological medicine and whether that should be the original ‘reference’ medicine or a biosimilar medicine. At the time of dispensing, a biosimilar medicine should not be automatically substituted for the original ‘reference’ medicine or another biosimilar medicine. In line with MHRA guidelines, biological medicines, including biosimilar medicines, must be prescribed by brand name to ensure automatic substitution does not take place and to support ongoing pharmacovigilance of the individual products.

Continuing development of biological medicines, including biosimilar medicines, creates increased choice for patients and clinicians, increased commercial competition and enhanced value propositions for individual medicines. Biological medicines account for a significant expenditure within the NHS and, as a number of these medicines will lose their patent protection within the next five years, it seems an appropriate time to consider the pattern of prescribing across NHS Wales.

Where AWMSG or NICE has already recommended the ‘reference’ medicine, the same guidance will normally apply to a biosimilar of the ‘reference’. AWMSG has issued advice for a number of biosimilar medicines including:

- Infliximab products:
  - Inflectra® and Remsima® have undergone appraisal by AWMSG and are recommended for restricted use within NHS Wales.
- Filgrastim products:
  - Grastofil® and Accofil® have been issued with Statements of Advice and are not endorsed for use in NHS Wales.
  - Nivestim®, TevaGrastim®, Zarzio®, Ratiograstim® are recommended as an option for use within NHS Wales for the treatment of neutropenia.

As Inflectra® and Remsima® only received a positive recommendation by AWMSG in March 2015, prescribing data are currently not available to support this measure.
2.2 Costs and cost savings
The total spend across Wales in secondary care for the period April 2014–March 2015 was £8.9 million for infliximab and £440,000 for filgrastim.

Data suggest that biosimilar products are cheaper than the ‘reference’ product\textsuperscript{28}. The use of biosimilar medicines in place of the ‘reference’ biological medicine should therefore be associated with cost savings. It should be noted that individual hospital contracting prices for biosimilar medicine and also reference products may vary, which may affect the potential cost savings.

The appropriate use of biosimilars will drive greater competition to release cost efficiencies to support the treatment of an increasing number of patients and the uptake of new and innovative medicines\textsuperscript{18}.

See Appendix 2 for biosimilar data.

2.3 Examples of programmes undertaken
The University Hospital Southampton NHS Foundation Trust and the University College London Hospitals NHS Foundation Trust have collaborated with NICE and shared their learning and experiences of planning for and managing the introduction of biosimilar medicines, in particular biosimilar versions of infliximab. The University Hospital Southampton NHS Foundation Trust undertook a programme whereby patients were reviewed and switched to an infliximab biosimilar during a routine clinic appointment by a specialist nurse. The team concluded that large cost savings could be achieved by using biosimilar versions of infliximab and some of the cost savings could be re-invested in improvements to patient care. The University College London Hospitals NHS Foundation Trust has considered the introduction of biosimilar versions of infliximab and reached an agreement that patients starting a new course of infliximab will be prescribed a biosimilar. This will be monitored and reviewed at a later date. For more information, refer to NICE technology appraisal support (HTTA329) on introducing biosimilar versions of infliximab: Inflectra\textsuperscript{®} and Remsima\textsuperscript{®}.
3.0 ANTIBIOTICS

**Purpose:** An NPI focusing on antibiotic prophylaxis in surgery supports one of the key elements of the Welsh Antimicrobial Resistance Programme: to inform, support and promote the prudent use of antimicrobials.

**Unit of measure:** Proportion of elective colorectal patients receiving surgical prophylaxis for more than 24 hours.

**Aim for 2016–2017:** Maintain performance below the Welsh average (PPS data) or show a reduction towards the Welsh average.

**Data collection:** Data will be collected quarterly using an agreed data collection form (Appendix 3). Data collection will be undertaken by the antimicrobial pharmacist, or other suitably qualified pharmacists. An initial pilot will be undertaken (sample size 10 patients). Patient numbers will be reviewed following the pilot.

3.1 Background and evidence

The goals of administration of antibiotic prophylaxis to surgical patients are to reduce the incidence of surgical site infection, use antibiotics in a manner that is supported by evidence of effectiveness and minimise adverse effects to the patient. Antibiotic prophylaxis in surgery is an adjunct to, not a substitute for, good surgical technique and is just one component of an effective policy for the control of healthcare associated infection.

Antibiotic prophylaxis should be given to patients before:
- clean surgery involving the placement of a prosthesis or implant
- clean-contaminated surgery
- contaminated surgery

Antibiotic prophylaxis is not routinely recommended for clean non-prosthetic uncomplicated surgery.

Advice from national organisations, including Public Health Wales, Scottish Intercollegiate Guidelines Network (SIGN) and NICE, recommend that antibiotic prophylaxis to surgical patients should be a single therapeutic dose of intravenous antibiotics in the majority of cases. This should be administered up to 60 minutes prior to incision to enable peak blood levels to be present at the start of the surgical procedure. A repeat dose of prophylaxis antibiotic is recommended when the operation is longer than the half-life of the antibiotic given. Certain circumstances, such as prolonged surgery, major blood loss, or specific surgery (e.g. hip arthroplasty), may require a longer course of antibiotic prophylaxis: when a maximum of 24 hours is recommended.

There is, however, a tendency to continue antibiotic prophylaxis for longer than necessary. The PPS for November 2014 reports that the proportion of surgical prophylaxis administered for greater than 24 hours ranged from 17% to 48% across health boards. The Wales average, however, is reducing. Data from the PPS indicate that the proportion of surgical prophylaxis administered for greater than 24 hours has reduced from 42% in 2012 to 30% in 2013 and 27% in 2014.

In common with therapeutic use, the use of antibiotics for prophylaxis carries a risk of adverse drug reactions (including *Clostridium difficile*-associated diarrhoea) and increased prevalence of antibiotic resistant bacteria. The choice of antibiotic prophylaxis should be influenced by the strength of the association between the antibiotic used and *C. difficile* diarrhoea. Therefore, antibiotic choice should minimise *C. difficile* risk whilst ensuring adequate coverage of the expected pathogens for the
operative site\textsuperscript{31}. Antibiotic choice should reflect local, disease-specific information about the common pathogens and their antimicrobial susceptibility\textsuperscript{31}. Narrow-spectrum, less expensive antibiotics should be the first choice\textsuperscript{31}.

See Appendix 4 for antibiotic data.

3.2 Useful resources and good practice
In 2011, the Healthcare Associated Infection Taskforce in Scotland introduced a new \textit{C. difficile} infection target. To support NHS boards in achieving and maintaining this target, the Scottish Antimicrobial Prescribing Group (SAPG) reviewed the supporting prescribing indicators to evaluate their success in assuring that antibiotics with a high risk of \textit{C. difficile} infection were not routinely used.

SAPG developed a prescribing indicator monitoring surgical prophylaxis in elective colorectal patients: with the aim being for antibiotic prescriptions to be compliant with the local surgical antimicrobial prophylaxis policy in $\geq 95\%$ of sampled cases. A case was considered compliant if a single dose of surgical antibiotic prophylaxis was given that was compliant with the local surgical antimicrobial prophylaxis policy.

By June 2014, all eight health boards participating in the audit had achieved $\geq 95\%$ compliance with the measure “Single Dose” and three of the eight health boards had achieved $\geq 95\%$ compliance with the measure “Antibiotic choice compliant with policy”. SAPG state that they will continue to focus on surgical prophylaxis in high risk surgical procedures where compliance with policy requires improvement\textsuperscript{37}.
REFERENCES


11 Holden SE, Poole CD, Morgan CLI et al. Evaluation of the incremental cost to the National Health Service of prescribing analogue insulin. BMJ Open 2011. Available at: http://bmjopen.bmj.com/content/1/2/e000258.full.pdf+


15 Cumbria CCG. Basal Analogue Insulin. 2014.


APPENDIX 1. DIABETES PRESCRIBING DATA

Table 1. Proportion of long-acting insulin analogue prescribing in primary care

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>ABMU</td>
<td>92.37</td>
<td>92.55</td>
<td>0.19</td>
</tr>
<tr>
<td>Aneurin Bevan</td>
<td>87.47</td>
<td>86.38</td>
<td>-1.25</td>
</tr>
<tr>
<td>BCU</td>
<td>95.53</td>
<td>94.68</td>
<td>-0.90</td>
</tr>
<tr>
<td>Cardiff and Vale</td>
<td>93.73</td>
<td>93.04</td>
<td>-0.74</td>
</tr>
<tr>
<td>Cwm Taf</td>
<td>81.88</td>
<td>79.61</td>
<td>-2.77</td>
</tr>
<tr>
<td>Hywel Dda</td>
<td>95.17</td>
<td>94.76</td>
<td>-0.43</td>
</tr>
<tr>
<td>Powys</td>
<td>90.29</td>
<td>88.61</td>
<td>-1.87</td>
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<tr>
<td>National average</td>
<td>91.45</td>
<td>90.55</td>
<td>-0.98</td>
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Figure 1. Trend in long-acting analogue prescribing as a percentage of total long and intermediate-acting insulin prescribing in primary care

Table 2. Proportion of long-acting insulin analogue prescribing – April 2014–March 2015

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<thead>
<tr>
<th></th>
<th>ABMU</th>
<th>Aneurin Bevan</th>
<th>Betsi Cadwaladr</th>
<th>Cardiff and Vale</th>
<th>Cwm Taf</th>
<th>Hywel Dda</th>
<th>Powys</th>
<th>Velindre</th>
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<tr>
<td>Primary care (items)</td>
<td>93%</td>
<td>87%</td>
<td>95%</td>
<td>93%</td>
<td>80%</td>
<td>95%</td>
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<td>N/A</td>
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<td>Secondary care (number)</td>
<td>76%</td>
<td>72%</td>
<td>86%</td>
<td>80%</td>
<td>55%</td>
<td>84%</td>
<td>N/A</td>
<td>76%</td>
<td>77%</td>
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## APPENDIX 2. BIOSIMILAR DATA

### Table A. Quantity and cost of filgrastim (Neupogen®) and filgrastim biosimilars prescribed within NHS Wales

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Biosimilar</th>
<th>AWMSG Advice</th>
<th>Total quantity</th>
<th>Total cost (£)</th>
<th>Cost/quantity (£)</th>
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<tbody>
<tr>
<td>Filgrastim (prescribed generically)*</td>
<td>unknown</td>
<td></td>
<td>362</td>
<td>5,889</td>
<td>16.26</td>
</tr>
<tr>
<td>Filgrastim (Neupogen®)</td>
<td>-</td>
<td>Recommended (March 2011)</td>
<td>539</td>
<td>27,816</td>
<td>51.61</td>
</tr>
<tr>
<td>Nivestim®</td>
<td>Recommended (Sept 2011)</td>
<td></td>
<td>4439</td>
<td>67,793</td>
<td>15.27</td>
</tr>
<tr>
<td>TevaGrastim®</td>
<td>Recommended (Sept 2010)</td>
<td></td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Zarzio®</td>
<td>Recommended (Sept 2010)</td>
<td></td>
<td>19538</td>
<td>340,041</td>
<td>17.40</td>
</tr>
<tr>
<td>Ratiograstim®</td>
<td>Recommended (Sept 2009)</td>
<td></td>
<td>0</td>
<td>0</td>
<td>0</td>
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* All Velindre NHS Trust (Velindre NHS Trust confirmed use of Zarzio®)

### Figure A. Filgrastim (Neupogen®) and filgrastim biosimilar medicines as a proportion of total filgrastim prescribed

[Graph showing the proportion of filgrastim prescribed by different hospital trusts.]
APPENDIX 3. DATA COLLECTION PRO-FORMA: ANTIBIOTIC SURGICAL PROPHYLAXIS (UPDATED MAY 2016)

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<th>Month</th>
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**Data**

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<td>Duration of prophylaxis consistent with health board guidelines?</td>
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**APPENDIX 4: ANTIBIOTIC DATA**

**Figure i. Proportion of antibiotics for surgical prophylaxis given > 24 hours – health board level (PPS data November 2014)**

**Figure ii. Proportion of antibiotics for surgical prophylaxis given > 24 hours – hospital level**

Key:
A – Bronglais
B – Princess of Wales
C – Royal Glamorgan
D – Royal Gwent
E – Morriston
F – University Hospital of Wales
G – Withybush
H – Wrexham Maelor
J – Glanwyl
K – Ysbyty Gwynedd
L – Ysbyty Glan Clwyd
M – Nevill Hall
N – Prince Charles
P – University Hospital Llandough
R – Prince Philip
S – Singleton
T – Neath Port Talbot
X – Powys Community Hospitals