Biosimilar Uptake by British Local Formularies: a Cross Sectional Study

Saja Alnahar (1)
Rachel A Elliott (2)
Murray D Smith (3)

1 University of Nottingham and corresponding author
2 University of Manchester
3 University of Lincoln

Cover Page

Manuscript Title: Biosimilar Uptake by British Local Formularies: a Cross Sectional Study

Keywords: biosimilars, biological medicines, local formularies, Great Britain

Total number of words - abstract: 250

Total number of words - paper: 2256

Abstract

Background: Biological medicines are starting to lose their patent protection, so similar, inexact copies (biosimilars) are being developed and licensed. The high acquisition costs of biologics for healthcare providers could be reduced by switching to biosimilars, thus alleviating budgetary pressures and increasing patient access. Therefore, the acceptance of biosimilars by prescribers in Great Britain (GB; England, Scotland, Wales) needs to be described and understood.

Objective: To determine uptake of the first wave of biosimilars (somatropin, epoetin, filgrastim) by local formularies (lists of preferred medicines for prescribing in local healthcare settings).

Settings: This study targeted local formularies in GB.

Method: In November 2014, local formularies (medicines formularies of Acute Trusts and Health Boards in GB) were screened for their approach to listing of biologics and their biosimilars as well as recommendations on usage of these pharmaceuticals.

Main Outcomes Measures: Listing frequencies of biosimilars.

Results: One hundred and forty-six British local formularies were screened. Amongst the 80% of formularies in which brand names were specified, biosimilar filgrastim was the most frequently listed when compared to the other targeted biosimilars. Biosimilars were listed in preference to reference biologic medicine in 49% of local formularies for filgrastim, 11% for somatropin and in only 6% for epoetin.

Conclusion: Although the market for biosimilars can act in parallel to the generic market, their uptake measured using local British formularies was less than what is expected given that the British market for medicines has a strong focus on generics. Finally, geographical variability within GB requires further investigation.

Impacts of findings

- As the use of brand names in prescribing and reporting adverse drug reactions is part of active monitoring of biological medicines safety, including the biosimilar medicines, local formularies must actively list these medicines using brand name;
- Specifying preferred brand for prescribing facilitates and promotes local formularies in guiding cost effective and rational medicines utilisation.

Introduction

Biological medicines (BMPs) provide an innovative method for treating chronic and life-threatening diseases such as cancers, rheumatoid arthritis and multiple sclerosis. Their rapid adoption into clinical practice has resulted in a substantial share of the pharmaceutical market; for example, in 2012-2013, 27% of total pharmaceutical sales in Europe were BMPs [1]. Moreover, eight of the top ten bestselling pharmaceuticals in 2013 in Europe were BMPs. It is expected that BMPs will maintain the same market share into 2016 [2,3] and likely beyond. BMPs have significantly improved health and disease outcomes, but their widespread utilisation is financially challenging to healthcare providers worldwide [4].

In 2013-2014, in England, seven out of the top ten most prescribed medicines in terms of cost to the National Health Service (NHS) were BMPs [5]. Notable though is that all seven will lose their patent protection by 2018 [6]. Patent expiry creates an opportunity for developing and licensing similar copies of off-patent BMPs-called biosimilar medicines (BSPs) [7]. Unlike conventional generic medicines, BSPs are not identical but similar copies of their reference BMP (R-BMP). The inability to produce identical copies is related to the complex and heterogenic molecular structure of these medicines, and being produced by not fully controllable living systems [4,8].

In their analysis of the European BSP market, Rovira et al reported that BSPs offer price reductions of between 10% and 35% [9]. Although this is a modest price reduction in comparison to conventional generic medicines, the overall cost saving to health service providers is expected to be significant due to the high unit costs and extensive use of BMPs [9]. The European Generic Medicines Association reported that the European Union might save upwards of €1.6 billion/year for the scenario in which a 20% price reduction occurs on five off-patent BMPs [10]. Furthermore, it has been suggested that the availability of BSPs might alter medical practice and increase compliance to clinical guidelines [11,12].

In Europe, BSPs can be launched after being centrally assessed and licensed by the European Medicines Agency (EMA) for safety, quality and efficacy [8,11]. While the EMA mandates full quality submission in order to license a BSP, it does permit evidence based extrapolation of the clinical outcomes from one tested indication to closely related others [13,14].

In Great Britain (GB), the Medicines and Healthcare products Regulatory Agency (MHRA) directs prescribers to use brand name in prescribing any BMP and its BSPs [15]. Brand name-based prescribing and reporting facilitates capture of safety issues related to BMPs including BSPs [15].

Despite being a generically-driven market [16], the uptake of BSPs in Britain seems to have been relatively limited when compared to other European countries [14]. According to the British Generic Manufacturers Association factors related to physicians' lack of confidence in prescribing BSPs, absence of encouraging national policies and banned substitution at pharmacy level have resulted in slow adoption of BSPs [14]. Lack of confidence might relate to physicians questioning the safety and efficacy of BSPs [11]. This might be at least partly explained by the abridged approach the EMA follows in assessing clinical efficacy of BSPs [13]. One exception is granulocyte-colony stimulating factor (G-CSF)-filgrastim BSP, which is achieving an uptake rate similar to that of conventional generic medicinal products [2].

One approach to evaluating prescribers' acceptance of BSPs is through assessing uptake of BSPs in local medicines formularies. The National Institute for Health and Care Excellence (NICE) defines local formularies as "the output processes to support the managed introduction, utilisation or withdrawal of healthcare treatments within a health economy, service or organisation" [17]. Local formularies are working documents that are subject to regular review and change. They tend to be robust on treatments used frequently and weak on occasionally used ones (that need to be available for a complete and comprehensive service). Local formularies can act as prescribing guiding tool at local settings [18]. Heal et al (2004) reported

that more than 80% of their study participants were guided by local formularies [19]. Accordingly, assessing BSP listing in local formularies might reflect acceptance of these products by prescribers.

Aim of the study

To determine uptake acceptance of first wave BSPs licensed and marketed in GB prior to 2015 (somatropin (HGH), epoetin (EPO) and filgrastim (G-CSF)) by local formularies.

Ethics approval

Ethical approval was not needed as local formularies throughout the UK are publically available documents included in the freedom of information scheme.

Method

During November-December 2014, a list of 157[1] Acute Trusts (accountable organisations within NHS England that manage and control the performance, services quality and financial efficiency of clusters of hospitals in England) was acquired from the NHS England website. Details of the 14 Regional Health Boards in Scotland and 7 Local Health Boards in Wales (accountable organisations within NHS Scotland and NHS Wales that are responsible for the delivery of healthcare services to the local population) were acquired from Scottish Government and NHS Wales websites[2].

[1] As of November 2014, the total number of Acute Trusts in England was 157. It was not possible to obtain the formulary list of two Acute Trusts since one was dissolved and the other one was still in process of developing a formulary list.

[2] Northern Ireland was excluded as there was an initiative underway to develop a joint formulary for the whole country, and some of its chapters were still under development.

The most recent versions of local medicines formularies were downloaded and examined for their listing of targeted R-BMPs and BSPs according to the criteria given in Table 1. These criteria enabled assessment of: (i) uptake of BSPs, (ii) compliance to the MHRA recommendation on brand name prescribing of BMPs, and (iii) the consideration given to population or indication-specific recommendations.

The assessment process started by examining whether the listing approach of R-BMP and BSPs was based on using brand name, molecular name or both, as per the British National Formulary (BNF) 68th edition. Then the availability of prescribing guidance in terms of speciality of the prescriber and/or the clinical settings was recorded. Finally, formulary entries were classified and compared according to preferred brand for prescribing. Formulary uptake of targeted BMPs and BSPs was analysed using descriptive statistics in an Excel® 2010 spreadsheet.

Results

One hundred and forty-six formularies were identified: 129 in England, 10 in Scotland and 7 in Wales. Forty-three percent (63/146) of these were joint formularies (the term given to a local formulary developed and/or used simultaneously by more than one healthcare providing organisation).

Formulary uptake and listing approaches varied across the three targeted groups. HGH was listed in 126 formularies achieving the highest percentage of medicine listing, EPO achieved the highest brand name based listing with 60 formularies using brand names. Despite BSP G-CSF being the last of the three groups to be authorised by the EMA, it was most commonly listed in preference to the R-BMP. Table 2 provides more details.

Variations between the countries of GB were seen, with 27% of English formularies listing BSP G-CSF in preference to the R-BMP, versus 12.5% and 14.3% amongst Scottish and Welsh

formularies, respectively. In the cases of HGH and EPO, 6% and 4% of English formularies preferred BSP over R-BMP; respectively, but no Scottish or Welsh formularies did so.

Only six formularies listed at least one BSP from all three targeted groups. There were no instances of BSPs being preferred to R-BMPs across all three targeted groups, but at the opposite extreme there were only two formularies in which R-BMPs were always preferred over BSPs.

Discussion

In this study, formulary uptake of BSPs in three different groups was employed as an indicator of clinical acceptance of BSPs in GB. The uptake of BSPs by British local formularies was less than what might be predicted from a classical generically driven market for medicines, and there appeared to be geographic variability in uptake which requires further investigation.

Most frequently listed was HGH, the first licensed BSP [20], however the maximum preference for BSPs over R-BMP was achieved by G-CSF BSPs. On the other hand, brand name-based listing was more frequent in the case of EPO. Despite it not being possible to gain a complete understanding of the variations between targeted groups, it might be explained in large part by the molecular nature, therapy duration and/or patients' demographics, preferences and life style.

Having several other medicinal products within the same group where each has different dosing frequencies, administration devices and storage conditions might affect acceptance of BSPs. For example, one HGH product is a needleless device making it more attractive to paediatric and needle-phobic patients. Another HGH product can be stored out of the refrigerator [21] which might make it the brand of choice for frequent travellers.

G-CSF's molecular structure and short duration of therapy might increase the acceptance of its BSPs. It is a small, easily characterised non-glycosylated molecule that is indicated for short

158 therapeutic periods [22, 23]. However, special population considerations in terms of patient
159 age and therapeutic indications were flagged in those instances when the R-BMP was listed in
160 preference to BSPs. Specifically, the R-BMP was listed as the preferred product for paediatric
161 patients and for stem cell mobilisation. Reluctance to use BSPs in these settings may be because
162 of the lack of clinical trial evidence of their efficacy and/or safety.

163 EPO achieved the highest percentage of brand name-based listing. This is most likely due to
164 EPO being a glycosylated protein, in which case each brand has a different glycosylation
165 pattern and hence a different immunogenic profile [24]. In addition, previously reported cases
166 of the life threatening pure red cell aplasia might encourage the use of brand name based listing
167 for EPO whether for the R-BMP or the BSPs [24].

168 The MHRA has considered several measures in the monitoring of BMPs, including BSPs, such
169 as: demanding brand name-based prescription, and requiring specification of a product's
170 identifiers (brand name, batch number and manufacturer) in reporting adverse drug reactions.
171 Furthermore, prescribers are directed to inform patients and/or carers about a product's brand
172 name and batch number [15]. However, more than one third of local formularies did not specify
173 brand names when listing BMPs in the groups examined in this study. Unintentional switching
174 between brands might affect patients' safety, if not carefully monitored and managed. Such
175 harm might be avoided in the cases of G-CSF and EPO because of their short duration
176 prescription, but possibly not otherwise for HGH which is typically used for prolonged periods.

177 The limited clinical evidence of BSPs' efficacy has been highlighted as a factor hindering
178 BSPs' acceptance in clinical practice [22]. However, the BSP G-CSF brand that was approved
179 based on results of a pharmacokinetics/pharmacodynamics trial in healthy volunteers instead
180 of patients, and in a non-comparative safety-focussed study in patients [25] -was recommended
181 for use ahead of R-BMP G-CSF in more local formularies than was any other
182 biosimilar/reference pairing.

As there is a proposal to assign different international non-proprietary name (INN) for BSPs, BSPs' manufacturers argue that a differing INN might limit the uptake of BSPs by giving suggestion to the view that BSPs are completely different instead of being a highly similar molecule [26]. The effect of different INN was noted in the case of epoetin zeta and epoetin alfa, where despite both being EPO BSP the latter was more often listed than the former. Moreover, 50% of formularies that preferred BSP EPO over the R-BMP have not listed epoetin zeta, while the remaining 50% listed it without brand specification. Of the 27 formularies that did list EPO using its molecular name none included epoetin zeta.

Variations in listing BSPs were observed between England, Scotland and Wales. Although both the Scottish Medicines Consortium and the All Wales Medicines Strategy Group have been actively involved in evaluating BSPs [27, 28], Scottish and Welsh formularies were less likely to list BSPs in preference to the R-BMP compared with their English counterparts.

Research data and analysis indicate that some formularies encourage BSP prescribing. However, variations and lack of specificity in some formularies may suggest a vague understanding of the concept and nature of BMPs in general, and BSPs in particular, by the professionals involved in developing local formularies.

The principal limitation of this study is that the uptake of BSPs has been estimated using local medicines formularies as a proxy for actual prescribing practice. This may not necessarily provide a highly accurate reflection of BSP prescribing, as it is not known to what degree these lists are adhered to.

If equally safe and effective as the originator BMP, lower prices for BSPs could potentially increase access to treatment for more patients, or reduce drug spending in an increasingly constrained financial environment. Engagement is required with prescribers, formulary managers and commissioners to understand the basis for formulary decision-making, identify reasons for variation in prescribing behaviour and develop strategies for more uniform uptake

of BSPs. Educational interventions are also needed around adherence to standards of pharmacovigilance to assure drug monitoring and patient safety.

Conclusion

The results of this study suggest that the uptake of BSPs in Britain is highly variable, and generally less than what is expected, given historically that its market for pharmaceuticals is very much generically driven. Further work is needed to understand why there is such low and variable uptake.

Table 1

Table 1- Formulary assessment criteria

No.	Assessment Criterion	Definition	
1.	Is this formulary a joint formulary? (Yes/No)	Formulary list that is developed and/or used by more than one healthcare setting (primary and/or secondary care).	
2.	Is the targeted medicine listed? (Yes/No)	BNF chapter 6.5.1*: somatropin (HGH) BNF chapter 9.1.3**: epoetin alfa (EPO) BNF chapter 9.1.6***: filgrastim (G-CSF)	
3.	How it is listed? (formulary/non-formulary)	Formulary	Medicinal product that is routinely available for prescription.
		Non-formulary	Medicinal product that is not routinely available for prescription. However, if it is deemed needed, it will be made available for the patient.
4.	What is the listing approach? (Brand name/INN/Both)	As per brands listed in BNF chapters 6.5.1, 9.1.3 and 9.1.6.	
5.	What are the listed brands? (R-BMP/BSP/Both)	BNF chapter 6.5.1: 1 R-BMP and 1 BSP BNF chapter 9.1.3: 1 R-BMP and 2 BSPs BNF chapter 9.1.6: 1 R-BMP and 3 BSPs	

6.	What is the preferred type? (R-BMP/BSP/Not specified*)*	Being the only listed brand/type; Clearly stated that this brand/type is the preferred for prescription; or Brand/type listed as formulary while other brands/type listed as non-formulary.
7.	Are there clear restrictions in prescribing? (Yes/No)	Whether or not there are specified restrictions in terms of who can prescribe these products and/or prescribing settings i.e. primary or secondary care.
8.	Is there specified brand of choice? (Yes/No)	If it is clearly stated that a specific brand is considered as the brand of choice.
9.	Are there special population considerations? (Yes/No)	If there are considerations related to patients' age, medical history and/or life style factors that might affect type/brand of preference (R-BMP or BSP).
10.	Are there special indications' considerations? (Yes/No)	If there are considerations related to indications that might affect type/brand of preference (R-BMP or BSP).

BNF: British National Formulary 68th Edition; **BMP:** Biological medicinal product; **BSP:** Biosimilar medicinal product; **INN:** International non-proprietary name(molecular name); **R-BMP:** Reference biological medicinal product

***6.5.1:** Drugs used in hypothalamic and anterior pituitary hormones and anti-oestrogen; 1 R-BMP and 1 BSP brand
****9.1.3:** Drugs used in hypoplastic, haemolytic, and renal anaemias; 1 R-BMP and 2 BSP brands
*****9.1.6:** Drugs used in neutropenia; 1 R-BMP and 3 BSP brands

Table 2

Table 2- Results Summary

Investigated Attributes		Medicine Group		
		Filgrastim (G-CSF)	**Epoetin alfa (EPO)**	**Somatropin (HGH)**
Medicine being listed				
	Not listed	27 (18%)	31 (21%)	20 (14%)
	Listed as Formulary	115 (79%)	107 (73%)	120 (82%)
	Listed as Non-formulary	4 (3%)	8 (6%)	6 (4%)
	Total	**146**	**146**	**146**
Clear Prescription Restrictions				
	Yes	78 (66%)	77 (67%)	84 (67%)
	No	41 (34%)	38 (33%)	42 (33%)
	Total	**119**	**115**	**126**
Listing approach				
	INN name	58 (49%)	44 (38%)	64 (51%)
	Brand names	49 (41%)	60 (52%)	59 (47%)
	Mixed Listing	12 (10%)	11 (10%)	3 (2%)
	Total	**119**	**115**	**126**
Listed Brands				
	Both	36 (59%)	21 (30%)	25 (40%)
	R-BMP Only	11 (18%)	48 (68%)	4 (7%)
	BSPs Only	14 (23%)	2 (3%)	33 (53%)
	Total	**61**	**71**	**62**
Preferred Type				
	R-BMP	10 (16%)	52 (73%)	29 (47%)
	BSPs	30 (49%)	4 (6%)	7 (11%)
	Unclear	21 (34%)	15 (21%)	26 (42%)
	Total	**61**	**71**	**62**
Specified Brand of Choice				
	Yes	13 (21%)	4 (6%)	9 (15%)
	No	48 (79%)	67 (94%)	53 (85%)
	Total	**61**	**71**	**62**
Special Population Considerations[3]				
	Yes	3 (5%)	8 (11%)	10 (16%)
	No	58 (95%)	63 (89%)	52 (84%)
	Total	**61**	**71**	**62**
Special Indication Considerations				
	Yes	9 (15%)	7 (10%)	0 (0%)
	No	52 (85%)	64 (90%)	62 (100%)
	Total	**61**	**71**	**62**

BSP: Biosimilar medicinal product; **INN:** International non-proprietary name (molecular name); **R-BMP:** Reference biological medicinal product

[3] Factors related to patient population or indication that might affect prescriber brand/product of choice.

List of Declarations:
The authors declare no potential conflicts of interest.

Funding:
This study is part of a PhD project funded by Yarmouk University- Jordan

REFERENCES

1. Committee for Medicinal Products for Human Use, 2006. Guideline on similar biological medicinal products containing biotechnology-derived proteins as active substance: non-clinical and clinical issues. London: European Medicines Agency
2. Assessing biosimilar uptake and competition in European markets [Internet]. Intercontinental Marketing Services Health (IMS)-Institute for Healthcare Informatics.; 2014. Available from: https://www.imshealth.com/files/web/IMSH%20Institute/Healthcare%20Briefs/Assessing_biosimilar_uptake_and_competition_in_European_markets.pdf
3. Generating value in generics: Finding the next five years of growth [Internet]. www.mckinsey.com. 2013 [cited 8 April 2017]. Available from: http://www.mckinsey.com/~/media/mckinsey/dotcom/client_service/pharma%20and%20medical%20products/pmp%20new/pdfs/generating%20value%20in%20generics_final.ashx
4. Declerck PJ, Simoens S. European perspective on the market accessibility of biosimilars. Biosimilars. 2012;2:33-40
5. Prescribing Team-Health and Social Care Information Centre (HSCIC). Hospital Prescribing England 2013-14 [Internet]. London: Health and Social Care Information Centre (HSCIC); 2014. Available from: http://content.digital.nhs.uk/catalogue/PUB15883/hosp-pres-eng-201314-rep.pdf
6. US$67 billion worth of biosimilar patents expiring before 2020 [Internet]. Generics and Biosimilars Initiative (GaBI). 2012 [cited 8 April 2017]. Available from: http://www.gabionline.net/Biosimilars/General/US-67-billion-worth-of-biosimilar-patents-expiring-before-2020
7. Authorisation of medicines [Internet]. European Medicines Agency (EMA). [cited 8 April 2017]. Available from: http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/general/general_content_000109.jsp&mid=WC0b01ac0580028a47
8. Brussels MR. Difficulties with Biosimilar Drugs. European Journal of Cancer. 2005;41(15):2203
9. Rovira J, Espín J, García L, Olry de Labry A. The impact of biosimilars' entry in the EU market. Andalusian Sch Pub Health. 2011 Jan;30:1-83
10. European Generic Medicines Association. EGA handbook on biosimilar medicines. European Generic Medicines Association, Brussels. 2010. [cited 8 April 2017]. Available from: http://www.bogin.nl/files/ega_biosmilarshandbook.pdf
11. Aapro MS. What does a prescriber think of biosimilars?. Oncologie. 2011 May 1;13(5):234.
12. Gascón P, Tesch H, Verpoort K, Rosati MS, Salesi N, Agrawal S, Wilking N, Barker H, Muenzberg M, Turner M. Clinical experience with Zarzio® in Europe: what have we learned?. Supportive Care in Cancer. 2013 Oct 1;21(10):2925-32.
13. Biosimilars - Biosimilar medicines [Internet]. Ema.europa.eu. [cited 9 April 2017]. Available from: http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/document_listing/document_listing_000318.jsp
14. British Generic Manufacturers Association (BGMA). Biosimilar medicines-Maximising benefits for patients and the NHS [Internet]. London: British Generic Manufacturers Association (BGMA); 2013. Available from:

http://www.britishgenerics.co.uk/admin/files//1403704797_BGMA-Biosimilars-Briefing-Paper.pdf
15. Reporting suspected adverse drug reactions to vaccines and biological medicines Drug Safety Update - GOV.UK [Internet]. Gov.uk. 2012 [cited 9 April 2017]. Available from: https://www.gov.uk/drug-safety-update/reporting-suspected-adverse-drug-reactions-to-vaccines-and-biological-medicines
16. Prescribing and Primary Care Services. Prescriptions Dispensed in the Community [Internet]. London: Health and Social Care Information Centre; 2013. Available from: http://content.digital.nhs.uk/catalogue/PUB11291/pres-disp-com-eng-2002-12-rep.pdf
17. Developing and updating local formularies. The National Institute for Health and Care Excellence (NICE); 2015 p. London
18. Duerden M, Walley T. Prescribing at the interface between primary and secondary care in the UK. Pharmacoeconomics. 1999 May 1;15(5):435-43
19. Heal SJ, Challinor N, Roome C, Gammie S, Thorne J, Wilcock M. What do GPs think about joint formularies?. Pharmaceutical Journal (Vol 276). 2006 Feb 11.
20. Committee for Proprietary Medicinal Products (CPMP). Opinion following an Article 7(5) referal for Genotropin International Non-Proprietary Name (INN): Somatropin: Background information [Internet]. London: European Medicines Agency (EMA); 2003. Available from: http://www.ema.europa.eu/docs/en_GB/document_library/Referrals_document/Genotropin_7_5/WC500013685.pd
21. London New Drugs Group. Comparison of growth hormone products and devices [Internet]. London: UK Medicines Information (UKmi); 2013. Available from: http://www.medicinesresources.nhs.uk/upload/documents/Evidence/Comparison%20of%20growth%20horm
22. Müller R, Renner C, Gabay C, Cassata G, Lohri A, Hasler P. The advent of biosimilars: challenges and risks. Swiss Med Wkly. 2014 Jul 1;144:w13980
23. Rickwood S, Di Biase S. Searching for Terra Firma in the Biosimilars and Non-Original Biologics Market. Insight for the Comming Decade of Change IMS Health Biosimilars and Non--Original Biologics Dostupné na www ims com. 2013:24
24. Schellekens H. Biosimilar therapeutics—what do we need to consider?. NDT plus. 2009 Jan 1;2(suppl 1):i27-36.
25. Jimenez AG, Brake B. Biosimilars in the European Union -Regulatory perspectives. ICH GCG ASEAN Training Workshop. 2011
26. Ramachandra S. Lessons for the United States: Biosimilar Market Development Worldwide [Internet]. Hospira Pharmaceuticals; 2013. Available from: https://www.ftc.gov/system/files/documents/public_events/Follow-On%20Biologics%20Workshop%3A%20Impact%20of%20Recent%20Legislative%20and%20Regulatory%20Naming%20Proposals%20on%20Competition/ramachandra.pdf
27. Scottish Medicines Consortium Biosimilar Medicines [Internet]. Scottishmedicines.org.uk. 2015 [cited 9 April 2017]. Available from: https://www.scottishmedicines.org.uk/About_SMC/Policy_statements/Biosimilar_Medicines

28. All Wales Medicines Strategy Group (AWMSG). Form B Guidance Note-Appraisal Submission. Vale of Glamorgan: All Wales Medicines Strategy Group (AWMSG); 2013