

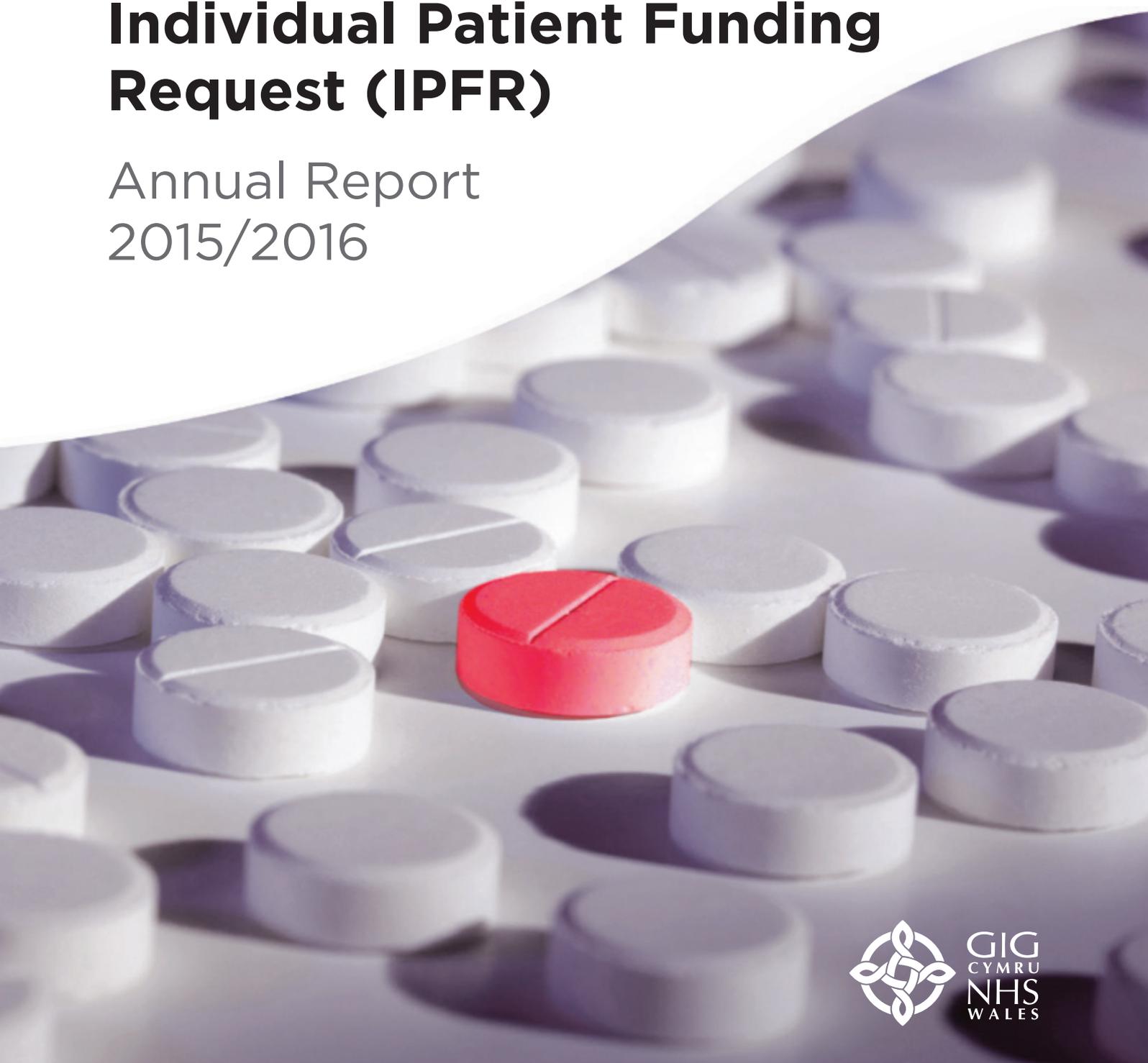


AWTTC

All Wales Therapeutics & Toxicology Centre
Canolfan Therapiwteg a Thocsicoleg Cymru Gyfan

Individual Patient Funding Request (IPFR)

Annual Report
2015/2016



PAMS

Patient Access to Medicines Service
Mynediad Claf at Wasanaeth Meddyginiaethau

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AWTTC Clinical Director's Statement 2015/2016 – A Year of Progress



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In 2015-16, we have all worked together in NHS Wales to seek to implement the recommendations which came out of the 2014 review of the Individual Patient Funding Request (IPFR) process. With the support of the All Wales Therapeutics and Toxicology Centre (AWTTC), IPFR teams in health boards across NHS Wales have sought to strengthen and improve the IPFR process, particularly in relation to transparency and inter-panel consistency. Having visited every IPFR panel in Wales during 2015/2016, I am pleased that the process for considering IPFRs is broadly consistent across all health boards, and I am looking forward to sharing the notes of good practice which are currently being compiled.

First of all, I would like to acknowledge the enthusiasm and commitment of the panel co-ordinators who continue to work extremely hard to support the IPFR process. We have been extremely grateful to the co-ordinators for submitting information to AWTTC in order for it to be compiled centrally. This has been invaluable in identifying clinical need for particular medicines and has highlighted potential patient “cohorts”.

One key area of work was the update of the NHS Wales IPFR policy and supporting guidance. I am sure that the amended document will provide more clarity in relation to what constitutes an appropriate IPFR panel application. The policy and supporting guidance were launched at an IPFR Training Workshop held in Cardiff on 19th April 2016.

Thanks to all the IPFR panel Chairs and members who participated in this event and the presenters at that meeting for their valuable contributions. Feedback showed that IPFR panel Chairs and members found the training day valuable, so we will ensure it becomes an annual event.

There are clearly continuing challenges in taking forward the medicines agenda in a changing national and global environment. However, with the implementation of the recommendations following the 2014 review of the IPFR process we are taking positive steps to ensure there is a robust, consistent and patient-focused approach to decision-making for individual patients, based on the best available evidence. I am confident that we will all continue to work together to improve the IPFR process to obtain the best outcomes for patients in Wales.

Background

Health boards in Wales have a statutory responsibility for the health of their populations and they discharge this duty, in part, through the provision of safe and high quality clinical services. They are also required to ensure the efficient use and application of their workforce and financial resource.

A comprehensive range of NHS healthcare services are routinely provided across Wales. In addition, the Welsh Health Specialised Services Committee (WHSSC), working on behalf of the seven health boards in Wales, commissions specialised services at national level. IPFRs are defined as 'requests to a health board to fund healthcare for an individual who falls outside the range of services and treatments that a health board has agreed to provide routinely', for example equipment or a device, a service or a specific non-drug treatment (e.g. a surgical intervention) or a medicine.

Assessment of the clinical and cost-effectiveness evidence for clinical interventions (i.e. for medicines, treatments or procedures) is very important when making decisions in relation to services that will be offered by health boards within a resource-constrained environment. Where there is evidence of clinical and cost-effectiveness for an intervention, it will normally be made generally available in the NHS in Wales in line with clear criteria, often based on the outcome of an assessment of the evidence by the National Institute of Health and Care Excellence (NICE) or the All Wales Medicines Strategy Group (AWMSG). However, there is also a clinical need (and a legal requirement) for a robust policy and process to consider requests for individual patients when a medicine, treatment or procedure is not generally available throughout the service.

In 2010, the Director General, Health and Social Services, Chief Executive, NHS Wales requested that health boards would work together with WHSSC and Public Health Wales (PHW) to develop an all Wales policy and standard documentation for the IPFR process. That policy has been in place since September 2011.

In October 2013, the Minister for Health and Social Services announced a review of the IPFR process in Wales to explore how it could be strengthened and an independent review group was established in April 2014. Their report was published for formal consultation. The report concluded that the IPFR process in Wales was comprehensive and supported rational, evidence-based decision making for medicine and non-medicine technologies which are not routinely available in Wales. However, the review group also made several recommendations to strengthen and improve the IPFR process and in March 2015 the Welsh Government asked health boards to work with AWTTTC to implement the report's recommendations.

Implementing recommendations following the 2014 review of the IPFR process

AWTTC developed an implementation plan and, in conjunction with health boards IPFR co-ordinators, work commenced on implementing the ten recommendations.

Recommendation 1: The NHS Wales policy and supporting guidance should be updated to define what constitutes an appropriate application to the IPFR panel

Action taken in reporting period:

- The NHS Wales policy and supporting guidance has been updated to help define what constitutes an appropriate application to the IPFR panel.
- An IPFR training day was held on the 27th January 2016 to support panel members in improving their skills in appraising the types of evidence submitted as part of IPFR applications.

Recommendation 2: AWTTC should be placed at the heart of the IPFR process supporting IPFR panels to work more cohesively, collating and monitoring all IPFR applications for appropriateness, identifying emerging trends and compiling the annual report for the process. This arrangement will also strengthen the position of AWTTC to support training for panel members and clinicians

Action taken in reporting period:

- AWTTC commenced their central co-ordinating role in April 2015.
- AWTTC staff and the lead IPFR co-ordinator for Wales attended meetings of all IPFR panels.
- NHS Wales Informatics Service (NWIS) initiated the development of a bespoke IPFR database.
- A common dataset was agreed for use to identify emerging trends within IPFR applications.

Recommendation 3: For medicines, AWTTC should establish and maintain a central data store for search strategies and key evidence. For non-medicine technologies and other interventions PHW should establish and maintain a central data store for search strategies and key evidence

Action taken in reporting period:

- AWTTC commenced the development of a central repository for evidence; this will be developed as part of the IPFR database.

Recommendation 4: The existing IPFR panels linked to the seven health boards and WHSSC should continue. A move to hold joint meetings of neighbouring panels may be considered further once the recommendations of this report have been implemented and reviewed

- No specific action was required during the reporting period.

Recommendation 5: IPFR panels should increase their lay representation to two voting members whilst the Community Health Council (CHC) representative should become a non-voting member. This will allow the CHC representative to focus, unfettered, on their role as a patient representative

Action taken during reporting period:

- A person-specification has been agreed outlining the roles and responsibilities of the lay member(s).
- The recruitment process for further lay members has commenced.

Recommendation 6: Each IPFR panel should have a mechanism in place to ensure appropriate clinical advice is available on or before the day of the panel to clarify clinical issues and avoid unnecessary delays in reaching a decision

Action taken during reporting period:

- The IPFR application form has been updated to include a clinical contact section.

Recommendation 7: IPFR applications should be screened for appropriateness prior to submission and countersigned by the relevant Clinical Lead/Head of Department

Action taken during reporting period:

- All actions have been undertaken including the requirement for appropriate support and/or additional sign off where necessary from the relevant clinical lead, head of department or multi-disciplinary team. This has been written into the policy and supporting guidance.

Recommendation 8: AWTTTC should work with health boards and WHSSC to establish a common dataset and patient consent process, for local and national reporting

Action taken during reporting period:

- Advice on patient consent processes has been received from the Information Commissioner's Office and incorporated into the revised IPFR policy and supporting documentation.
- A dataset has been agreed and a reporting process has been established.

Recommendation 9: AWTTTC, in conjunction with IPFR co-ordinators and panel members, should update the NHS Wales policy and supporting guidance on IPFR panels to reflect the recommendations of this report

Action taken during reporting period:

- NHS Wales IPFR policy and guidance has been updated accordingly.

Recommendation 10: Patient outcomes linked to IPFR decisions should be monitored. AWTTTC and health boards should work together to devise a process to collect this information for all technologies

Action taken during reporting period:

- A patient outcome data form has been produced with input from clinicians and IPFR panel members.
- A process for the collection of patient outcome data has been developed.

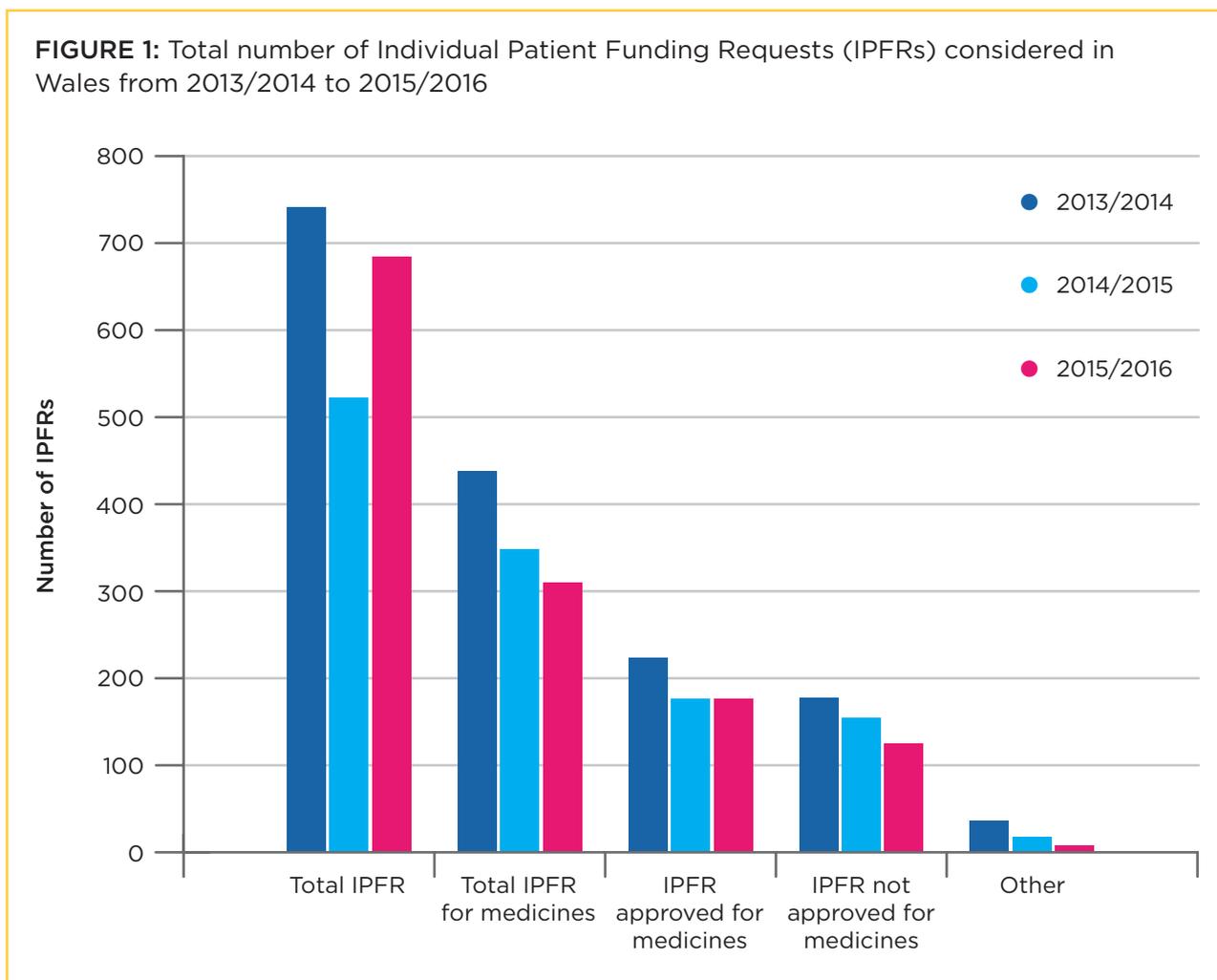
Total IPFRs considered in Wales

A total of 683 IPFRs were considered between 1 April 2015 and 31 March 2016, 309 (45%) were for medicines and the remainder (n = 374; 55%) were for non-medicine related requests (e.g. surgical interventions, medical devices etc.).

Compared with 2013/14 and 2014/15, the number of IPFRs for medicines in Wales in 2015/16 decreased by 29% and 11%, respectively. In contrast, the number of requests for non medicines varied over the same period, with the greatest number of requests for non-medicines occurring in 2015/2016. Refer to Figure 1 below.

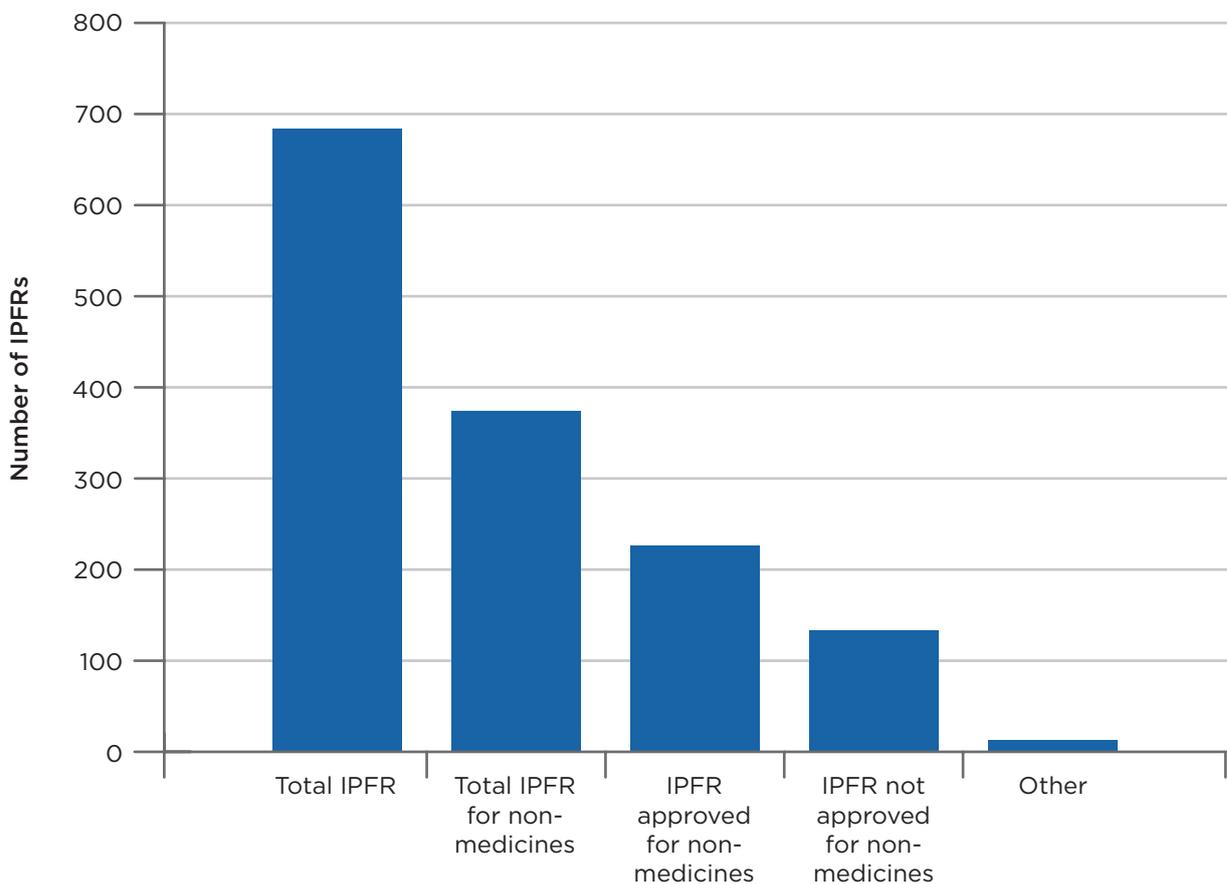
Although the number of IPFRs for medicines has decreased over the last three years, the proportion of requests approved has risen in 2015/16 so that 57% of IPFR requests for medicines were approved compared with 51% in 2013/14 and 2014/15.

The 'other' outcomes shown in Figure 1 include IPFRs for medicines that have been considered but the panel were unable to make a decision whether to approve or not approve funding at the initial consideration. This may be due to several reasons, including deferral of a decision pending receipt of further required information. The number of medicines with 'other' outcomes has decreased since 2013 and made up only 2.6% of total IPFR requests in 2015/16.



The outcomes of the non-medicine IPFRs considered in 2015/2016 are illustrated in Figure 2 below. Of the total IPFRs for non-medicines (n = 374), 226 (60%) were approved and 134 (36%) were not approved. The 'other' outcomes (n = 14; 4%) shown in Figure 2 include IPFRs for non-medicines that were considered initially, but the panel were unable to make a decision whether to approve or not approve funding - this is most often due to insufficient information being available to the IPFR panel. Data were not available for 2013/2014 and 2014/2015 to provide comparison.

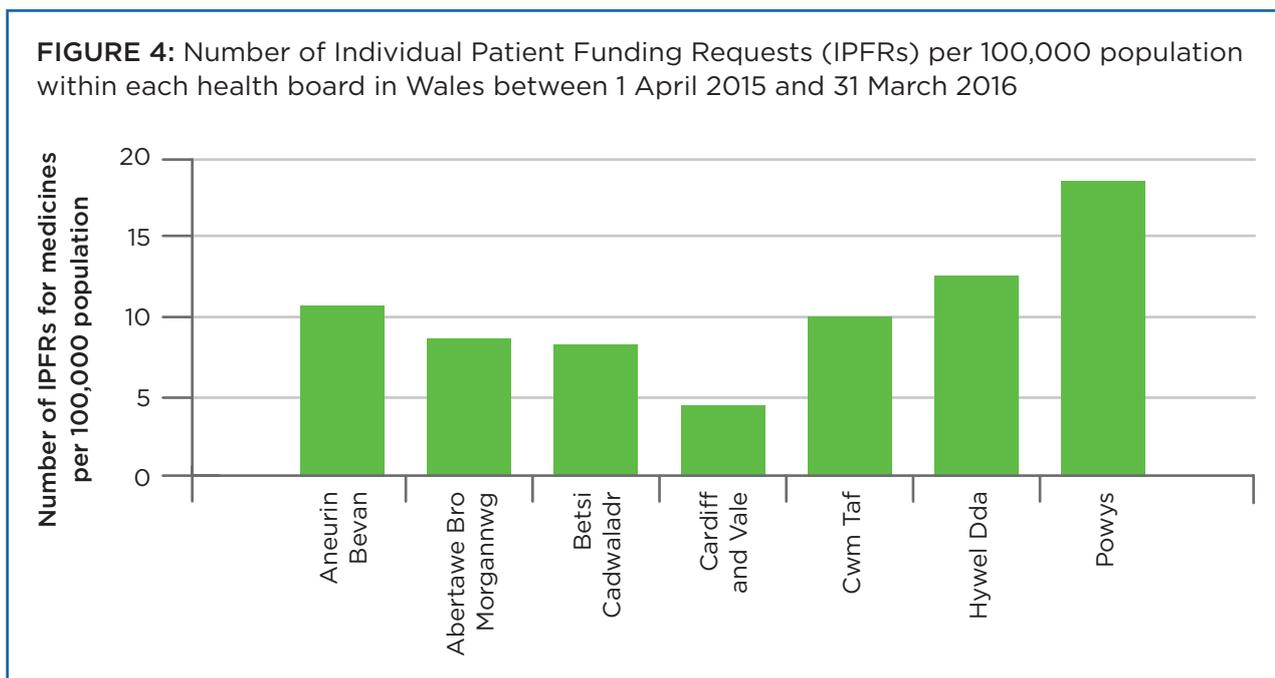
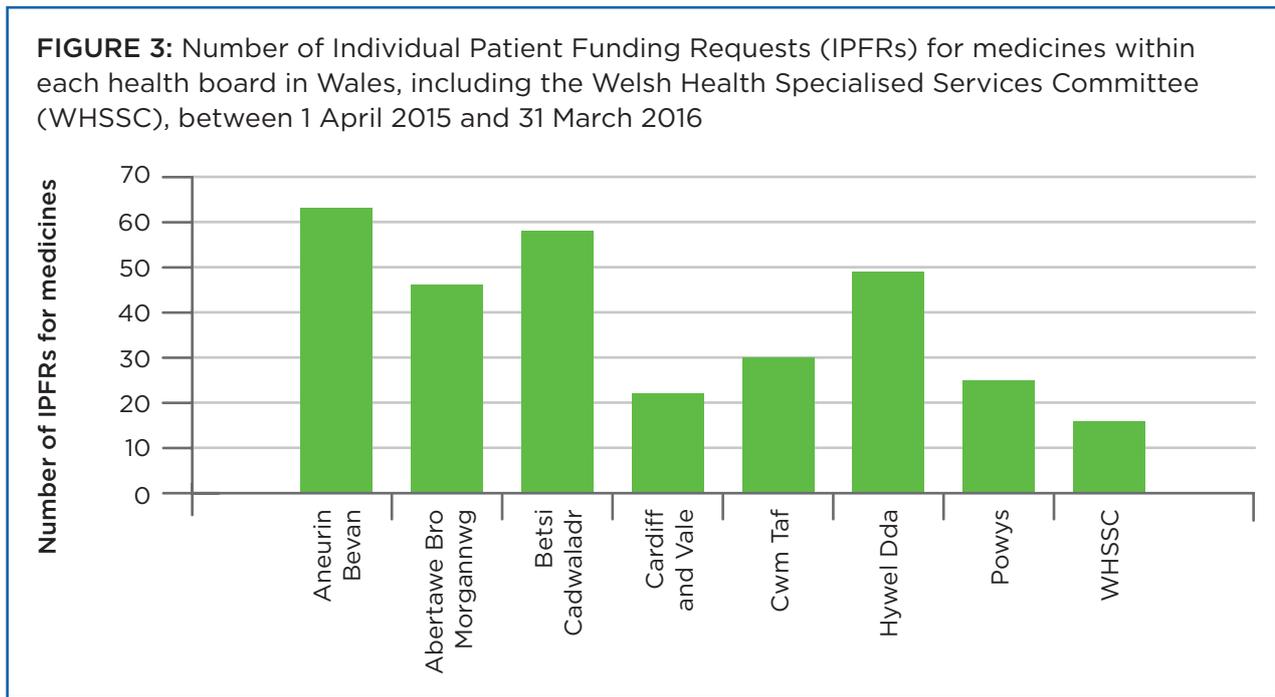
FIGURE 2: Total number of Individual Patient Funding Requests (IPFRs) considered in Wales in 2015/2016



IPFRs for medicines by health board and the Welsh Health Specialised Services Committee (WHSSC)

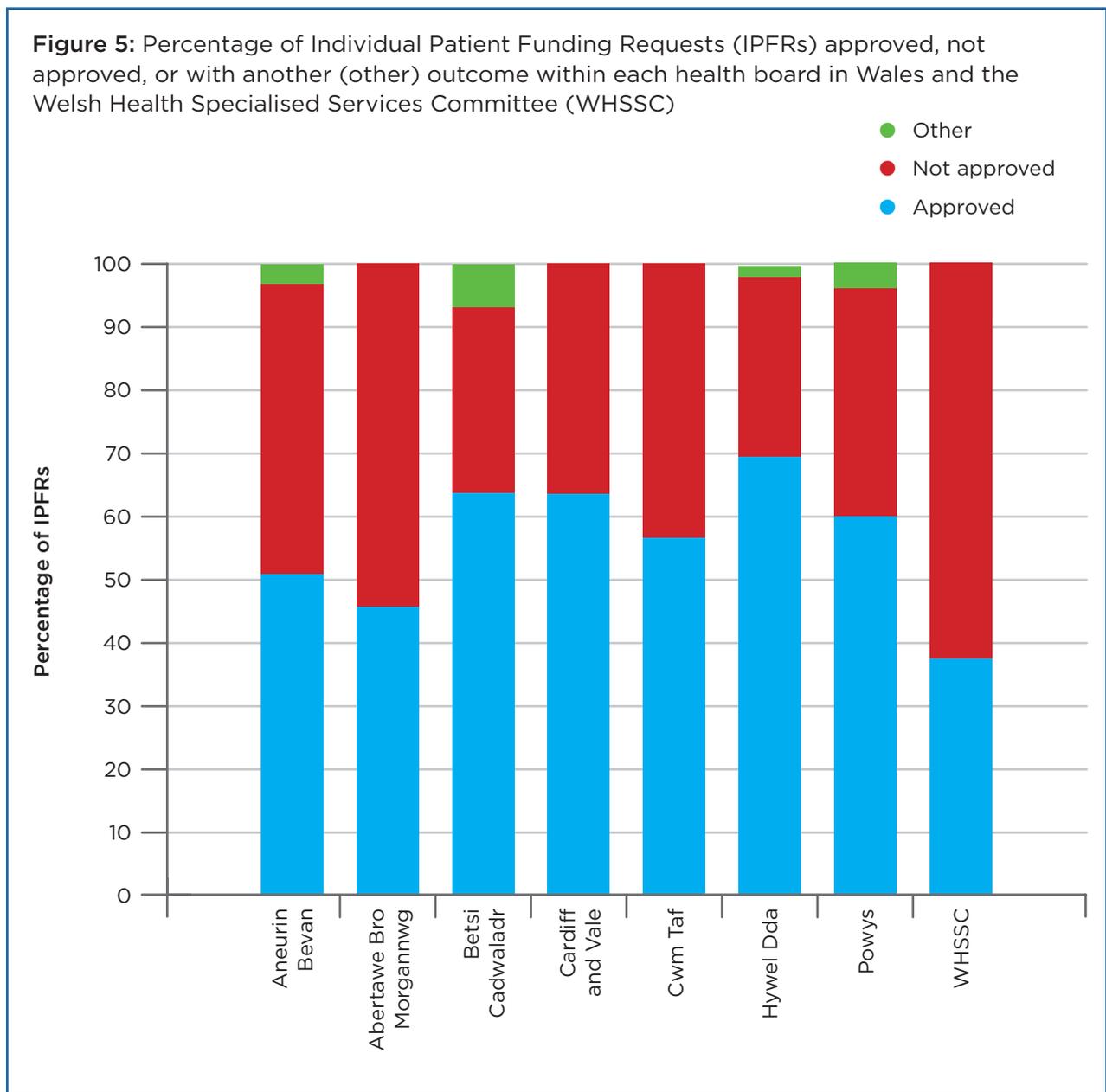
The highest absolute number of IPFRs for medicines was considered by Aneurin Bevan health board (n = 63) and the fewest was considered by WHSSC (n = 16) as shown in Figure 3.

To acknowledge the different population sizes within each health board, these data were expressed as IPFR requests per 100,000 population. The population data were derived from *StatsWales* (mid-year 2015) and the population-corrected data are shown in Figure 4.



These data demonstrate that Powys health board received the highest number of IPFR applications for medicines per head of population (19 per 100,000 population) and Cardiff and Vale health board received the fewest number of applications corrected for population size (5 per 100,000). Reasons for such wide variation in the number of IPFRs considered by each health board may include differences in local commissioning policies and the availability of services (including specialised services) in each health board.

The outcomes of the IPFRs for medicines considered by each health board and WHSSC are shown in Figure 5.



The medicines most frequently considered annually between 1 April 2013 and 31 March 2016 are shown in Table 1. Bevacizumab has been the most frequently requested medicine each year since 2013/2014. However, it is important to note that many of the medicines applied for via the IPFR process, including bevacizumab, are indicated for multiple indications, different treatment regimens and for different stages of the treatment pathway in relation to those different clinical indications.

Table 1: The most commonly requested medicines in rank order

2013/2014	2014/2015	2015/2016
Bevacizumab	Bevacizumab	Bevacizumab
Cetuximab	Axitinib	Cetuximab
Rituximab	Brentuximab	Adalimumab
Axitinib	Bendamustine	Pertuzumab
Adalimumab*	Cetuximab	Rituximab*
Eribulin*	NR	Bendamustine*
Infliximab*	NR	Trastuzumab emtansine

* The same numbers of applications were reported for these medicines in the relevant column. NR = not reported.

Requests for an IPFR occur for three main reasons;

1. Advice in relation to a licensed indication is not available from AWMMSG or NICE.
2. AWMMSG or NICE has given advice, and has not recommended the technology.
3. The medicine is being used 'off-label', i.e. medicine used outside the terms of their marketing authorisation (product licence).

The differences in the medicines requested between each year may be due, in part, to the fact that a proportion of the requests occurred prior to advice being given by AWMMSG or NICE, and following positive advice the IPFR route was no longer required for the particular medicine/indication.

Table 2 shows the medicines most frequently either approved or not approved by IPFR panels from 1 April 2015 to 31 March 2016.

Table 2: The medicines most frequently approved or not approved between 1 April 2015 and 31 March 2016 in rank order

Approved	Not approved
Bevacizumab	Bevacizumab
Adalimumab	Cetuximab
Rituximab	Pertuzumab
Apremilast	Trastuzumab emtansine
Bendamustine	Bendamustine*
Ibrutinib*	Ruxolitinib*
Ruxolitinib*	Sorafenib*

* The same numbers of applications approved/not approved were reported for these medicines in the relevant column

The top ten indications for which the most commonly requested medicines were considered are outlined in Table 3 below.

Table 3: Top 10 medicine-indication combinations considered by IPFR panels in 2015/2016

Medicine	Indication	License Status
Pertuzumab [†]	First-line treatment of metastatic advanced breast cancer	Licensed
Apremilast	Severe psoriasis	Licensed
Bevacizumab 7.5mg	First-line treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer	Off-label
Ruxolitinib*	Myelofibrosis	Licensed
Cetuximab [‡]	≥ 2nd line treatment of advanced colorectal cancer	Licensed
Ibrutinib [†]	Mantle cell lymphoma	Licensed
Bevacizumab [‡]	Metastatic colorectal cancer	Licensed
Vedolizumab*	Crohn's disease	Licensed
Adalimumab	Severe uveitis	Off-label
Enzalutamide*	Prostate cancer	Licensed

* IPFR requests prior to Health Technology Appraisal (HTA) advice becoming available, [†]HTA in progress, [‡]HTA negative recommendation

In the majority of cases, requests were made prior to publication of Health Technology Appraisal (HTA) advice by NICE or AWMSG. Two of the indications were associated with negative HTA advice and two were for off-label use, so that IPFR would be considered the only route for access to those treatments at that time. Both of the off-label medicines have since been taken forward via the One Wales interim Commissioning Process (refer to section 7).

IPFRs for medicines for the treatment of cancer

Medicines for treating cancer were the most commonly requested medicines (58%) via IPFR in 2015/16. Indication data were missing for five (1.6%) of the total medicines considered this year (n = 309) and, therefore, these could not be classified.

The greatest number of IPFRs for medicines for the treatment of cancer was received by Aneurin Bevan health board (n = 39) and the fewest were by WHSSC (n = 8) as shown in Figure 6. The data were also expressed as the number per 100,000 population in the health board and are shown in Figure 7. Powys health board received the greatest number of IPFRs for cancer medicines per 100,000 people (9.8) and Betsi Cadwaladr health board received the fewest (3.0). The percentage of IPFRs for cancer medicines within each health board and WHSSC are shown in Figure 8. At least 50% of IPFRs considered by five health boards and WHSSC, but excluding Betsi Cadwaladr health board and Hywel Dda health board, were for cancer medicines. Indeed, more than 80% of IPFRs considered by Cardiff and Vale health board (n = 19) and Cwm Taf health board (n = 25) IPFR Panels were for cancer medicines. In contrast, fewer than 40% of IPFRs considered by Betsi Cadwaladr health board (n = 21) and Hywel Dda health board (n = 17) were for cancer medicines. Possible reasons for the wide variation in the percentages of IPFRs for cancer medicines between the health boards may be due to differences in commissioning arrangements and in the delivery of cancer treatment services. There may also be differences in local policies or treatment pathways.

FIGURE 6: Number of Individual Patient Funding Requests (IPFRs) for cancer medicines within each health board in Wales and the Welsh Health Specialised Services Committee (WHSSC) between the 1 April 2015 and 31 March 2016

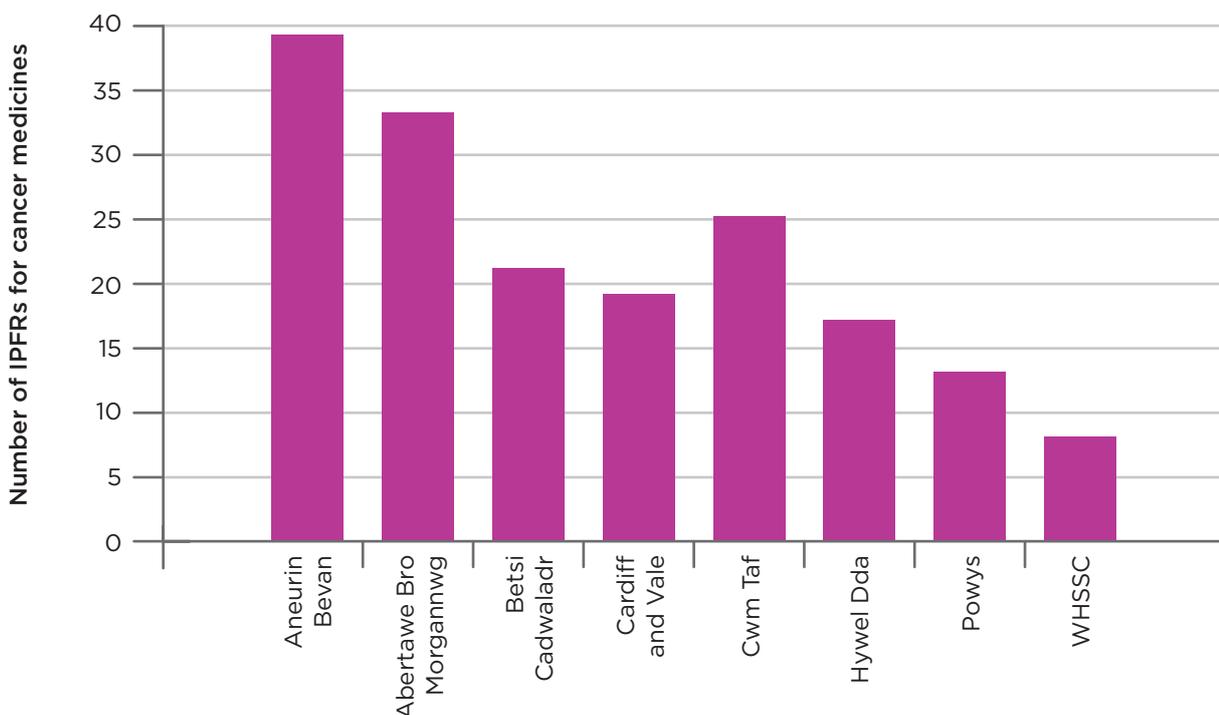


FIGURE 7: Number of Individual Patient Funding Requests (IPFRs) for cancer medicines per 100,000 population within each health board in Wales between 1 April 2015 and 31 March 2016

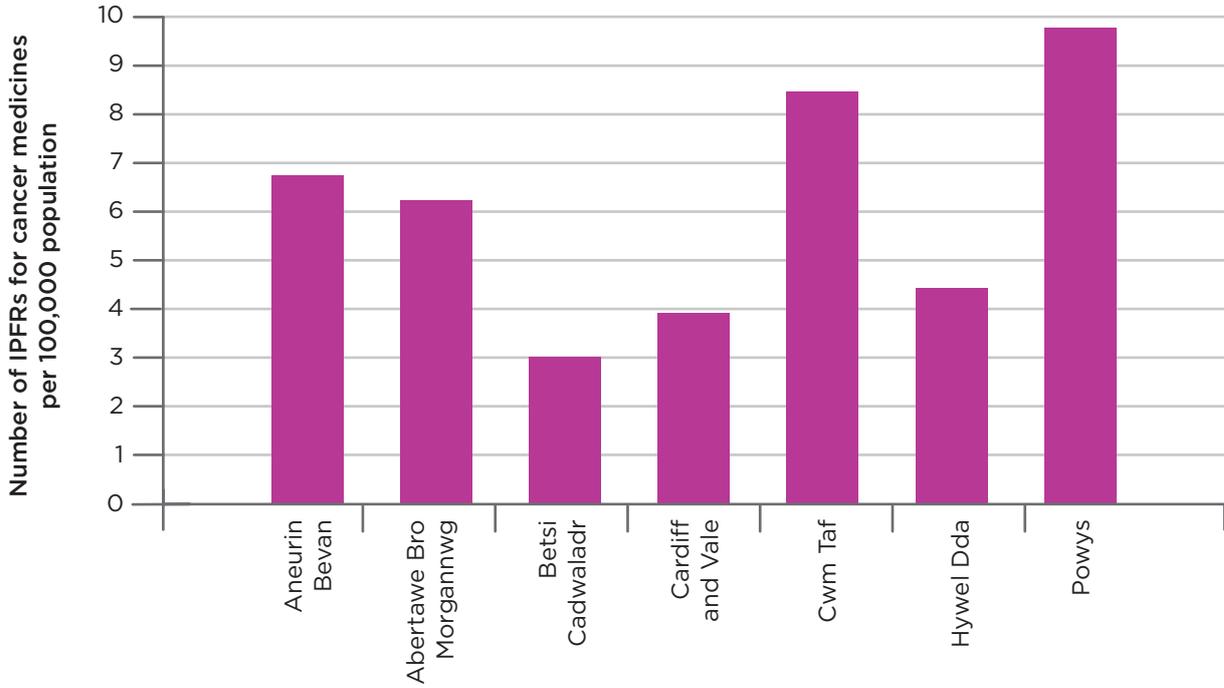
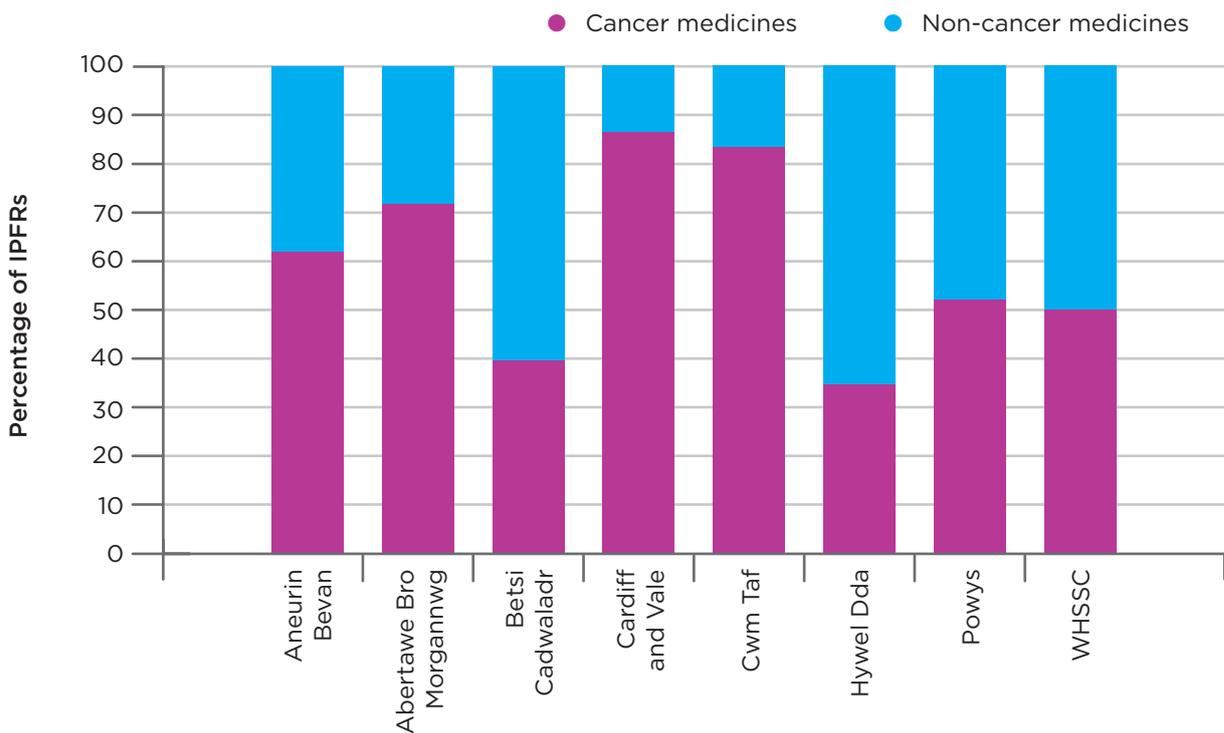
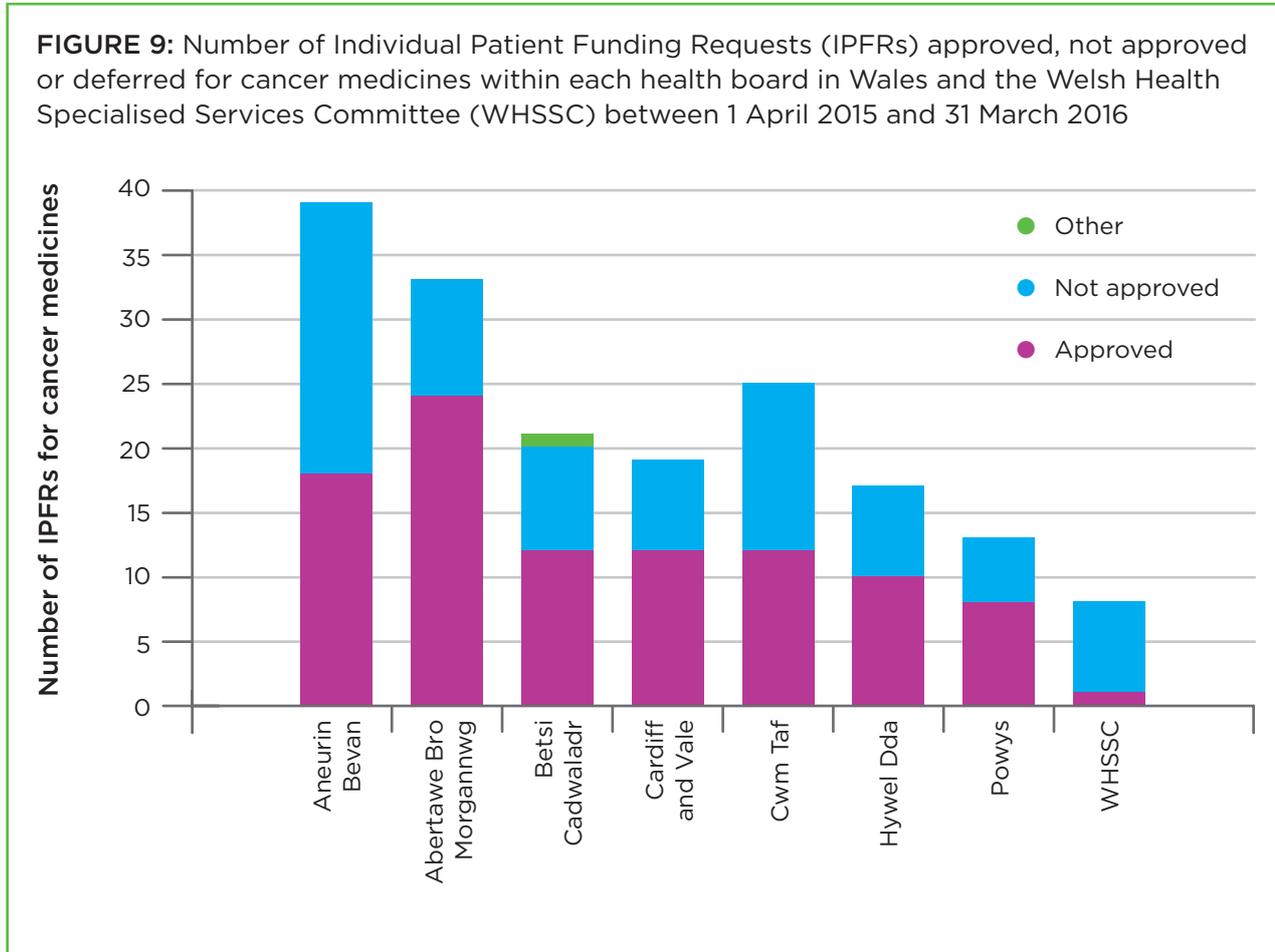


FIGURE 8: Percentage of Individual Patient Funding Requests (IPFRs) for cancer and non-cancer medicines within each health board in Wales and the Welsh Health Specialised Services Committee (WHSSC) considered by IPFR panels between 1 April 2015 and 31 March 2016



The outcomes of the IPFRs for cancer medicines considered by health boards and WHSSC are shown in Figure 9. More than 50% of IPFRs for cancer medicines were approved by five of the health boards.



IPFR and the One Wales Interim Commissioning Process

Analysis of the 2015-16 IPFR submission data from health boards across Wales has been used to inform other aspects of the AWTTTC work programme, and in particular the new One Wales Interim Commissioning Process.

The One Wales Interim Commissioning Process has been developed to facilitate one decision for NHS Wales on access to medicines for a group of patients (a patient “cohort”) where an unmet clinical need for treatment of the condition has been identified. A patient cohort is defined as several patients with the same clinical presentation who may benefit from a particular medicine. In such circumstances the IPFR process, with its emphasis on exceptionality, may not be considered appropriate and may result in a variation in access to a medicine across Wales. The main aim of the One Wales process is to ensure equity of access to medicines not routinely available in NHS Wales for a patient cohort.

Medicines not routinely available may include licensed medicines for which there is no HTA advice (either from NICE or AWMSG); medicines used off-label, i.e. outside their licensed indications (as defined in the product-licence); or unlicensed medicines i.e. medicines which have no product licence for use for that specific indication in the UK.

The preferred route for accessing licensed medicines is via HTA. However, in a small number of cases a One Wales interim commissioning decision may be appropriate, providing there is a commitment to HTA by the licence holder within a specified timeframe. An interim commissioning decision ahead of HTA enables the collection of patient outcome data which can be used to provide more robust clinical and cost-effectiveness evidence for subsequent HTA. For off-label or unlicensed medicines, where there is no suitable licensed medicine available which will meet the patient’s needs, the One Wales process enables interim commissioning, which is reviewed on an annual basis.

If a medicine meets the criteria for the One Wales process, AWTTTC compiles an Evidence Status Report (ESR). The ESR is the body of evidence considered by the Interim Pathways Commissioning Group (IPCG) when making a recommendation to NHS Wales Chief Executives as to whether or not the medicine should be made available within NHS Wales for a patient cohort. Membership of the IPCG includes representation from every IPFR panel in Wales. The IPCG reports to the NHS Wales Executive Board of Chief Executives, which makes the final decision concerning interim commissioning in Wales.

Medicines and patient cohorts are identified for the One Wales process by signals from activity in the IPFR panels, from WHSSC, the Committee of Chief Pharmacists or clinician groups. Collation and analysis of data from IPFR panels across Wales enables AWTTTC to identify potential patient cohorts – thus if several applications for IPFR are submitted across NHS Wales for the same medicine and indication, AWTTTC is alerted to a potential patient cohort.

A total of 36 patient cohorts were identified in the year 2015-16; 23 of these were not considered appropriate for One Wales interim commissioning for the reasons shown in Table 4:

Table 4: Patient cohorts identified between 1 April 2015 and 31 March 2016 not considered appropriate for One Wales interim commissioning

Number of patient cohorts	Reasons not considered appropriate for One Wales interim commissioning
14	NICE or AWMSG HTA advice had already been published (IPFR requests are predominantly made before HTA advice had been published or within the three month implementation window)
8	The medicine was already on either the NICE or AWMSG HTA work programmes
1	Positive AWMSG advice had already been published for a licensed alternative

The analysis of IPFR data by AWTTTC has also been invaluable in informing the HTA process. Five medicines have been identified as being suitable for HTA and a submission from the manufacturer for appraisal by AWMSG has been requested. It has also been invaluable in identifying differences in prescribing and variation in access to medicines across NHS Wales.

Exceptionality

The word ‘exceptional’ is defined in the Oxford English Dictionary as being “of the nature of or forming an exception: out of the ordinary course, unusual, special”. There are situations that occur where the patient is clearly different from other patients with the same clinical condition or where an individual patient might benefit from a treatment in a different way to other patients.

Recognising that it can never be possible to anticipate all unusual or unexpected circumstances, the decision-making guidance contained within the NHS Wales IPFR policy asks;

1.	What is the clinical presentation of the patient?
2.	Is the evidence supplied to explain why the clinical presentation of this patient is unusual and different to that expected for this disease and this stage of disease?
3.	Is evidence supplied to demonstrate why the patient would gain a greater clinical benefit?

In developing a common dataset as part of the review recommendations, AWTTTC can report that, of the 176 IPFR cases for medicines approved in 2015/16, “exceptionality” was recorded to have been demonstrated in 110 cases and not demonstrated in 25 cases. The rationale for the decision has not been recorded for the remaining 41 cases - this will be a mandatory (required) field for completion on the new shared database.

Reasons for exceptionality included:

1.	The patient had a rare disease or rare variant of a disease
2.	Co-morbidity contraindicated the usual recommended treatment for a condition
3.	The patient had experienced a severe adverse reaction to the normally recommended treatment for the condition
4.	The patient was younger than usual for the condition and had a performance status which meant that he/she was more able to tolerate a particular treatment (and therefore was expected to do better on that treatment)

In cases where exceptionality had not been proven and treatment was approved, access had been granted on grounds of 'good governance', 'NICE advice pending (and expected to be positive)', or 'continuation of treatment previously approved'.

Of the 125 medicines not approved between April 2015 and March 2016 exceptionality was said not to be demonstrated in 109 cases. The reason for not approving the remaining 16 requests was not provided and, as stated previously, this will be a mandatory (required) field for completion on the shared new database.

Reasons for not approving an IPFR included:

1.	Patient presented with normal disease progression
2.	Patient had adherence (compliance) issues with existing treatment
3.	Patient had not exhausted the alternative treatments available
4.	Lack of evidence for use of the treatment in the particular presentation
5.	Conflicting evidence that treatment may do more harm than good
6.	Negative HTA advice published by NICE or AWMSG
7.	Patient to be enrolled in a clinical trial

Patient Outcomes

Of the data collected during 2015-16 patient outcome information was available for 17 people.

- Ten individuals improved in association with the approved treatment (6 were requests for continued funding)
- Three individuals did not improve or experienced an adverse drug reaction
- Four people died (two prior to receiving treatment, but it should be noted that no delays in treatment were recorded for any person)

The collection of outcome data is very important in order to monitor and analyse whether or not a treatment has been effective and it will be a mandatory (essential) part of the IPFR reporting process in the future. In addition, the IPFR policy has been updated to reflect the requirement for (and obtain a commitment from) the requesting clinician to provide outcome data as part of the IPFR application process.

Summary of the data

Overall the data for 2015/16 indicate:

- *A decline in the number of IPFRs across Wales compared with previous years*

Possible reasons for the decline in requests for medicines may be a greater awareness by the submitting clinicians of HTA advice, or a better understanding of the most appropriate route(s) for accessing a medicine on behalf of patients.

- *A decline in the number of IPFRs for which a decision could not be made at the initial meeting*

This may be because the quality of IPFR applications has improved so that panels are better informed and have sufficient information available to make a decision.

- *Health boards approved a similar number of IPFRs for cancer medicines in 2015-2016 compared with previous years.*
- *The most commonly requested medicines were for the treatment of cancer and in that group of medicines, bevacizumab remains the most commonly requested cancer medicine via IPFR.*

In compiling this 2015-16 report, health boards have submitted information to AWTTTC on a regular basis. It is envisaged that the new IPFR database, which is currently in development and due to be launched in 2016, will improve reporting functionality. It will also enable greater consistency of data across the health boards, collation and audit of outcome data and will provide a search facility for evidence relating to a specific medicine and indication.

Glossary and additional note

AWMSG	All Wales Medicines Strategy Group
AWTTC	All Wales Therapeutics and Toxicology Centre
CHC	Community Health Council
ESR	Evidence Status Report
HTA	Health Technology Appraisal
IPCG	Interim Pathways Commissioning Group
IPFR	Individual Patient Funding Request
NHS	National Health Service
NICE	National Institute of Health and Care Excellence
NWIS	NHS Wales Informatics Service
PHW	Public Health Wales
WHSSC	Welsh Health Specialised Services Committee

Additional note

Where small numbers are involved, we are unable to provide the names of specific treatments as the potential risk of identifying individual patients becomes significant. Therefore, this information is considered personal information and is withheld under Section 40(2) of the Freedom of Information Act 2000. This information is protected by the Data Protection Act 1998, as its disclosure would constitute unfair and unlawful processing and would be contrary to the principles set out in Schedules 2 and 3 of the Act.