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RESEARCH ARTICLE

Use of non-formulary high-cost medicines in an Australian public hospital

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Abstract

Background Clinicians prescribe high-cost medicines for rare diseases and nonapproved indications when conventional therapies have failed. *Objective* To examine the use of non-formulary high-cost medicines at an Australian public hospital. *Methods* Retrospective audit of individual patient use applications for nonformulary medicines costing more than $5000 AUD per year at a large tertiary referral hospital in Adelaide, South Australia over a 12-month study period from January 2015 to December 2015. *Main outcome measures* Total cost of non-formulary high-cost medicines, medication class, indications for use, level of supporting evidence and proposed monitoring outcomes. *Results* Eighty-seven individual patient use applications were examined. All except one were approved, at a total cost of $1,339,203 AUD. The most common drug classes were anti-CD20 (n = 33, 38%), combined antiretrovirals (n = 10, 11%) and TNF-alpha antagonists (n = 10, 11%). There were 56 indications for these medicines with the majority being inflammatory conditions (n = 52, 60%), followed by infections (n = 14, 16%) and malignancies (n = 14, 16%). Of the first-time individual patient use applications (n = 63), there were 25 applications (40%) that provided a case series as supporting evidence. Approximately half of new individual patient use applications (n = 32) proposed an objective monitoring outcome, but few (n = 13, 21%) contained sufficient information to allow a third party to determine efficacy of the medication. *Conclusions* Non-formulary high-cost medicines are being used for a broad range of indications based largely on low levels of evidence. Prospective definition of an adequate response to treatment and reporting of these outcomes is required to improve the evidence-base and to aid decision-making for subsequent treatment courses.

Keywords High-cost medicines · Hospital pharmacy · Australia · Formulary

Impact on practice

- In Australian public hospitals, non-formulary high-cost medicines seem to be used for a broad range of indications, often off-label, with limited supporting evidence.
- Prospective determination of what constitutes an efficacious response to treatment with non-formulary medicines and reporting of these outcomes would build the evidence-base and aid Drug and Therapeutics Committees in deciding whether to fund subsequent treatment courses.

Introduction

Although there is no standard definition for high-cost medicines, they can account for up to 25% of public hospital expenditure on drugs in Australia [1]. Clinicians often prescribe high-cost medicines outside the hospital formulary for rare diseases and non-approved indications when conventional therapies have failed.

In Australia, prescription medicines are funded by the Australian government through the Pharmaceutical Benefits Scheme (PBS), following demonstration of their efficacy, safety and cost-effectiveness compared with other treatments

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[2]. High-cost drugs for rare diseases and non-approved indications are rarely listed on the PBS and the high pricing of these medicines is prohibitive to accessing these medicines for some patients. In many instances, access to these medicines can be provided by Australian public hospitals with the cost of supplying non-approved high-cost medicines borne by Australian public hospitals.

Individual patient use (IPU) of high-cost medicines that are prescribed outside of the hospital formulary is obtained by clinicians through applying to the Drug and Therapeutics Committee (DTC) at their hospital [3, 4]. The DTC is responsible for maintaining the hospital formulary and promoting the quality use of medicines, which is a central objective of Australia's National Medicines Policy [5]. The IPU application form ("Appendix A") requires the submitting clinician to provide evidence that supports the use of the high-cost medicine for the requested indication. They must also nominate a monitoring outcome that could be used to judge the efficacy of the treatment course and estimate the number of similar applications that might be expected per year in their hospital population.

Previous research has demonstrated a significant increase in spending on non-formulary high-cost medicines between 1999 and 2001, through an IPU scheme at St Vincent's Hospital, NSW [6]. Since then, there has been a growth in Australia's expenditure on high cost medicines as a result of the aging population and the introduction of an array of high-cost biological medicines, such as monoclonal antibodies and tyrosine kinase inhibitors [7, 8]. As medicine expenditure grows, hospitals are striving to ensure that their limited resources are being used to provide the best outcomes for their patients [9]. To the best of our knowledge, there are no studies examining the use of non-formulary high-cost medicines in Australia in the current pharmaceutical landscape.

Aims of the study

We aimed to describe the use of non-formulary high-cost medicines at a large tertiary referral hospital in Australia. Our primary measure was the overall cost of funding these medicines. We also examined the types of high-cost medicines used and their indication, evidence to support their use and the nominated monitoring outcomes.

Ethics approval

This audit was conducted as a quality assurance activity of the Drug and Therapeutics Committee. For this type of study formal consent is not required.

Methods

Within South Australia a state-wide formulary exists [10] and medicines not listed on the formulary must be approved through a state-wide application form ("Appendix A"), which is submitted to the local DTC.

A retrospective audit of all IPU applications for high-cost medicines between January 2015 and December 2015, inclusive was conducted at the Royal Adelaide Hospital (RAH), an 800-bed tertiary referral hospital in Adelaide, South Australia. For the purposes of this audit, we defined high-cost as any medicine which would cost more than $5000 AUD per year or course of treatment if not ongoing. This cut-off was chosen as requests above this value required additional approval by the chief operating officer.

Our methodology is an adaption of that previously described by Gallego et al. [6]. We collected all IPU applications for high-cost medicines that had been considered by the DTC during the 2015 calendar year. The original IPU applications, supporting evidence and approval status were obtained from the pharmacy department records.

Data extracted from the IPU applications included the drug name, position of the requesting clinician, indication for use, nominated monitoring outcome, cost of the treatment course and whether approved by the DTC. Information regarding the TGA approval status for the requested indication was obtained from the Australian Register of Therapeutic Goods [11]. The indications for high-cost medicines were categorised into inflammatory conditions, infections and malignancies.

We then analysed the evidence supporting use for the proposed indications, the nature of the nominated monitoring outcomes and whether these were reported in applications for renewals. This was an extension of the aforementioned methodology which allowed us to examine the level of evidence supporting the use of non-formulary high-cost medicines and whether sufficient information was being collected to audit efficacy using the predetermined monitoring outcomes.

The evidence supporting use for the proposed indications were classified as either systematic review of randomised controlled trials (RCTs), RCTs, cohort studies or case series. This is in accordance with the National Health and Medical Research Council (NHMRC) Evidence Hierarchy ("Appendix C") [12].

The IPU applications were divided into two groups. First-time applications for a high-cost medicine for an individual patient were classified as 'new applications' and applications that requested an extension of previously funded treatment courses were classified as 'renewal applications'.

The nominated monitoring outcomes were classified as objective or subjective. An objective outcome was defined

as an objective investigation, validated severity score or examination finding. For objective outcomes, we determined whether the application contained sufficient detail for a third party to ascertain efficacy of the treatment course from the medical records, in order to be able to allow independent assessment of response, in the case of renewal request. For instance, if the indication was for psoriasis then stating an improvement in symptoms would be a subjective outcome, whereas reporting the Psoriasis Area Severity Index (PASI) [13] would be an objective outcome but would not allow a third party to independently judge whether the criteria for improvement had been met. Conversely, nominating a 50% reduction in PASI as a clinically significant response is an objective outcome that could be independently assessed by a third party. Renewal applications were reviewed to determine whether the efficacy of the previously funded treatment course had been described and if so, whether it included the nominated monitoring outcome.

Descriptive statistics were used to describe the characteristics of the applications for individual patient use of high-cost medicines. These include the medicine name, class, monitoring outcome, indications for use, TGA-approval status for the selected indication and level of supporting evidence. This also included the nature of the monitoring outcome provided and whether these nominated outcomes were being included in renewal applications. A subgroup analysis was conducted for individual medicines that accounted for greater than 30% of the total number of IPUs. This examined the total cost of these most commonly used high-cost non-formulary medicines, indications for their use and TGA-approval status for these indications.

Results

Characteristics of IPU applications

A total of 87 IPU applications for high-cost medicines were requested and examined in the study period. This included 63 new applications and 24 requests for extension of previously approved applications. The requesting clinician was usually a consultant (n = 56, 64%) or registrar (n = 25, 29%) with a smaller proportion of fellows (n = 2, 2%) and junior medical officers (n = 4, 4%). All except one (n = 86) of these applications were approved by the DTC equating to an approval rate of 99%. The total cost for non-formulary medicines costing more than $5000 AUD per year or treatment course was $1,339,203 AUD in 2015.

IPU applications by drug and class

The high-cost medicines most commonly requested were rituximab (n = 33, 38%), abacavir/dolutegravir/lamivudine (n = 10, 11%) and infliximab (n = 8, 9%) (Table 1). There were a further 27 different drugs ranging from anti-infectives to monoclonal antibodies and antivirals. The most common classes of medicines requested were anti-CD20 (n = 33, 38%), combined antiretrovirals (n = 10, 11%), tumor necrosis factor (TNF)-alpha antagonists (n = 10, 11%), azoles (n = 5, 6%), tyrosine kinase inhibitors (n = 4, 5%) and immunoglobulins (n = 3, 3%).

Indications for use of high-cost medicines

There were 56 different indications for these drugs ranging from inflammatory conditions (n = 52, 60%) to infections (n = 14, 16%) and malignancies (n = 14, 16%). Of these, there were 11 indications with two applications each and 39 indications with a single application each. Table 1 lists the indications for the eight most frequently used non-formulary high-cost medicines (see "Appendix B" for the complete list of indications).

Evidence supporting the use of high-cost medicines

The level of supporting evidence was evaluated for the 63 new IPU applications. There were 21 applications (33%) where the drug was TGA approved for the requested indication. There were 2 applications (3%) that provided no supporting evidence. Of the remainder, the level of evidence provided was classified according to the NHMRC Evidence Hierarchy. Lower levels of evidence, case series (n = 25, 40%) and cohort studies (n = 7, 11%), were more common than the ideal of either randomised controlled trials (RCTs) (n = 7, 11%) or systematic reviews of RCTs (n = 1, 2%) (Fig. 1).

Monitoring outcomes for new IPU applications

Of the 63 new applications, approximately half (n = 32, 51%) proposed an objective monitoring outcome to assess efficacy of the treatment, such as platelet count in thrombotic thrombocytopaenic purpura or measurement of proteinuria in membranous glomerulonephritis. Only 13 applications (21%) contained sufficient detail for a third party to make a determination on whether the treatment course had been successful, such as maintaining platelet count $> 30 \times 10^9$/L in idiopathic thrombocytopaenic purpura or maintaining haemoglobin level > 100 g/L in haemolytic anaemia. The remaining applications did not specify what constituted a clinically significant change in the nominated outcome.

Outcomes provided for renewal IPU applications

There were 22 renewal applications requesting continuation of a previously funded treatment course. The efficacy

Table 1 Most frequently used non-formulary high-cost medicines

High-cost medicine	Applications for use (N)	Cost in 2015 (AUD)
Rituximab	33 (38%)	$317,132 (24%)
Focal segmental glomerulosclerosis (n = 4)		
Membranous glomerulonephritis (n = 3)		
Myasthenia gravis (n = 3)		
Systemic lupus erythematosus (n = 3)		
Chronic inflammatory demyelinating polyneuropathy (n = 2)		
Graft-versus-host disease (n = 2)		
Thrombotic thrombocytopenic purpure (n = 2)		
Autoimmune autonomic neuropathy (n = 1)		
Autoimmune encephalitis (n = 1)		
Autoimmune-mediated necrotising myopathy (n = 1)		
Castleman disease (n = 1)		
Haemolytic anaemia (n = 1)		
Haemophilia A (n = 1)		
Idiopathic thrombocytopaenia purpure (n = 1)		
IgM paraproteinemic polyneuropathy (n = 1)		
Inflammatory myositis (n = 1)		
Multiple sclerosis (n = 1)		
Pemphigus vulgaris (n = 1)		
Systemic sclerosis (n = 1)		
Neuromyelitis optica spectrum disorder (n = 1)		
Grave's orbitopathy (n = 1)		
Abacavir/dolutegravir/lamivudine	10 (11%)	$128,991 (10%)
Human immunodeficiency virus (n = 10)		
Infliximab	8 (9%)	$185,668 (14%)
Hidradenitis suppurativa (n = 3)		
Pyoderma grangrenosum (n = 2)		
Sarcoidosis (n = 2)		
Bechet's disease (n = 1)		
Posaconazole	5 (6%)	$81,783 (6%)
Acute myeloid leukaemia (n = 1)		
Aspergullus fumigatus (n = 1)		
Malignant otitis exterma (n = 1)		
Mucormycosis (n = 1)		
Myelodysplastic syndrome (n = 1)		
Intravenous immunoglobulin	3 (3%)	$36,000 (3%)
Antibody-mediated rejection (n = 1)		
Idiopathic inflammatory myelopathy (n = 1)		
Peripheral neuropathy (n = 1)		
Febuxostat	2 (2%)	$16,498 (1%)
Gout (n = 2)		
Octreotide	2 (2%)	$19,416 (1%)
Thyroid cancer (n = 2)		
Ponatinib	2 (2%)	$48,000 (4%)
Chronic myeloid leukaemia (n = 1)		
Acute lymphoblastic leukaemia (n = 1)		

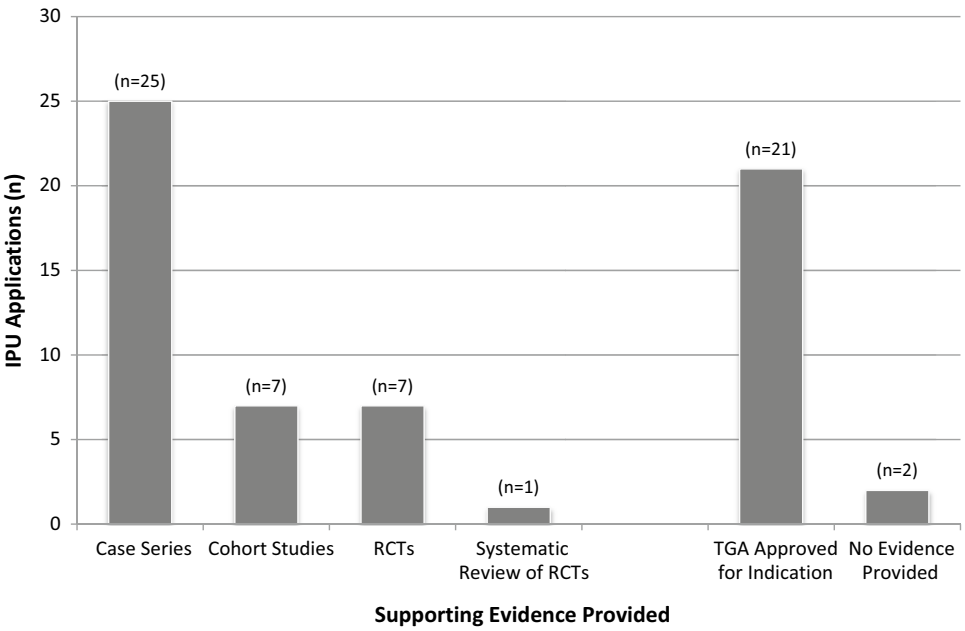

Fig. 1 Evidence supporting the use of non-formulary high-cost medicines. Evidence ranked in accordance with the NHRMC Evidence Hierarchy with two further categories for medicines that are TGA approved for the selected indication and applications where no evidence was provided. TGA, Therapeutic Goods Administration; NHMRC, National Health and Medical Research Council; RCT, Randomised Controlled Trial

of the previous funded treatment course was described in 15 renewal applications (68%) with the result of the nominated monitoring outcome being provided in all but one case, which reported a different outcome.

Subgroup analysis for IPU medicines accounting for > 30% of total number of IPUs

Rituximab accounted for over one-third of all applications (n = 33, 38%) resulting in a cost of $317,132 AUD over the study period. There were 21 different indications for rituximab use with the most common being focal segmental glomerulosclerosis (n = 4, 12%), membranous glomerulonephritis (n = 3, 9%), myasthenia gravis (n = 3, 9%) and systemic lupus erythematosus (n = 3, 9%). Fourteen of the 21 indications had one application each.

Rituximab was not TGA approved for any of these indications. Of the 33 applications for rituximab, the majority of supporting evidence was in the form of case studies (n = 21, 64%) followed by cohort studies (n = 8, 24%) and RCTs (n = 4, 12%).

Discussion

This study demonstrates that high-cost medicines are being used for a very broad range of indications, based largely on low levels of evidence, making it difficult for DTCs to prospectively assess the benefit and cost-effectiveness of funding these treatments. Our data demonstrates the cost of funding high-cost medicines outside of the hospital formulary through an IPU scheme for an individual hospital. Furthermore, the monitoring outcomes to determine the efficacy of the treatments were provided in only half of the applications, with few able to be appropriately assessed by a third party. This clearly poses challenges when auditing the efficacy of treatments funded, to help guide subsequent applications to DTCs.

The composition of high-cost medicines being prescribed off-label has changed significantly over the last two decades. In the late 1990 and early 2000s, the most frequently used high-cost non-formulary medicines were conventional immunosuppressants (such as mycophenolate, cyclosporine and tacrolimus), antiresorptives (such as pamidronate), anticonvulsants (such as gabapentin) and somatostatin agonists (such as octeotide) [6]. However, in more contemporary studies including ours, biological agents (particular rituximab) have become more common and are being used for a range of inflammatory and malignant conditions [14–16]. The rate of reporting of monitoring outcomes was provided in half of cases in our study. This is significantly improved compared to a previous Australian study which found clinical outcomes provided in only 18% of cases [6].

The IPU scheme allows patients to access high-cost medicines that are not covered through conventional funding arrangements. Clearly off-label prescribing requires a control system to ensure that these medicines are being used appropriate [17]. The DTC plays this role by conducting their own risk–benefit assessment, determining the monitoring for adverse events and influencing the duration of prescription. Many of these high-cost drugs are unlikely to be listed on the PBS for a range of indications due to the requirement for the pharmaceutical company to apply to the PBAC and demonstrate the cost-effectiveness of their drug

[18]. Submission to the PBAC for high-cost drugs for rare diseases and off-label indications are unlikely, especially when they are already being funded by Australian public hospitals through IPU schemes.

The limited evidence supporting the use of high-cost drugs and inadequate reporting of monitoring outcomes highlights the challenges facing DTCs. The low levels of evidence to support use of high-cost non-formulary medicines is similar to that seen in previous studies [6, 14]. This reflects the difficulty of performing randomised controlled trials for rare conditions and non-approved indications. Despite this low level of evidence, nearly all (99%) of the applications were approved, as these patients have often failed multiple conventional lines of treatment, and continue to be symptomatic, hence the evidence threshold for a therapeutic trial, may be low. Given that the supportive evidence is at high risk of bias, it is difficult for DTCs to prospectively judge the efficacy of funding these treatments. Furthermore, we report that half of the pre-determined monitoring outcomes were being captured following approval and funding of high-cost medicines. These outcomes must be collected in order to build the evidence-base not only for DTCs but for all treating clinicians.

Some of the medication use through the IPU system was occurring while the medications were being considered by PBAC or for addition to the hospital formulary. This was evident in our data by the multiple applications for one combined antiretroviral agent for HIV that was PBS listed in 2015 but was not yet available on the hospital formulary [19]. Clinicians were using the IPU system to prescribe this high-cost medicine before it had been added to the hospital formulary. While it is necessary for a hospital formulary to be sufficiently restrictive to achieve its goals of quality use of medicines, this also creates additional paperwork when the formulary process is not sufficiently responsive for new drugs [20]. Fortunately, the IPU scheme facilitates the timely access to new and efficacious therapies in exceptional cases. We predict that similar circumstances would have occurred for novel drugs with demonstrated efficacy and widespread uptake such as antivirals for hepatitis C and targeted therapies for cystic fibrosis.

There were a large number of applications for rituximab in contrast to the limited evidence base to support these indications. Similar to previous studies, we have found that rituximab is used for a range of renal, autoimmune and rheumatologic disorders based on predominantly case series and cohort studies [15, 16]. Rituximab is becoming the agent of choice for second- or third-line therapy in patients with a range of inflammatory conditions who have failed conventional immunosuppressive agents. With the majority of these applications being approved in our hospital, there is a large pool of data that could be generated on the efficacy of rituximab for these diseases. Given the large number of individual indications, these data would be most useful if collected into a state-wide or national registry as first suggested by Danes et al. [14]. Data within such a registry would then be available to inform prescribers and DTCs when presented with future applications for rituximab given the scarcity of supporting evidence in the literature.

The advent of biosimilar agents for monoclonal drugs may improve patient access to high-cost non-formulary medicines. Since this study, both rituximab and infliximab have come off patent and now have biosimilars on the market. Biosimilars have a lower acquisition cost for pharmaceutical companies and therefore it may become more feasible for them to be licensed for rare conditions and non-approved indications. As biosimilars become more available, clinicians may increasingly use these biologic agents in conditions where their place has been less established to date [21].

The rising cost of new drugs and expanding indications for their use mandates a reconsideration of the approach by which DTCs evaluate IPU applications for high-cost medicines. These findings have informed change to the IPU application process at the study institution. Clinicians are now mandated to provide an objective monitoring outcome and timeframe for assessment. It is hoped that reporting of the clinical outcomes of these treatment courses will assist the DTCs in assessing future applications. There remains an ongoing challenge in enforcing the reporting of clinical outcomes to the DTC by the prescribing clinician.

In conclusion, non-formulary high-cost medicines are being used for a broad range of indications, often off-label, with limited supporting evidence. Prospective determination of what constitutes an efficacious response to treatment and reporting of these outcomes would build the evidence-base and aid DTCs in deciding whether to fund subsequent treatment courses.

Funding None.

Conflicts of interest Joshua Inglis, Gillian Caughey and Sepehr Shakib declare that they have no conflict of interest.

Appendix A

SA Health

Individual Patient Use (IPU) Medicine Request Form

NOT URGENT review at next Drug & Therapeutics Committee or equivalent committee ☐ URGENT within 24 hours ☐ within 1 to 3 days ☐ within 4 to 7 days ☐ AND reason for urgency:

1 GENERAL INFORMATION

The following information is required by the Drug & Therapeutics Committee (DTC) or equivalent committee, before consideration will be given for Individual Patient Use medicine supply. Failure to complete all details may result in a delay in consideration of the application by the Committee, and therefore delay availability of the medicine. Please note:

- The signature of the relevant Clinical Director or Division Head or nominee and Hospital/Health Service Chief Operating Officer (or delegate) must be obtained to indicate endorsement of application and funding approval.
- You can contact your clinical pharmacist for assistance in completing this form.
- The signed, completed forms should be forwarded to your DTC (or equivalent committee).

1.1 Patient details

Name:		
UR #:	Date of birth:	Gender:
Patient location (site/hospital):		

1.2 Application Details

New application ☐	Renewal ☐	Application Date:

1.3 Details of medicine

Drug Name (generic):
Dosage form(s) and strength(s):

1.4 Indication(s) for use

Define the indication(s) for which approval for individual patient use is being sought:		
Is the medicine registered by the TGA **for the requested indication**?	Yes ☐	No ☐
Is the medicine registered by the TGA?	Yes ☐	No ☐
If not, will this medicine be accessed by the SAS scheme? *If yes, SAS form to be completed in addition to IPU Medicine Request Form.* *Additional consent may be required for off licensed / off label use.*	Yes ☐	No ☐

1.5 Details of PBS listing

Is the medicine listed on the PBS **for this indication**?	Yes ☐	No ☐

Government of South Australia
SA Health

1.6 Patient history

Relevant patient background (duration and severity of disease):

1.7 Reason for request

Explain your reasons for requesting this medicine:

1.8 Alternative therapy and treatment history

List any formulary alternative(s) available, and indicate why they are not suitable:
Indicate therapies that have been tried and reasons supporting use of requested medicine {including duration of previous treatment(s)}:
What alternative therapies (including non-pharmacological) may be used for treating this the condition in a similar patient population:
If renewal of previous IPU, please provide objective/subjective measures showing effectiveness of previous treatment and reason for renewal:

1.9 Treatment details

Dosage and frequency:	
Concomitant therapy for this indication:	
Duration of therapy requested:	Expected time to evaluate response:
Intended outcome of treatment:	
How will you monitor response:	
Treatment to commence (date):	

1.10 Evidence to support use of medicine for proposed indication

Evidence for use in this treatment population **(attach relevant supporting documentation to demonstrate** safety and efficacy):

1.11 Costs of medicine (obtain information from Pharmacy)

Please fill out appropriate section for either ongoing or intermittent/cyclical treatment.

Cost per day	$
Cost per treatment course or per annum	$
Additional costs e.g. monitoring, additional medicine or equipment	$
Is this a high cost medicine approval* Yes ☐ No ☐ Unknown ☐	

* High Cost medicines are those for which the predicted cost to SA Health per year is:

- $10,000 per patient per treatment; or
- $100,000 for an individual hospital; or
- $300,000 within SA Health.

1.12 Applicant details

Applicant name: Position:
Clinical unit, hospital:
Telephone No: Pager No: Email:
Conflict of interest: Financial or other resulting from contact with pharmaceutical companies, which have a bearing on this submission. Yes ☐ No ☐ If yes tick relevant box and explain Conference Funding ☐ Gifts ☐ Travel Expenses ☐ Samples ☐ Honoraria ☐ Industry paid food/refreshments ☐ Research support ☐ Other support (describe) ☐ Please provide a brief but clear description of each potential conflict:
I declare, that to the best of my knowledge, all of the information contained in this application is true and accurate. Applicant signature: Date:
If applicant not Treating Consultant; Consultant Name: Signature: Date: Telephone No: Pager No: Email:

AUTHORISATION

2.1 Authorisation by Clinical Director or equivalent

Name:
Signature: Date:

2.2 Authorisation by Head of Division or equivalent (High Cost Medicines)

Name:	
Signature:	Date:

2.3 Authorisation by Chief Operating Officer or equivalent (High Cost Medicines)

Name:	
Signature:	Date:

2.4 Authorisation by Chair of Drug & Therapeutics Committee or Director of Pharmacy (or delegate)

DTC USE ONLY		
Application received (date):	APPROVED ☐	REJECTED ☐
If approved, please state conditions of approval:		
Details of outcome(s) to be reported to DTC:		
Date that outcome(s) needs to be reported to DTC:		
Name:		
Delegation:		
Signature:	Date:	

2.5 Authorisation by Chief Medical Officer or Chief Pharmacist (or delegate) (High Cost Medicines)

Application received (date):	APPROVED ☐	REJECTED ☐
Name:		
Delegation:		
Signature:	Date:	

2 PHARMACY USE INFORMATION

Cytotoxic or hazardous substance If yes was a risk assessment completed	Yes ☐ Yes ☐	No ☐ No ☐	 N/A ☐
List precautions: Signature:			
Entered in iPharmacy	Yes ☐	No ☐	N/A ☐
Entered in IPU database	Yes ☐	No ☐	N/A ☐
Stock ordered	Yes ☐	No ☐	N/A ☐
Applicant informed of outcome	Yes ☐	No ☐	N/A ☐
Dispensary / Production informed	Yes ☐	No ☐	N/A ☐
Clinical Pharmacist informed	Yes ☐	No ☐	N/A ☐
Name:			
Signature:	Date:		

Appendix B: Complete list of indications for non-formulary high-cost medicines

Indication	Applications for use (N)
Human immunodeficiency virus	10 (11%)
Focal segmental glomerulosclerosis	4 (5%)
Myasthenia gravis	3 (3%)
Membranous glomerulonephritis	3 (3%)
Systemic lupus erythematosus	3 (3%)
Hidradenitis suppurativa	3 (3%)
Thyroid cancer	2 (2%)
Thrombotic thrombocytopenic purpura	2 (2%)
Sarcoidosis	2 (2%)
Pyoderma grangrenosum	2 (2%)
Myelodysplastic syndrome	2 (2%)
Idiopathic thrombocytopaenia purpura	2 (2%)
Graft-versus-host disease	2 (2%)
Gout	2 (2%)
Chronic inflammatory demyelinating polyneuropathy	2 (2%)
Breast cancer	2 (2%)
Acute myeloid leukaemia	2 (2%)
Systemic sclerosis	1 (1%)
Peripheral neuropathy	1 (1%)
Pemphigus vulgaris	1 (1%)
Osteosarcoma	1 (1%)
Neurosarcoid	1 (1%)
Nephrotic syndrome	1 (1%)
Multiple sclerosis	1 (1%)
Mucormycosis	1 (1%)
Melanoma	1 (1%)
Malignant otitis exterma	1 (1%)
Inflammatory myositis	1 (1%)
IgM paraproteinemic polyneuropathy	1 (1%)
Idiopathic inflammatory myelopathy	1 (1%)
Hyperparathyroidism	1 (1%)
Hereditary angioedema	1 (1%)
Hepatitis B virus	1 (1%)
Haemophilia A	1 (1%)
Haemolytic anaemia	1 (1%)
Deep vein thrombosis	1 (1%)
Chronic myeloid leukaemia	1 (1%)
Castleman disease	1 (1%)
Blau syndrome	1 (1%)
Bechet's disease	1 (1%)
Autoimmune-mediated necrotising myopathy	1 (1%)
Autoimmune encephalitis	1 (1%)
Autoimmune autonomic neuropathy	1 (1%)
Aspergullus fumigatus	1 (1%)
Antibody-mediated rejection	1 (1%)
Angiodysplasia	1 (1%)
Amylodosis	1 (1%)
Essential thrombocytosis	1 (1%)
Chronic idiopathic urticaria	1 (1%)
Acute lymphoblastic leukaemia	1 (1%)
Neuromyelitis optica spectrum disorder	1 (1%)
Cystic fibrosis	1 (1%)
Grave's orbitopathy	1 (1%)
Bronchiectasis	1 (1%)
Antibody-mediated rejection	1 (1%)
Hodgkin's lymphoma	1 (1%)

Appendix C: NHMRC evidence hierarchy

Level	Intervention
I	A systematic review of level II studies
II	A randomised controlled trial
III-1	A pseudorandomised controlled trial
III-2	Comparative study with concurrent control
	Non-randomised, experimental trial
	Cohort study
	Case–control study
	Interrupted time series with a control group
III-3	Comparative study without concurrent controls
	Historical control study
	Two or more single arm study
	Interrupted time series without a parallel control group
IV	Case series with either post-test or pre-test/post-test outcomes

NHMRC National health and medical research council

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