The use of Dermagraft® in neuropathic foot ulcers in people with diabetes: an economic analysis for Australia

Segal L PhD, MEcon • John S MBus, Cert in Health Econ

Summary

The purpose of this study was to establish the costs of conventional management of neuropathic foot ulcers in people with diabetes and evaluate the cost effectiveness of Dermagraft®, a living human dermal replacement, as an adjunct therapy. The cost of conventional management of foot ulcers was established by surveying specialist clinics for typical resource use and applying published unit costs. A Markov model was used to estimate expected cost per ulcer healed, with and without Dermagraft, drawing on effectiveness data from the pivotal clinical trial. The expected use of Dermagraft in Australian specialist clinics was based on an observational case study of 27 hard to heal ulcers. The data from this study was also used to establish an alternative cost-effectiveness estimate, using a pre-post own control study design.

Using the Markov model, the mean cost per ulcer healed is estimated at $10,906 using conventional management and $12,128 using Dermagraft as an adjunct or $9,393 if Dermagraft is cut and used to treat two ulcers. In the case studies, a mean 7.6 applications of Dermagraft were used per ulcer, with healing achieved in 85 per cent of ulcers. Based on the case studies, the mean cost of managing an ulcer after commencement with Dermagraft – until healing was achieved or to 24 weeks – was $4,682, compared with an estimated $12,500 incurred under conventional management prior to Dermagraft use.

The use of Dermagraft as an adjunct to conventional management in the specialist clinic setting for hard to heal ulcers results in a similar average cost per ulcer healed and a lower cost per week in a healed state to conventional management alone. A shorter treatment period, fewer complications and fewer inpatient episodes will, in some cases, offset the cost of Dermagraft making the treatment cost saving.

Leonie Segal PhD, MEcon
Deputy Director, Health Economics Unit
Monash University
PO Box 477
West Heidelberg, Vic 3081
Tel: (03) 9496 4438
Fax: (03) 9496 4424
E-mail: Leonie.Segal@Buseco.monash.edu.au

Sue John MBus in Management, Cert in Health Econ
Health Economics Manager
Smith + Nephew Pty. Ltd.
PO Box 150
Clayton, Vic 3168

Introduction

Neuropathic foot ulcers in people with diabetes are a serious health problem compromising normal daily activities, negatively impacting on quality of life and imposing significant costs on the health care system. The subject of this paper is the cost effectiveness of the use of Dermagraft®, a living human dermal replacement, in the management of neuropathic foot ulcers in people with diabetes, by Australian specialist wound care/high risk foot clinics.

Foot ulceration is particularly common in persons with diabetes due, in part, to the effects of neuropathy and an impaired healing process. Each year, approximately 1.9 per cent of persons with diabetes will develop a foot ulcer [1]. Complete healing of these ulcers often remains an elusive goal; an open ulcer predisposes the patient to infection which can require hospital admission for medical or surgical

intervention. Ulceration is the most common precursor to amputation and has been identified as a factor in 85 per cent of lower extremity amputations [2].

Even with best practice management, ulcer healing can be slow and costly to the individual and the health care system due to regular ambulatory clinic visits and community care/district nursing support. Extended or repeated inpatient care is not uncommon. In 1997/8 there were 1,606 admissions to hospital in Australia requiring management of a diabetic neuropathic foot ulcer. The average length of stay for the 18 per cent of admissions where the foot ulcer was the primary reason for admission was 14.8 days, with 50 per cent of patients having an inpatient stay of greater than 10 days [3]. The average length of stay in Australian public acute hospitals in 1997/98 was 4 days [4].

The occurrence of neuropathic foot ulcers is likely to become more common due to an increase in the incidence and prevalence of diabetes. The prevalence of diabetes has nearly doubled between 1983 and 1995 [5, 6] which reflects a rise in the two dominant risk factors for type 2 diabetes: a sedentary lifestyle and obesity (Body Mass Index >30). Obesity has risen from 7.1 per cent of adults in 1980 to 17.1 per cent of adults in 1995 [6, 7].

At the same time, there is concern with the rising cost of health care. In Australia, health care costs have been increasing at an average 4 per cent per annum over the period 1989/90 to 1996/97 [8]. Concern with these costs has spurred development of strategies to promote best practice management and more cost effective approaches in order to optimise health outcomes within health care budgets.

Appropriate and timely management of neuropathic foot ulcers in people with diabetes can greatly enhance healing. Conventional best practice management (conventional management) consists of sharp debridement, infection control, moist wound dressings and the use of aids to reduce pressure at the ulcer site. The aim of treatment is to provide an optimal environment for the patient's own fibroblast cells to trigger the wound healing process and structurally integrate collagen and other matrix proteins into a new dermal and epidermal layer to achieve a healed ulcer. Human fibroblasts have been shown to have impaired functioning in the presence of high glucose levels, thereby inhibiting the wound healing potential of the patient with diabetes and reducing the effectiveness of conventional ulcer management [9].

Recent advances in tissue engineering make it possible to enhance the healing process of full-thickness plantar surface foot ulcers in people with diabetes mellitus. US clinical trial outcomes demonstrate that the use of Dermagraft as an adjunct to conventional management results both in faster healing and more ulcers completely healed, as well as a trend towards delay in ulcer recurrence [10-13].

Dermagraft provides the necessary collagen, human dermal matrix, proteins and growth factors (some of which are known to be deficient in chronic wounds) to facilitate the wound healing process. A suitable wound treated with Dermagraft is able to generate a healthy dermal layer that can initiate epithelialisation and closure of the wound.

The aim of the research reported in this paper was to establish the costs of conventional management of neuropathic foot ulcers in people with diabetes by Australian specialist wound care/high risk foot clinics and to evaluate the cost effectiveness of Dermagraft as an adjunct therapy. This involves a comparison between the additional costs of management when Dermagraft is used, recognising potential cost offsets, and the improved clinical outcomes demonstrated in US clinical trials and Australian case studies.

Methods

The costs associated with conventional foot ulcer management by Australian specialist clinics were determined from a survey of typical resource use, to which published unit costs for each resource type were applied. These costs were used in a Markov model to estimate the expected annual costs of treatment and, together with the results from the pivotal US trial, were used to estimate cost per ulcer healed, with and without Dermagraft. An observational study of 27 hard to heal ulcers managed in Australian specialist clinics was used to establish expected patterns of use of Dermagraft and to derive cost effectiveness estimates based on actual clinical practice.

Australian costs

The average cost of conventional ulcer management was derived from a survey of clinicians from ten leading specialist foot and wound clinics around Australia. The survey covered typical patterns of neuropathic foot ulcer management and reflected input from medical practitioners, podiatrists and wound care nurses. A 100 per cent response rate was obtained.

The survey covered diagnostic tests performed, dressings used, medications prescribed, off-weight bearing devices used, frequency of visits, expectation of hospitalisation and rate of lower extremity amputation. Responses to the survey

were collated and sent to half the initial respondents for confirmation or suggested modification. These consensus responses were deemed to represent conventional management of foot ulcers in the Australian specialist clinic setting.

Unit costs were derived from published databases and reimbursement schedules and attributed to the resources identified. Hospital inpatient costs were derived from national AN-DRG data [14], the cost of medical tests and consultations from reimbursement rates in the Commonwealth Medical Benefits Schedule [15] and the cost of pharmaceuticals as reported in the Pharmaceutical Benefits Schedule [16]. Unit costs were combined with treatment patterns to calculate average weekly management costs for ulcers with various complications.

Markov model

The York Health Economics Consortium developed a Markov model to simulate the clinical progression of a foot ulcer between six discrete health states over a 52 week period. A Markov model is a mathematical model commonly used in health economics to trace a cohort of patients with a particular medical condition over time.

A set of transition probabilities is defined that describe the probability of moving between the nominated health states within a given timeframe. The ulcer is presumed to start in an open state with no infection and progresses through alternative possible health states of healed, open with superficial infection (e.g. cellulitis), open with deep infection (e.g. osteomyelitis) and amputation.

The pattern of health states over time is described by weekly transition probabilities derived from the US pivotal trial [11]. They reflect the probability of an ulcer moving between the different health states on a week by week basis. The sixth health state in the model is death. While it is possible for death to be the outcome of a ulcer as a logical progression after amputations, there were no ulcer related deaths reported in the US clinical trial.

Two separate transition matrices for progression of a foot ulcer were developed; one to represent conventional management informed by the control arm of the clinical trial, and the other to represent the use of Dermagraft as an adjunct, based on the experimental arm of the trial. The transition probabilities for superficial and deep infection from the control arm were used to represent both cohorts due to the small number of infections in the experimental arm. Thus the proportion of ulcers that become infected is solely attributable to the time spent with an ulcer in an unhealed state. Similarly, the rate of amputation for the control group was used to determine the probability of amputation for both cohorts.

The Markov model utilises Australian clinical practice to estimate resource use and costs and clinical outcomes from the pivotal US trial, modelled over a 52 week period. The primary outputs of the model are:

- Average annual treatment costs,
- Average cost per ulcer healed and
- Average cost per healed week, for conventional management with and without Dermagraft.

A mean of seven pieces of Dermagraft is assumed for patients in the experimental cohort, as per the pivotal US trial.

Australian case studies

A series of observational case studies was used to explore the expected patterns of Dermagraft utilisation and likely cost effectiveness in the Australian specialist clinic setting and to determine the feasibility and practicality of using Dermagraft on more than one ulcer.

Dermagraft was clinically evaluated at 11 specialist wound care/high risk foot clinics around Australia. The inclusion criteria for patient selection were absence of infection (based on clinical signs), adequate blood supply (an ankle brachial index >0.8) and a long-standing (>8 weeks) diabetic neuropathic foot ulcer that had failed to respond satisfactorily to conventional management. Patients were recruited sequentially over the study period.

A total of 27 ulcers were identified that met the criteria and treated with Dermagraft as part of their management between December 1998 and April 2000. Clinical management, healing progress and treatment cost were documented for the episode of care associated with the ulcer prior to and after the application of Dermagraft.

A retrospective/prospective analysis of resource use and cost was conducted in conjunction with the clinical evaluation in order to compare the cost of treating the ulcers conventionally, with the cost of management using Dermagraft as an adjunct. The total cost of ulcer management prior to Dermagraft treatment was based on treatment documented in patients' medical records supplemented by clinician and patient interviews. Cost of management following the first application of Dermagraft was recorded until healing was achieved or for 24 weeks follow-up. This

study design represents a matched control design, with each patient acting as their own control.

Results

Costs of managing neuropathic foot ulcer in Australian wound care/high risk foot clinics

The average cost of conventional ambulatory management for an open uninfected ulcer was calculated at $182 for the first week of management and $81 per week for subsequent weeks. The first week of presentation includes a diagnostic work-up which is not usually required in subsequent weeks. For an ulcer with superficial infection, e.g. cellulitis, the estimated average cost of ambulatory management is $369 for the first week and $217 for each subsequent week.

The total average cost of conventional ulcer management, for an ulcer with superficial infection, is $1,187 for the initial week and $1,096 for each subsequent week in this health state. This cost incorporates a small probability of inpatient care and an amount for district nursing.

For an ulcer with deep infection, e.g. osteomyelitis, the estimated average cost of treatment is $2,937 for the first week and $2,881 for each subsequent week, including ambulatory care, likely inpatient care and district nursing care. The cost of Dermagraft is included at A$800 per piece. Detailed costs are presented in Table 1.

Markov model results

Clinical effectiveness used in the Markov model simulation is based on the US pivotal trial. The median time to heal an ulcer (including same site recurrences) is 28 weeks with conventional management and 14 weeks using Dermagraft as an adjunct. This represents a 50 per cent reduction in time to heal. Over 52 weeks, the expected mean time in the healed state is 18.8 weeks with conventional management, and 27.1 weeks using Dermagraft. On average, patients treated with Dermagraft can expect to spend 8.3 more weeks per year in a healed state.

Using Australian costs, the total cost of treatment is estimated at $9,123 for conventional care, $12,323 using also Dermagraft and assuming seven pieces per ulcer, or $9,523 if each piece of

Table 1. Average Australian costs for management of neuropathic foot ulcers A$ (to the nearest $, 2000 costs).

Cost item	Open, not infected	Superficial infection	Deep infection
Initial lab tests and diagnostic tests	72	193	273
Follow-up tests/week	3	73	12
Dressings/week	7	18	19
Medications/week	0	15	31
Clinician visits (physician/nurse)			
– initial week	103	143	103
– subsequent weeks	71	111	71
Subtotal ambulatory care			
– initial week	182	369	428
– subsequent weeks	81	217	235
Hospitalisation* mean weekly cost	0	967 40.4% of 2,393	2,812 70.9% of $3,967
Total mean cost of ulcer treatment:			
– initial week	182	1,187	2,937
– subsequent weeks	81	1,096	2,881
Lower limb amputation†	18,019		
Dermagraft Δ	800/piece		

* Costs from AN-DRGs 489, 490 & 491 cellulitis, for superficial infection; 444, 445 osteomyelitis for deep infection health states [14]. Probability of hospitalisation based on survey of specialist clinics.

† Cost of amputation based on AN-DRG 411 [14] plus estimated rehabilitation cost.

Δ Cost per piece as supplied by Smith+Nephew.

Dermagraft is cut to treat two ulcers. Average cost per healed week was estimated at $454 for conventional management, $486 with Dermagraft used at the rate of one per ulcer application and $352 per healed week, where each piece of Dermagraft is cut to treat two ulcers.

In addition to faster healing, more ulcers are expected to heal with Dermagraft – an additional 17.8/100 over a year [11]. The average cost to heal an ulcer based on the Markov model is estimated at $10,906 using conventional management, $12,128 with Dermagraft, assuming seven pieces per course of treatment, and $9,393 with Dermagraft, but allowing each piece of Dermagraft to be cut to treat two ulcers. The key economic results are presented in Table 2.

Australian case study results

The clinical outcomes of treating 27 hard to heal ulcers with Dermagraft in Australian specialist clinics were consistent with the outcomes of the US clinical trials in demonstrating improved healing rates and faster healing for hard-to-heal ulcers. Potential cost savings were also identified. Key results are summarised in Table 3.

Complete healing was achieved in 23 ulcers (85 per cent) by week 24, using a mean of 7.56 applications of Dermagraft per ulcer. Fourteen ulcers, 52 per cent, were healed by week 12, which is consistent with the 12 week healing rates achieved in the pivotal US clinical trial of 51 per cent [13]. These ulcers required a mean of 4.6 applications of Dermagraft to achieve healing.

The patients in the case studies had experienced mean ulcer duration of 84 weeks prior to Dermagraft treatment without achieving healing, despite receiving appropriate care at wound care/high risk foot clinics, (including sharp debridement, moist wound dressing, off-weight bearing strategies etc). Treatment to that time had involved a mean 15 inpatient days and 45 ambulatory clinic visits per ulcer, at a mean cost per ulcer of $12,500. This is based on 26 cases – one of the patients was lost to follow up following 12 applications of Dermagraft and his retrospective costs were not collated. This patient was assumed to be unhealed at 24 weeks.

The mean cost of ulcer management, once treatment with Dermagraft commenced, was $4,682 per ulcer and $5,496 per healed ulcer. None of these patients required admission to hospital once treatment with Dermagraft commenced. The mean cost of managing these ulcers once Dermagraft treatment commenced was 39 per cent of the costs incurred prior to Dermagraft application – and with a high healing rate of 85 per cent achieved.

For 18 of the 27 ulcers (67 per cent), pieces of Dermagraft were cut and used on multiple ulcers, so that a total of 125 pieces of Dermagraft were used in 204 applications on 27 ulcers. If this had not been possible and the full cost of a piece of

Table 2. Markov model – key economic results.

Attribute	Specialist clinic ulcer management		Difference*
	without Dermagraft	with Dermagraft	
Mean annual treatment cost per patient			
– Dermagraft course (7 pieces)		$5,600	+ $5,600
– Other treatments	$9,123	$6,723	– $2,400
Total cost @ 1 ulcer/piece of Dermagraft	$9,123	$12,323 (a)	+ $3,200 (a)
Total cost @ 2 ulcers/piece of Dermagraft	$9,123	$9,523 (b)	+ $400 (b)
Mean cost per ulcer healed	$10,906	$12,128 (a)	+ $1,222
	$10,906	$9,393 (b)	– $1,513
Healed weeks over 52 week period	18.8	27.1	+ 8.3 weeks
Mean cost per healed week	$486	$454 (a)	$32 (a)
		$352 (b)	– $134 (b)
Incremental cost per additional healed week			
– @ 1 ulcer/piece of Dermagraft			+ $383 (a)
– @ 2 ulcer/piece of Dermagraft			+ $50 (b)

* + more expensive with Dermagraft
– conventional therapy alone more expensive.

(a) using 1 piece of Dermagraft per ulcer (at each application)

(b) cutting each piece of Dermagraft to apply to two ulcers (at each application)

Table 3. Australian case studies – summary results.

Attributes	Prior to Dermagraft treatment (26 ulcers)	After starting Dermagraft treatment (27 ulcers)	
Mean ulcer duration	84 weeks	12 weeks	
Inpatient hospitalisation:			
– mean days	14.88	0	
– mean cost	$7,678	0	
Ambulatory clinic care:			
– mean visits	45	12	
– mean cost	$4,880	$978	
Dermagraft treatment:			
– mean applications/ulcer	0	7.56	
– mean cost/ulcer:	$0	$ 3,704*	($6,048†)
Total mean cost to treat an ulcer	$12,500	$4,682*	($7,022†)
Mean cost per healed ulcer	∞ (unhealed)	$5,496*	($8,244†)

* Based on costs actually incurred. In the clinics, pieces of Dermagraft were cut where appropriate and applied to more than one ulcer. In total, 125 pieces were used on 27 ulcers in 204 applications (mean cost = 125 x $800/27 = $3704).

† Maximum cost: assuming pieces of Dermagraft were not cut, with a whole piece used for each application mean cost would then be 7.56 x $800.

Dermagraft attributed to each ulcer (7.56 pieces x $800), the mean cost of treatment would be $7,022 per ulcer. This is still substantially less than the cost of conventional management incurred up until the time Dermagraft was applied.

Discussion

There are implications for the Australian health care system based on the cost effectiveness analyses presented in this paper, particularly in the context of an increasing prevalence of diabetes and an expected concomitant increase in neuropathic foot ulcers.

Determination of the costs of conventional management of foot ulcers in Australian specialist clinics is itself an informative exercise. It was also a prerequisite to the cost effectiveness analyses reported here because, to the authors' knowledge, this resource utilisation and cost data have not previously been assembled for publication.

The Markov model transition probabilities are derived from the clinical outcomes of the US pivotal trial. A supplemental trial reported a similar 12 week healing rate with the use of Dermagraft at 51 per cent, but a 32 week healing rate 11.5 per cent better than that of the pivotal study, 69.2 per cent compared and 57.5 per cent respectively [13]. The clinical outcomes are a major determinant of the economic outcomes, therefore the use of the earlier study data will tend to understate the relative cost effectiveness of treating foot ulcers with Dermagraft compared with conventional treatment alone. This conclusion is supported by the Australian case study material.

Cutting a piece of Dermagraft to use on two or more ulcers also substantially improves the cost effectiveness of supplemental Dermagraft therapy compared with conventional therapy alone. The Markov model suggests that, with pieces of Dermagraft cut to treat two ulcers, the cost of treatment per ulcer is slightly higher with Dermagraft compared with conventional management alone ($9,523 per ulcer compared with $9,123 per ulcer). However, given the improved healing rate associated with Dermagraft, a lower average cost per ulcer healed is achieved, representing an improvement in efficiency.

The analysis shows that the purchase price of Dermagraft is offset by the expectation that patients treated with the living human dermal replacement will spend less time than conventionally treated patients in the unhealed state, where the risk of infection (and thus cost of care) is higher. Based on the Markov model simulation of clinical progression of foot ulcers, patients treated with Dermagraft will spend an average of 8.3 more weeks per year in a healed state. This would be associated with substantial improvement in patients' quality of life, and can potentially be achieved at no net cost to the health care system. Higher costs in the ambulatory clinic setting may be more than offset by a reduction in hospital admissions.

The case studies also show Dermagraft to be clinically effective when applied to appropriately selected patients and

when used in the Australian specialist clinic setting. The retrospective/prospective cost analysis, using patients as their own control, demonstrated that early intervention with Dermagraft is highly cost effective relative to conventional management alone. The mean total cost to treat and heal ulcers after the application of Dermagraft was significantly less than the average cost of prior conventional management, irrespective of whether or not the cost of each piece of Dermagraft is attributed to one or more ulcers.

The implication of this analysis for the health care system is that early intervention with Dermagraft on ulcers that are unresponsive to conventional management is likely to reduce health care resource use and costs and improve outcomes.

The retrospective portion of the cost analysis reflected the cost of treatment without achieving healing. The prospective component of the analysis, after application of Dermagraft, was, in contrast, associated with 85 per cent of ulcers healed within 24 weeks. It is important that both outcomes and costs are considered in making choices about the allocation of health care budgets, not just the impact on costs.

The US clinical trials and the Australian case studies demonstrate that using Dermagraft as an adjunct to conventional management in the specialist clinic setting will achieve improved health outcomes for patients with hard to heal ulcers. And, based on Australian costing data and management practices, these improvements can potentially be achieved at a lower net cost to the health care system. The cost effectiveness result derived from the case studies is somewhat more favourable to Dermagraft in part because actual costs were used. While in the Markov model in relation to costs associated with infection, the experience of the control group was assumed to also apply to the intervention group.

The role for Dermagraft on appropriately selected patients in Australian specialist wound care and high risk foot clinics is justified on the basis of both clinical effectiveness and cost effectiveness. The improved healing rate and faster healing with Dermagraft results in a lower average cost per ulcer healed. The shorter treatment period, fewer complications and fewer inpatient episodes may also result in cost savings that more than offset the purchase price of Dermagraft.

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References

1. Ramsey SD, Newton K, Blough D, McCulloch DK, Sandhu N, Reiber GE & Wagner EH. Incidence, outcomes and cost of foot ulcers in patients with diabetes. Diabetes Care 1999; **22**(3):382-387.
2. Pecararo RE, Reiker GE & Burgess EM. Pathways to diabetic limb amputation: basis for prevention. Diabetes Care 1990; **13**(5):513-521.
3. Australian Institute of Health and Welfare (AIHW). National Hospital Morbidity Database. AIHW, Canberra, 1999.
4. Australian Institute of Health and Welfare (AIHW). Australian Hospital Statistics 1997-98. Health Services Series No. 12. AIHW Cat. No. HSE 6. AIHW, Canberra, 1999.
5. National Heart Foundation of Australia. Risk Factor Prevalence Study No 2 1983. National Heart Foundation, Canberra, 1984.
6. Australian Bureau of Statistics. National Health Survey 1995, ABS catalogue no 4368.0. Australian Bureau of Statistics, Canberra, 1997.
7. National Heart Foundation of Australia. Risk Factor Prevalence Study No 1 1980. National Heart Foundation, Canberra, 1981.
8. Australian Institute of Health and Welfare. Health Expenditure Bulletin no 15 1997-98. AIHW, Canberra, June 1999.
9. Bowering CK. The use of Dermagraft (in the treatment of diabetic foot ulcers). Today's Therapeutic Trends 1998; **16**(1):87-96.
10. Gentzkow GD, Iwasaki SD, Hershon KS, Mengel M, Prendergast JJ, Ricotta JJ, Steed DP & Lipkin S. Use of Dermagraft, a cultured human dermis, to treat diabetic foot ulcers. Diabetes Care 1996; **19**(4):350-354.
11. Naughton G, Mansbridge J & Gentzkow G. A metabolically active human dermal replacement for the treatment of diabetic foot ulcers. Artificial Organs 1997; **21**(11):1203-1210.
12. Pollack RA, Edington H, Jensen JL, Kroeker RO, Gentzkow GD & The Dermagraft Diabetic Ulcer Study Group (1997). A human dermal replacement for the treatment of diabetic foot ulcers. Wounds 1997; **9**(6):175-183.
13. Gentzkow GD, Jensen JL, Pollack RA, Kroeker RO, Lerner JM, Lerner M, Isawaki SD & The Dermagraft Diabetic Ulcer Study Group. Improved healing of diabetic foot ulcers after grafting with a living human dermal replacement. Wounds 1999; **11**(3):77-84.
14. Commonwealth Department of Health and Family Services. Casemix Development Program: Report on the Development of AN-DRG Version 3.1 Cost Weights; Report on The National Hospitals Cost Data Collection, 1996-97. Commonwealth Department of Health and Family Services, Canberra, August 1998.
15. Commonwealth Department of Health and Aged Care. Medical Benefits Schedule, November 1997. Commonwealth Department of Health and Aged Care, Canberra, 1997.
16. Commonwealth Department of Health and Aged Care. Schedule of Pharmaceutical Benefits, August 1998. Commonwealth Department of Health and Aged Care, Canberra, 1998.