

Nutritional Products

Drug utilisation sub-committee (DUSC)

October 2015

Abstract

Purpose

To assess the utilisation of food and nutritional products listed on the Pharmaceutical Benefits Scheme (PBS). This review focuses on products for cows' milk protein intolerance following the July 2012 changes to the PBS restrictions for these products. The DUSC requested an analysis of these products at its February 2015 meeting.

Date of listing on the Pharmaceutical Benefits Scheme (PBS)

There are 150 nutritional products listed on the PBS Schedule in August 2015. Approximately a third of these products have been listed since the previous DUSC analysis which assessed utilisation to April 2011 (that is listed since May 2011).

Data Source / methodology

The report used data from the Department of Human Services (DHS) Supplied Prescriptions Database for the majority of analyses. The DHS Authority Approvals database data was used to identify the restrictions for which patients use protein hydrolysate (PH) and amino acid (AA) formulae. At the time of the report, two years of data were available since the July 2012 changes to the PBS restrictions for nutritional products for cows' milk protein intolerance.

Key Findings

- There has been a substantial decrease in the utilisation of AA formulae for cows' milk protein intolerance and allergy following the July 2012 restriction changes. Between 2011 and 2014, the number of patients supplied AA formulae decreased by 31% and has since stabilised. At the same time the number of patients supplied PH formulae increased 24%.
- There is a large group of children supplied AA formulae who are aged 2 years and older. Almost 900 patients aged 2 years and older are supplied AA formulae each quarter. In 2014, this represented over 25% of patients supplied AA formulae. This is in contrast to PH formulae which have fewer than 300 patients aged 2 years and older supplied each quarter, representing less than 13% of PH patients in 2014. In 2014, this represented 30% and 19% of total expenditure for AA and PH formulae respectively.
- Infant formula products are the most widely used nutritional products on the PBS, accounting for almost half of PBS expenditure on nutritional products in 2014.

- The use of nutritional products for metabolic conditions or other conditions requiring strict dietary management is growing. From 2011 to 2014, the number of prescriptions for these products increased 7% while expenditure grew 25%.

Purpose of analysis

To assess the utilisation of food and nutritional products listed on the Pharmaceutical Benefits Scheme (PBS). This review focuses on products for cows' milk protein intolerance following the July 2012 changes to the PBS restrictions for these products. The DUSC requested an analysis of these products at its February 2015 meeting.

Background

The PBS funds nutritional products for patients with metabolic conditions, infants and children with intolerance or allergy to cows' milk protein, infants and children with lactose intolerance and other medical conditions requiring strict dietary management. Unlike registered medical products, infant formulae and substitute food product formulae do not require Therapeutic Goods Administration (TGA) approval. Foods for special medical purposes and infant formula products are regulated by the Australia New Zealand Food Standards Code. Foods for special medical purposes are regulated by Standard 2.9.5 of the Food Standards Code. Infant formula products are regulated by Standard 2.9.1 of the Code even where they might meet the requirements of the standards for foods for special medical purposes. For further information on the regulation of infant formula and food for special medical purposes, refer to the [Food Standards Australia New Zealand website](#).

The PBAC receives advice on submissions to list nutritional products on the PBS from its Nutritional Products Working Party (NPWP). The NPWP is chaired by a member of the PBAC and comprises nutritional and paediatric experts.

Conditions treated by nutritional products listed on the PBS

There are 150 nutritional product items listed on the PBS as at 1 August 2015. There are two main groups of food products listed on the PBS: food products used to manage the nutritional needs of those with metabolic conditions; and food products to assist with individuals who have food allergies or intolerances.

Infant formula products

There are three main types of infant formula products listed on the PBS. Protein hydrolysate (PH) formulae and amino acid (AA) synthetic formulae are PBS-listed for infants and children with cows' milk and soy protein intolerance, cows' milk enteropathy or allergy. Lactose free formulae are listed for children with lactose intolerance. PH and AA formulae are also listed for a number of conditions other than cows' milk protein intolerance. Infant formula products are the most widely used nutritional products on the PBS, accounting for almost half of PBS expenditure in 2014 on nutritional products.

An Australia consensus panel recommend soy formula as the first choice for cows' milk protein allergy in infants aged six months or older and extensively hydrolysed formula, also known as PH formula, in infants less than 6 months of age.¹ PH is the second choice of treatment where soy formula is not tolerated, followed by AA formula if PH formula is not tolerated. AA formula is the first choice of treatment for patients with anaphylactic

reactions to cow's milk protein. Where infants are breastfed, cows' milk protein may need to be eliminated from the mother's diet.¹

AA formulae may also be used for enteral feeding.²

Metabolic conditions

The majority of nutritional products listed on the PBS are for the dietary management of metabolic conditions. Most of these conditions are inborn errors of protein metabolism where life-long modified protein diets are required. These include:

- Amino acid disorders: phenylketonuria, maple syrup urine disease, tyrosinaemia and homocystinuria.
- Urea cycle disorders and gyrate atrophy of choroid and retina.
- Organic acidaemias: methylmalonic acidaemia, propionic acidaemia, isovaleric acidaemia and glutaric aciduria type 1.

There are PBS-listed nutritional products used to manage the following conditions:

- Carbohydrate disorders and conditions requiring high fat diets:
 - glycogen storage disease
 - intractable seizures (ketogenic diet)
 - glucose transport protein defects
 - pyruvate dehydrogenase deficiency
 - glucose-galactose intolerance and multiple monosaccharide intolerances
- Conditions benefitting from medium chain triglyceride supplementation:
 - chylous ascites
 - chylothorax
 - fat malabsorption conditions
 - long chain fatty acid oxidation disorders
 - hyperlipoproteinaemia type 1
- Peroxisomal biogenesis disorders
- Renal failure requiring a diet low in protein, phosphorus and/or potassium
- Products for unspecified inborn errors of metabolism or restrictive therapeutic diets.

PBS listing details (as at 1 August 2015)

There are 150 nutritional product items listed on the PBS as at 1 August 2015. Patients supplied PBS nutritional products pay a co-payment for each prescription. In 2015, the general patient co-payment is \$37.70 and the concessional co-payment is \$6.10. This section will provide an overview of the listings for AA and protein PH formulae for cows' milk protein and soy protein intolerance, cows' milk protein enteropathy or allergy. For a summary of the listings of other nutritional products, refer to Appendix 1. For full details of the current PBS listing refer to the [PBS website](#).

PH formulae are listed for:

- Cows' milk protein enteropathy and intolerance to soy protein in patients up to 24 months of age. The patient must be treated by or in consultation with a specialist allergist, clinical immunologist, specialist paediatrician or specialist paediatric gastroenterologist and hepatologist.
- Cows' milk protein enteropathy and intolerance to soy protein in patients over 24 months of age. The patient must be treated by a specialist allergist, clinical immunologist, specialist paediatrician or specialist paediatric gastroenterologist and hepatologist.
- Proven combined immunoglobulin E (IgE) mediated allergy to cows' milk protein and soy protein in patients up to 24 months age. For initial treatment, the patient must be treated by or in consultation with a specialist allergist, clinical immunologist, specialist paediatrician or specialist paediatric gastroenterologist and hepatologist. For continuing treatment, the patient must be treated by one of the aforementioned specialists. This restriction does not specify a maximum age limit.

PH formulae are also listed for:

- biliary atresia,
- chronic liver failure with fat malabsorption,
- chylous ascites,
- cystic fibrosis,
- enterokinase deficiency,
- proven fat malabsorption,
- severe diarrhoea of greater than 2 weeks duration in a patients aged less than 4 months, and,
- severe intestinal malabsorption.

Table 1 presents details of the PBS listings of PH formulae.

Table 1: PBS listing of PH formulae

Item	Name, form & strength, pack size	Max. quant.	Rpts	DPMQ	Brand name and manufacturer
8259Q	Protein hydrolysate formula with MCT, 450g	8	5	\$104.45	Karicare Aptamil Pepti-Junior Gold Nutricia Australia Pty Limited
2676W	Protein hydrolysate formula with MCT, 400g	8	5	\$160.93	Alfaré Nestle Australia Ltd

Source: the [PBS website](#). If a Special Pricing Arrangement is in place this should be noted.

AA formulae, including products supplemented with long chain polyunsaturated fatty acids (LCPs) and/or medium chain triglycerides (MTCs) are listed for the following conditions under the initial treatment item codes.

- Cows' milk enteropathy in patients up to the age of 24 months treated by, or in consultation with a specialist allergist, clinical immunologist or specialist paediatric gastroenterologist and hepatologist.
 - The patient must be intolerant to both soy protein and PH formulae; and
 - The condition must not be isolated infant colic or reflux.
- Proven IgE mediated allergy to cows' milk protein and PH in patients up to 24 months of age. The patient must be treated by, or in consultation with a specialist allergist, clinical immunologist or specialist paediatric gastroenterologist and hepatologist.
- Intolerance to cows' milk protein, soy protein and PH formulae in patients older than 24 months of age. These patients must be treated by a specialist allergist, clinical immunologist or specialist paediatric gastroenterologist and hepatologist. This restriction does not specify a maximum age limit.

The continuing treatment item codes allow for use in same conditions as the initial treatment item codes. Patients receiving continuing treatment of cows' milk enteropathy and who are less than 24 months old (including with failure to thrive) or IgE-mediated cows' milk protein allergy must be treated by a specialist allergist, clinical immunologist or specialist paediatric gastroenterologist and hepatologist or have an appointment to be assessed by one of these specialists. The continuing item codes have the following additional restrictions:

- Cows' milk anaphylaxis in patients up to 24 months of age. These patients must be treated by a specialist allergist or clinical immunologist, or in consultation with a specialist allergist or clinical immunologist.
- Severe intestinal malabsorption (including short bowel syndrome) where the patient has failed to respond to PH formulae or has been receiving parenteral nutrition.

The AA products with LCP supplementation, with or without MCT supplementation, also have a listing for cows' milk protein enteropathy with a failure to thrive. AA formulae are also listed for severe intestinal malabsorption that has failed to respond to PH formulae or for patients who are receiving total parenteral nutrition. Some AA formulae are listed for eosinophilic oesophagitis under different item codes. Table 2 presents the details of the AA formulae listings for cows' milk protein intolerance, cows' milk protein enteropathy and allergy.

Table 2: PBS listing of AA formulae for initial treatment of cows' milk protein intolerance, cows' milk protein enteropathy and allergy

Item	Name, form & strength, pack size	Max. quant.	Rpts	DPMQ	Brand name and manufacturer
1180D (initial) 1192R (cont.)	amino acid synthetic formula, 400g	8 ^a	5	\$347.17	Neocate Advance Vanilla Nutricia Australia Pty Limited
8574G (initial) 8575H (cont.)	amino acid synthetic formula, 400g	8 ^a	5	\$347.17	EleCare Abbott Australasia Pty Ltd
8754R (initial) 8755T (cont.)	amino acid synthetic formula, 400g	8 ^a	5	\$347.17	Neocate Advance Nutricia Australia Pty Limited
2246F (initial) 2560R (cont.)	amino acid synthetic formula with LCP, 400g	8 ^a	5	\$353.89	Neocate LCP Nutricia Australia Pty Limited
9339M (initial) 9340N (cont.)	amino acid synthetic formula with LCP, 400g	8 ^a	5	\$353.89	EleCare LCP Abbott Australasia Pty Ltd
2928D (initial) 2900P (cont.)	amino acid synthetic formula with LCP and MCT, 400g	8 ^a	5	\$353.89	Alfamino Nestle Australia Ltd
5466Q (initial) 5467R (cont.)	amino acid synthetic formula with LCP and MCT, 400g	8 ^a	5	\$353.89	Neocate Gold Nutricia Australia Pty Limited

Source: the PBS website.

^a Maximum quantities up to 20 may be authorised under the continuing treatment item codes. No increased maximum quantities or repeats are allowed for the initial treatment listings.

Date of listing on PBS

The majority of nutritional products were listed on the PBS prior to the previous DUSC analysis which assessed utilisation to April 2011. Approximately a third of the 150 nutritional products listed on the PBS as at August 2015 have been listed since May 2011. An overview of the number of new items is presented in Table 3. For further details, refer to Appendix 1.

Table 3: Nutritional products listed on the PBS May 2011 to August 2015 by condition

Condition	New items
Chronic renal failure	1
Cows' milk intolerance or allergy - AA	4 ^a
Eosinophilic oesophagitis	2
Homocystinuria	3
Inborn errors of protein metabolism	3
Ketogenic diet	4
Lactose intolerance	2 ^b
Maple syrup urine disease	5
Medium chain triglycerides	5
Organic acidaemias	2
Peroxisomal biogenesis disorders	2
Phenylketonuria	10
Restrictive therapeutic diet	1
Tyrosinaemia	3
Urea cycle disorders	1
Chronic renal failure	1

Source: PBS Schedule April 2011, PBS Schedule June 2015.

^a Refers to the listings of Neocate Advance Vanilla[®] and Alfamino[®] products for the initial and continuing treatment for cows' milk protein intolerance.

^b Refers to the listing of Karicare Aptamil Gold De-Lact[®] for acute and chronic lactose intolerance.

Relevant aspects of consideration by the Pharmaceutical Benefits Advisory Committee (PBAC) and changes to listing

This section will focus on PBAC considerations and changes to the restrictions for PH and AA formulae for cows' milk enteropathy/intolerance and allergy. For a summary of the PBAC consideration of other nutritional products, refer to Appendix 2.

July 2012 changes

At the July 2011 meeting, the PBAC recommended a number of changes to the restrictions for AA synthetic formulae and PH formulae for the treatment of combined intolerance to cows' milk protein, soy protein and PH formulae (in the case of the AA synthetic formulae) and severe intolerance to cows' milk protein on the advice of the NPWP. The PBAC subsequently considered feedback from sponsors, the Australasian Society of Clinical Immunology and Allergy (ASCIA) and a Clinical Immunologist at its November 2011 meeting.

The NPWP made the following recommendations to the restrictions which were accepted by the PBAC and implemented in July 2012:

- Different restrictions were recommended for PH formulae and AA synthetic formulae to reflect their differing places in therapy.
- The term 'cow's milk protein intolerance' was replaced by 'cow's milk protein enteropathy' in consultation with ASCIA.
- The initial treatment period was increased from 3 to 6 months.
- The patient age was changed to be specified in months: from 2 years to 24 months. The restriction for use in children aged 2 years and older remained unchanged.
- Prescribers are required to provide the patient's date of birth and the name of the specialist consulted.

Two additional restrictions were also created: one for severe cows' milk enteropathy with failure to thrive and another for cows' milk anaphylaxis. These restrictions do not require patients to have soy protein or PH formulae to be eligible for AA formulae. Prior to these changes, there were no specific restrictions for the use of either PH or AA formulae for cows' milk protein allergy. PH formulae with medium chain triglycerides were no longer listed for the treatment of severe cows' milk protein intolerance/enteropathy.

The PBAC noted the wording 'in consultation' is intended to require consultation with a specialist, which may include a telephone consultation. The PBAC requested the National Prescribing Service to educate prescribers on the appropriate use of AA synthetic formulae.

December 2012

At its December 2012 Special meeting, the PBAC reviewed the PBS restrictions for AA synthetic formulae and PH following receipt of correspondence from the ASCIA and the Royal Australasian College of Physicians. Concerns that were discussed included:

- Inconsistencies between the restrictions' description of specialist prescribers and the fields of specialty practice recognised by the Australian Health Practitioners Regulation Agency,
- The requirement to demonstrate intolerance to soy protein, and,
- Current restrictions not allowing subsidy for patients with for proven IgE mediated combined allergy to cows' milk protein and soy protein.

The PBAC recommended that no changes be made to the descriptions of specialist allergist and clinical immunologist in the restrictions as it was unclear whether qualified immunologists and allergists were currently all registered as such with the Australian Health Practitioners Regulation Agency. The PBAC considered doing so would result in a more restrictive restriction and may decrease access for patients. The PBAC recommended amending the specialist descriptor for paediatric gastroenterologists to paediatric gastroenterologist and hepatologist and paediatrician to be changed to specialist paediatrician.

The PBAC agreed to extend the restriction for AA synthetic formulae to include treatment for proven IgE mediated combined allergy to cows' milk protein and soy protein in a child up to the age of 24 months, who has failed a trial of PH formulae. Comparable restrictions should be added to the listings for PH formulae. The PBAC also recommended the addition of the severe cows' milk protein enteropathy indication to PH formulae with MCTs.

The new restrictions were implemented in December 2013 and January 2014.

March 2013 PBAC consideration

At its March 2013 meeting, the PBAC considered correspondence from Allergy and Anaphylaxis Australia regarding the July 2012 changes to AA formulae restrictions. The correspondence raised concerns general paediatricians who provide allergy services as a majority of their practice were unable to prescribe appropriate formulae for patients with cows' milk allergy. The PBAC stated there is no intention to disadvantage children with genuine allergy and reiterated that specialist consultation can take place through any appropriate means such as telephone or email.

Previous reviews by the DUSC

The DUSC previously reviewed the utilisation of nutritional products at its October 2011 meeting. The review found that the utilisation and cost of nutritional products on the PBS has been increasing steadily over the past 20 years. The majority of the growth has come from metabolic conditions and nutritional products for infants with cows' milk protein allergy or intolerance. While noting the increasing cost and utilisation associated with nutritional products, there was no evidence presented in the review to support a view that usage was not reasonable.

The review found that only a minority of patients with cows' milk protein intolerance or allergy trial PBS listed PH prior to commencing AA formulation. The DUSC suggested that practitioners often do not prescribe PH before AA preparations on the PBS because parents have already trialled these products over the counter whilst waiting for an appointment with a specialist. The DUSC did not consider that the use of AA preparations appeared excessive at the point in time and suggested that the products are not particularly palatable and thus are only resorted to in situations where they are necessitated. The DUSC also highlighted the cost associated around dietary changes for breastfeeding mothers whose child is lactose intolerant or allergic to cows' milk protein and that this cost tends not to be captured by reviews regarding cost of treatment.

Methods

The analysis used data from Department of Human Services (DHS) Supplied Prescriptions Database. This database includes data on all items supplied by the PBS and Repatriation Pharmaceutical Benefits Scheme (RPBS) where the DHS has made a payment. It includes data on the item supplied, the quantity, cost to Government, de-identified personal identification number (PIN) and patient date of birth. This database does not include data on the use of R/PBS medicines that cost below the patient co-payment. At the time of the report there were no nutritional products with a cost below the general patient co-payment. Prescription data from 2003 to March 2015 were used in the analyses.

The analysis used prescription data based on date of supply. There may be small differences compared with publicly available DHS - Medicare date of processing data.¹ Additionally, the data from one pharmacy was removed from the analysis due to unusual patterns of supply.

Data from the DHS Authority Approvals database was used to identify the restriction for which patients were prescribed PBS Authority Required items. This data is not available from the DHS Supplied Prescriptions data. Authority approval data are collected when a prescriber makes a telephone or written request for prior approval to prescribe an Authority Required item to DHS. As a result, this will include a number of prescriptions that are not dispensed. This data are complete to the end of June 2015.

Data on patient age are not included in the Authority Approvals database and were derived by linking the de-identified PIN to supply data. Where a patient has used a temporary Medicare number or did not have a PBS prescription supplied (including the medicine for which they received Authority approval), their date of birth is unknown. Temporary Medicare numbers are often used by infants until they are enrolled.

There are special PBS supply arrangements for clients of eligible remote area Aboriginal Health Services (AHSs). AHSs are able to receive bulk supplies of PBS medicines through an approved community or hospital pharmacy. Data on items supplied to AHSs include the item and quantity supplied, month of supply, the name of the AHS, State and cost to Government. The supply data relate to the pharmacy supplying the items to the AHS. For medicines supplied to AHSs, there are no data on whether the products were supplied to patients or any other patient-level data. Data on the number of packs supplied to AHSs are presented in a separate table. Data on the cost to Government of supply to AHSs are included with total expenditure.

Results

Analysis of drug utilisation

Overall utilisation

Figure 1 presents the number of patients receiving nutritional products on the PBS from 2003 to 2014.

The data for PH formulae also include use for biliary atresia, fat malabsorption, chylous ascites, cystic fibrosis, enterokinase deficiency and severe diarrhoea in patients aged less than 4 months. The data for AA formulae also include use for severe intestinal malabsorption. Some AA products are also listed for eosinophilic oesophagitis under separate item codes. The latter are classified separately under 'All other nutritional products'.

¹ PBS statistics. Australian Government Department of Human Services Medicare. Canberra. Available from <<http://www.medicareaustralia.gov.au/provider/pbs/stats.jsp>>.

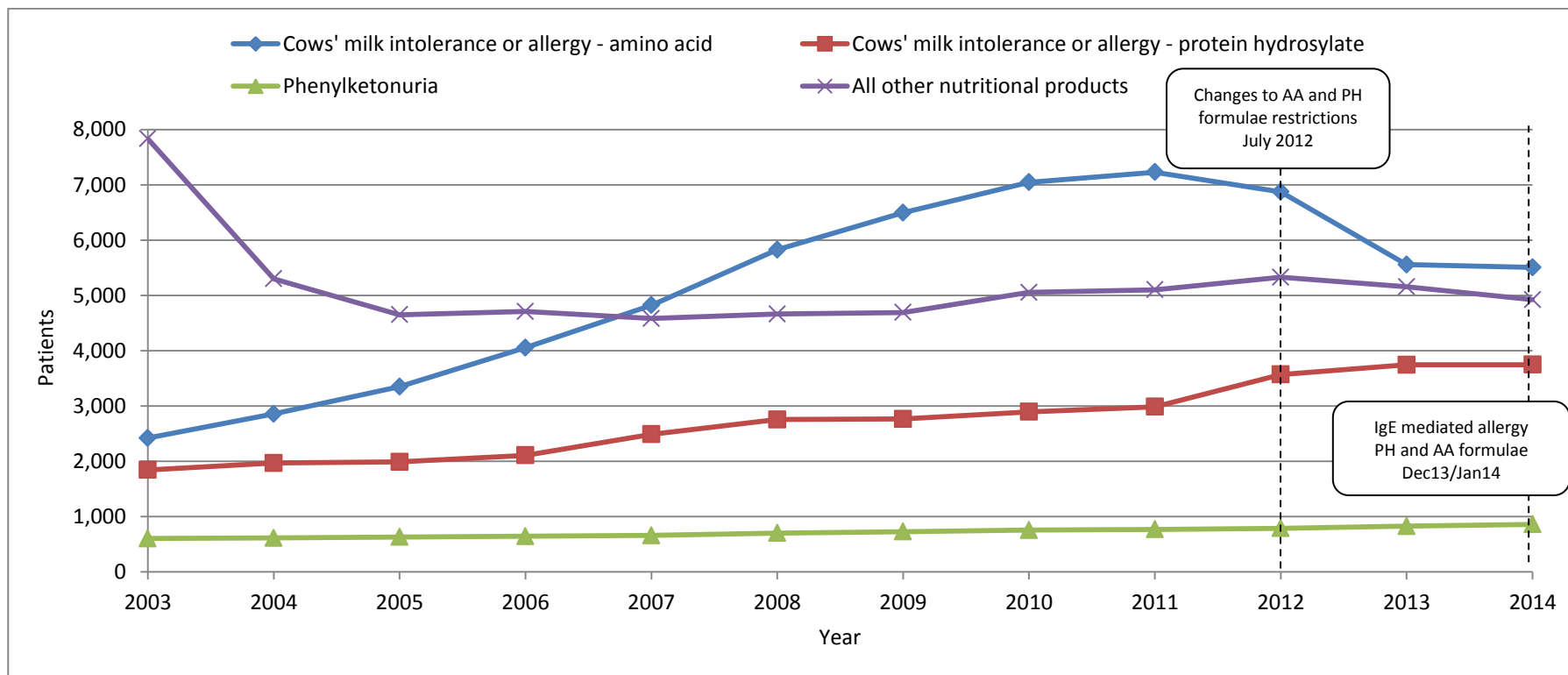


Figure 1: Patients supplied nutritional products on the PBS

Source: DHS Supplied Prescriptions Database, extracted July 2015.

Note: AA and PH formulae for cows' milk protein intolerance and allergy include utilisation for other indications.

Between 2003 and 2011, the number of patients with at least one dispensing of AA formulae for cows' milk protein intolerance or allergy grew at a rate of 15% per year. During the same period, the number of patients supplied PH formulae grew at 6% per year. Between 2011 and 2014, the number of patients supplied AA formulae decreased by 24% while the number of patients supplied PH formulae increased 26%. The number of patients supplied products for phenylketonuria and all other nutritional products has slowly increased. The large number of patients for 'All other nutritional products' in 2003 was due to a large number of patients supplied lactose-free formula products.

Figure 2 presents the number of patients starting treatment with PBS listed nutritional products by year from 2006 to 2014.

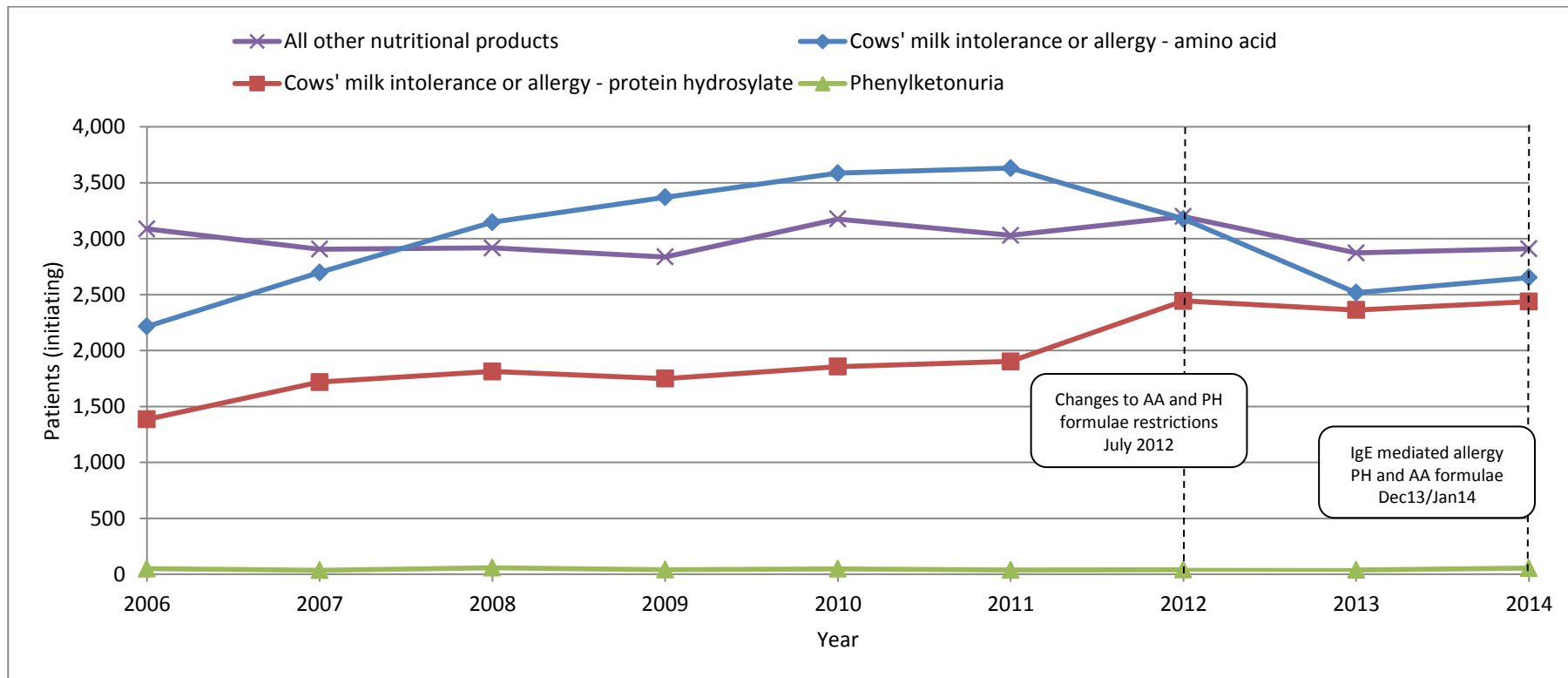


Figure 2: Patients starting nutritional products on the PBS

Source: DHS Supplied Prescriptions Database, extracted July 2015.

Note: AA and PH formulae for cows' milk protein intolerance and allergy include utilisation for other indications.

There was 10% per year growth in the number of patients starting treatment with AA formulae from 2006 to 2011. During the same period, the number of patients starting treatment with PH formulae increased 7% per year. Between 2011 and 2013, there was a 31% decrease in the number of patients starting treatment with AA formulae and a 24% increase in the number of patients starting PH

formulae. The number of patients starting treatment with products for phenylketonuria and other nutritional products has remained relatively stable.

Utilisation of products for cows' milk protein intolerance and allergy

Figure 3 presents new and total patients number receiving AA or PH formulae by quarter of supply.

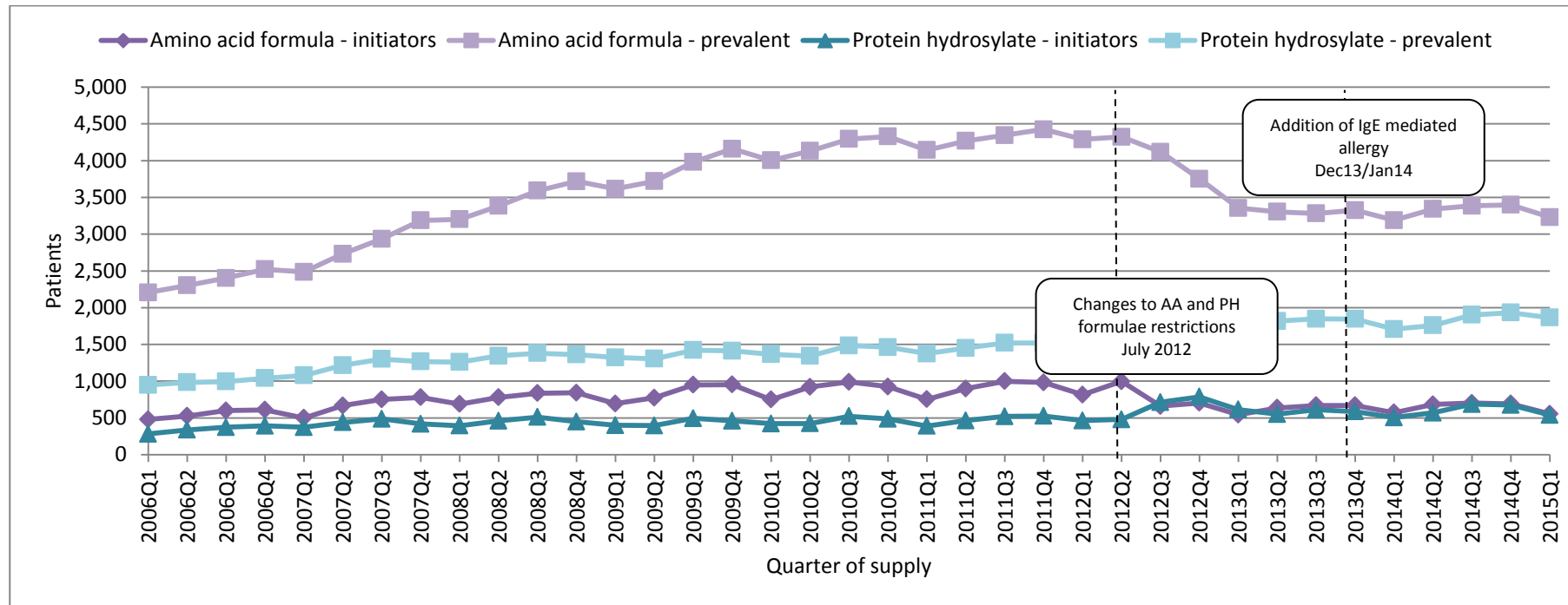


Figure 3: Initiating and prevalent patients for AA and PH formulae for cows' milk protein intolerance and allergy

Source: DHS Supplied Prescriptions Database, extracted July 2015.

Note: AA and PH formulae for cows' milk protein intolerance and allergy include utilisation for other indications.

There was a decrease in the number of new and total patients supplied AA formulae following the changes to the restrictions in July 2012. The new and total patients supplied PH formulae increased during the same period.

Figure 4 presents the number of patients starting treatment with PH formulae from 2006 to the first quarter of 2015 by age.

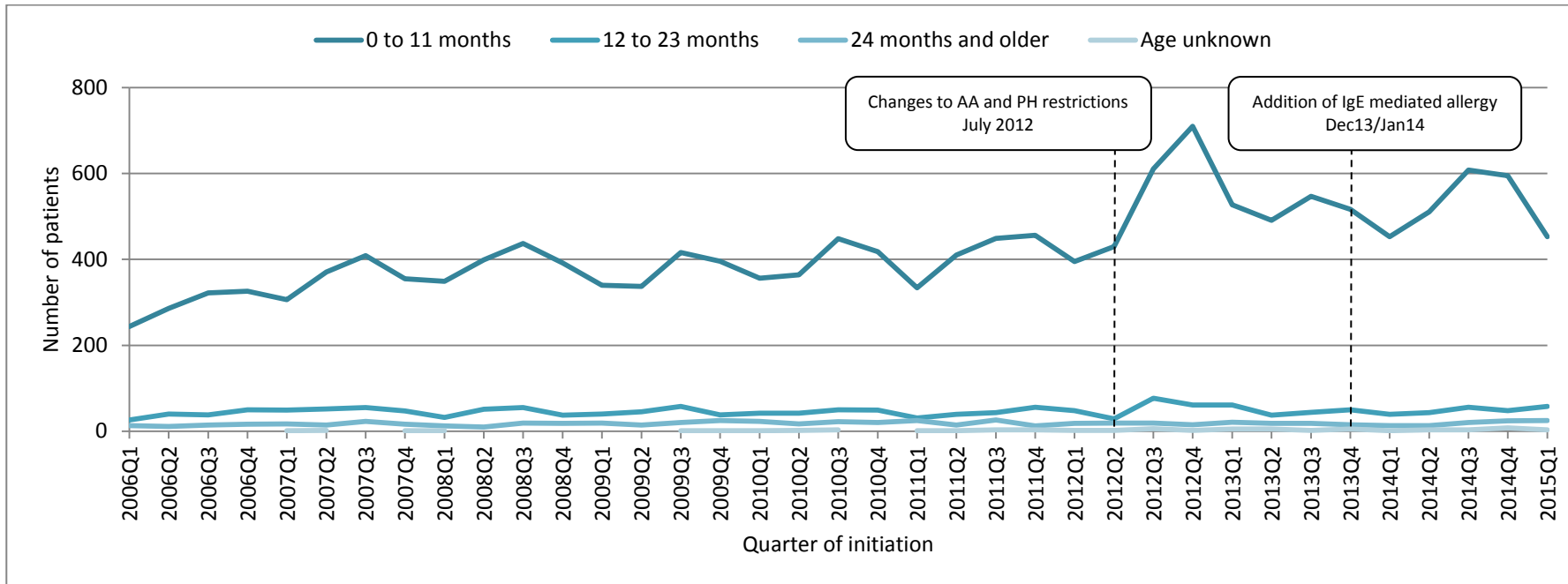


Figure 4: Initiating patients for PH formulae for cows’ milk protein intolerance and allergy by age

Source: DHS Supplied Prescriptions Database, extracted August 2015.

Note: PH formulae for cows’ milk protein intolerance and allergy include utilisation for other indications.

There was a substantial increase in the number of patients starting PH formulae on the PBS following the July 2012 restriction changes.

Figure 5 presents the total number of patients supplied PH formulae on the PBS by age.

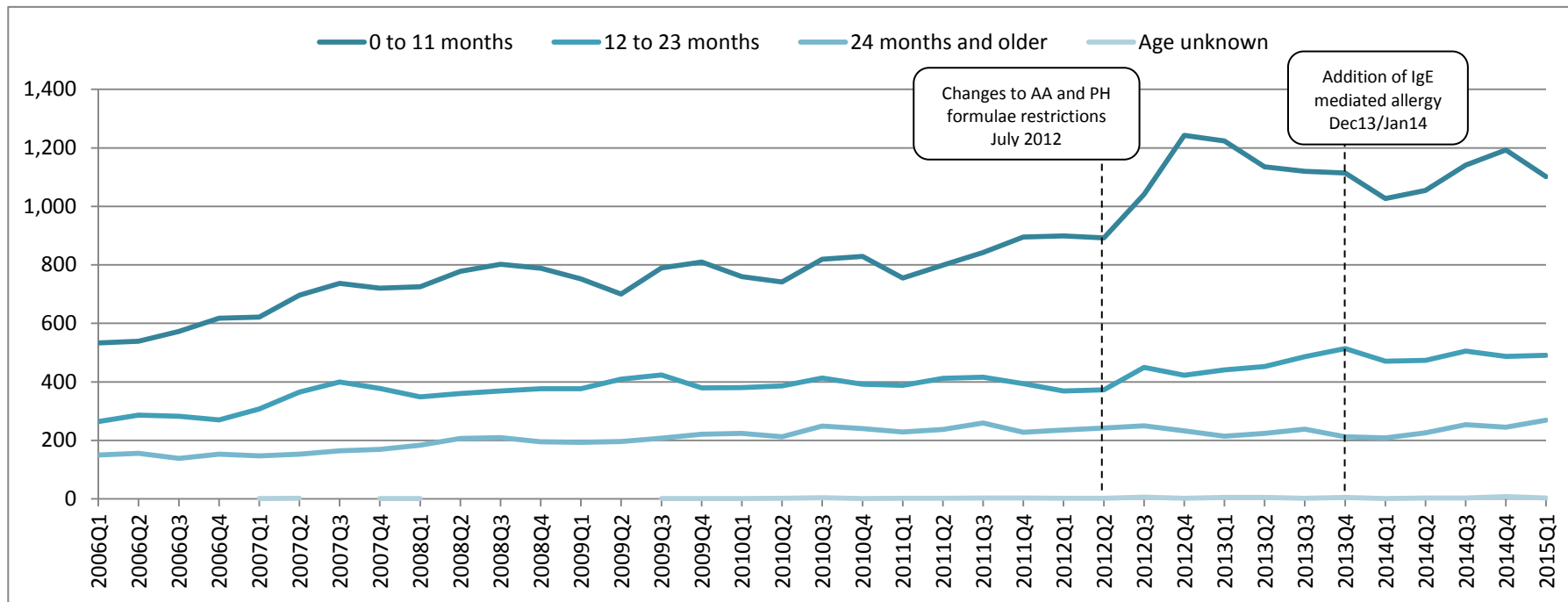


Figure 5: Prevalent patients for PH formulae for cows' milk protein intolerance and allergy by age

Source: DHS Supplied Prescriptions Database, extracted August 2015.

Note: PH formulae for cows' milk protein intolerance and allergy includes utilisation for other indications.

The total number of patients for PH formulae increased in the 0 to 11 months cohort and the 12 to 23 month cohort.

Figure 6 presents the number of patients starting AA formulae by age.

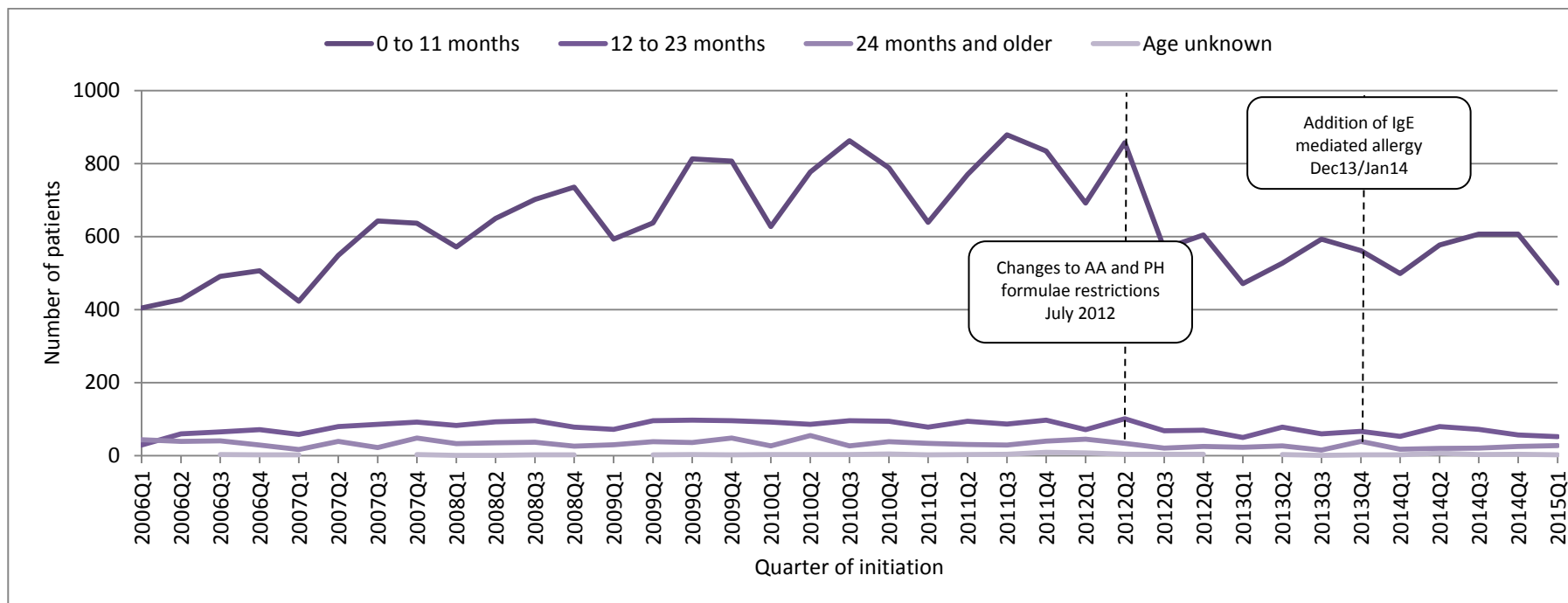


Figure 6: Initiating patients for AA formulae for cows' milk protein intolerance and allergy by age

Source: DHS Supplied Prescriptions Database, extracted August 2015.

Note: AA formulae for cows' milk protein intolerance and allergy includes utilisation for other indications.

There was a substantial decrease in the number of patients starting AA formulae on the PBS following the July 2012 restriction changes.

Figure 7 presents the total number of patients supplied AA formulae by age.

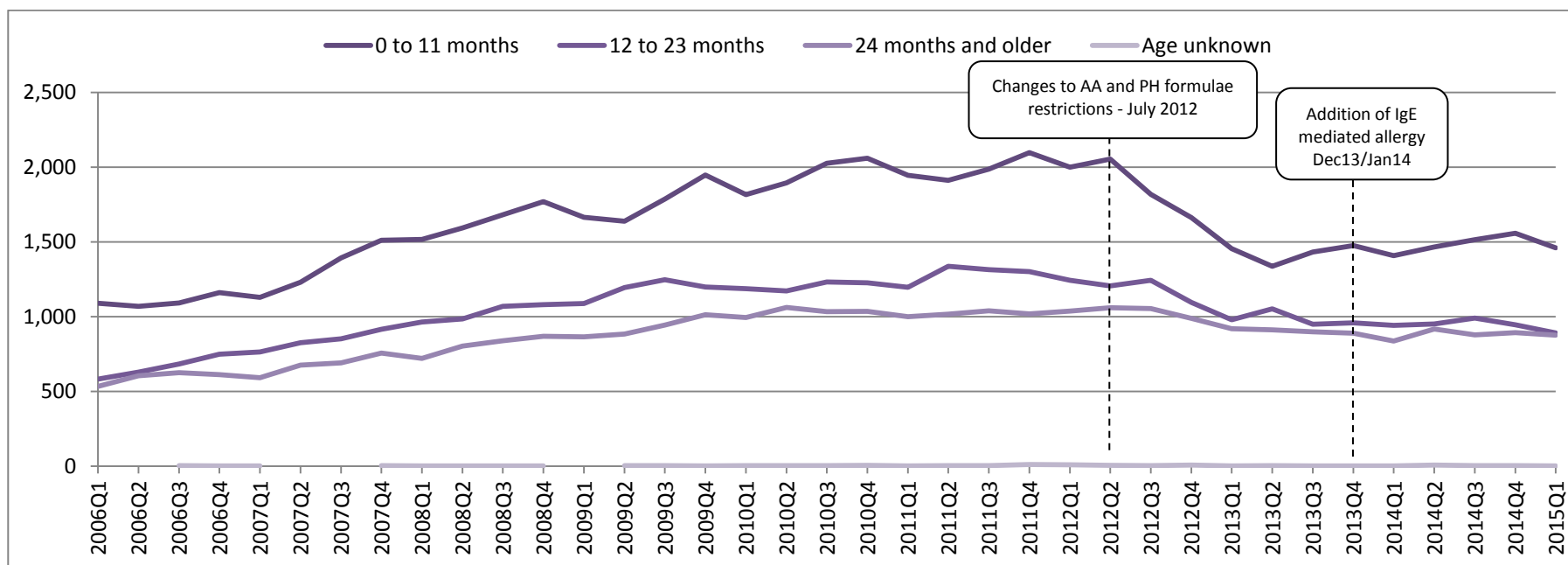


Figure 7: Prevalent patients for AA formulae for cows' milk protein intolerance and allergy by age

Source: DHS Supplied Prescriptions Database, extracted August 2015.

Note: AA formulae for cows' milk protein intolerance and allergy include utilisation for other indications.

The number of patients supplied AA formulae each quarter decreased substantially following the July 2012 changes to the restrictions. The decrease was greater for patients up to 1 year of age. There are a similar number of patients aged 2 years and older as there are patients aged 1 year supplied AA formulae. The absolute number of patients aged 2 years and over receiving AA formulae is 3-4 times greater than the number of patients aged 2 years and older supplied PH formulae. In the fourth quarter of 2014, there were 893 patients aged 2 years and older supplied AA formulae and 245 patients aged 2 years and older supplied PH formulae.

Figure 8 presents the number of prescriptions for AA and PH formulae for cows' milk intolerance and allergy.

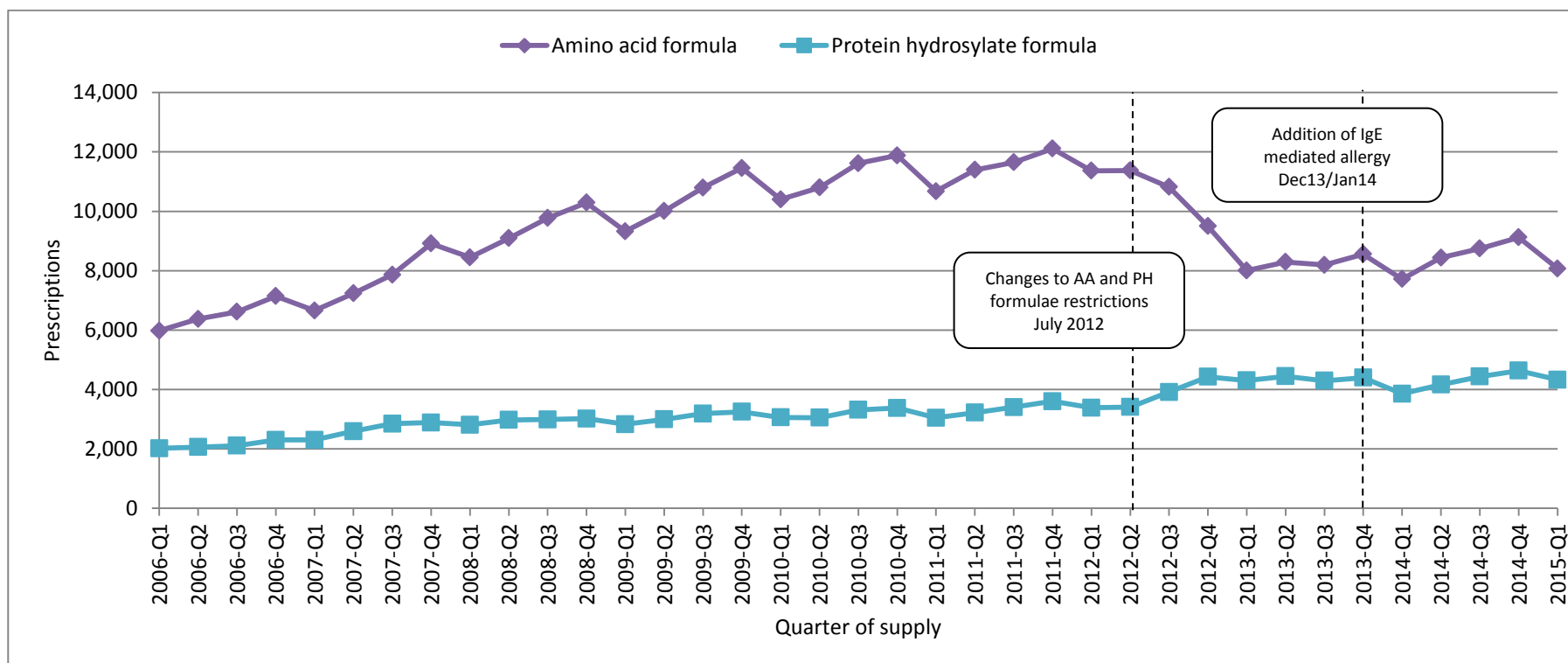


Figure 8: Prescriptions for AA and PH formulae for cows' milk protein intolerance and allergy

Source: DHS Supplied Prescriptions Database, extracted August 2015

Note: AA and PH formulae include small numbers of prescriptions for restrictions other than cows' milk protein allergy, enteropathy or intolerance

The number of AA prescriptions supplied was 27% lower in the second quarter of 2013 compared to the second quarter of 2012. During the same period, there was a 31% increase in the number of prescriptions for PH formulae.

Figure 9 presents the quarterly expenditure for AA and PH formulae for cows' milk protein intolerance and allergy.

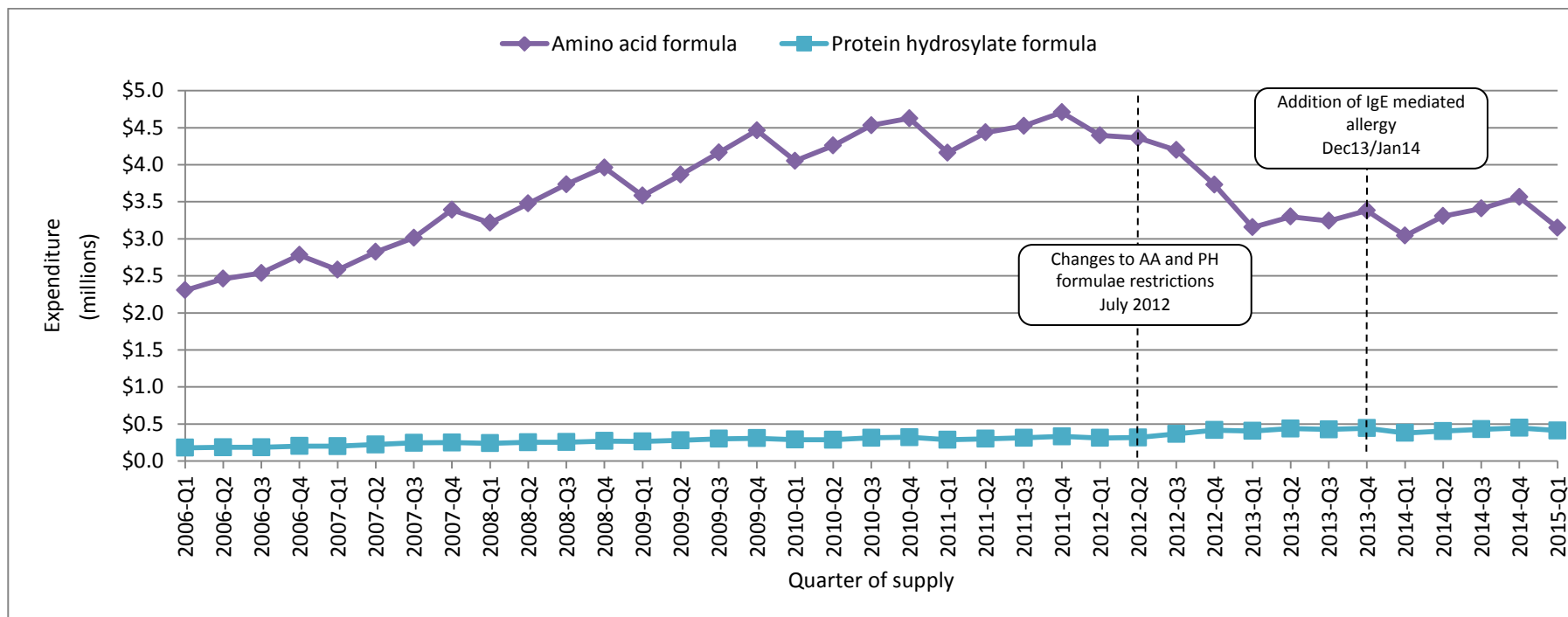


Figure 9: Expenditure for AA and PH formulae for cows’ milk protein intolerance and allergy

Source: DHS Supplied Prescriptions Database, extracted August 2015

Note: AA and PH formulae include small numbers of prescriptions for restrictions other than cows’ milk protein allergy, enteropathy or intolerance

There was a 24% decrease in expenditure on AA formulae from the second quarter of 2012 to the second quarter of 2013. During the same period, expenditure for PH formulae increased by 38%. Due to the substantially higher cost of AA formulae, this represented a saving of \$944,074 in the second quarter of 2012 compared to the second quarter of 2013.

Use of PH and AA formulae for other indications

PH and AA formulae are PBS listed for a number of conditions other than cows' milk protein enteropathy and allergy. The number of authority approvals for these indications are presented in Tables 4 and 5.

Table 4: Authority approvals for PH formulae (indications other than cows' milk protein intolerance or allergy)

Year	Severe intestinal malabsorption	Fat malabsorption	Severe diarrhoea in infant	Other indications ^a	Cows' milk protein restrictions (% of total)	Total approvals
2011	111	182	28	43	3,680 (91%)	4,044
2012	97	182	51	45	4,369 (92%)	4,744
2013	136	148	62	52	4,738 (92%)	5,136
2014	105	137	18	32	4,757 (94%)	5,049
2015 ^b	56	82	6	15	2,358 (94%)	2,517

Source: DHS Authority Approvals Database, extracted July 2015

^a Includes PBS indications biliary atresia, chylothorax, chylous ascites, cystic fibrosis, enterokinase deficiency and DVA special approvals.

^b Data complete to June 2015

Table 5: Authority approvals for AA formulae (indications other than cows' milk protein intolerance or allergy)

Year	Severe intestinal malabsorption	Cows' milk protein enteropathy and allergy	% Cows' milk protein enteropathy and allergy ^a	Eosinophilic oesophagitis ^a
2011	212	11,412	98%	31
2012	203	10,448	98%	105
2013	201	7,776	97%	183
2014	144	8,243	98%	134
2015 ^b	74	3,986	98%	59

Source: DHS Authority Approvals Database, extracted July 2015

^a Excludes eosinophilic oesophagitis approvals. AA formulae have separate item codes for use in eosinophilic oesophagitis

^b Data complete to June 2015

Authority approvals for conditions other than cows' milk protein intolerance, allergy and enteropathy accounted for 2-5% of approvals for AA formulae and 6-9% of approvals for PH formulae.

Approvals for PH and AA formulae by age

Tables 6 and 7 present the number of authority approvals for PH and AA formulae by restriction and by age from 2011 to 2015. A small percentage of approvals did not have age data. Age data are extracted by linking approvals data to prescription supply data. Age may

be missing because the patient is using a temporary Medicare number or if they have never received a PBS subsidised prescription, including the medicine for which they received an Authority approval.

Table 6: Approvals for PH formulae by restriction and age

Year and Restriction	Under 2 years (up to 23 months)	2 years or older	Age unknown
2011			
Cows' milk protein allergy	-	-	-
Cows' milk protein intolerance	3,067	305	308
Severe intestinal malabsorption	51	59	< 5
Fat malabsorption	45	130	7
Severe diarrhoea in infant	26	0	< 5
Other indications ^a	30	10	< 5
2012			
Cows' milk protein allergy	-	-	-
Cows' milk protein intolerance	3,692	316	361
Severe intestinal malabsorption	36	57	< 5
Fat malabsorption	59	119	< 5
Severe diarrhoea in infant	45	< 5	6
Other indications ^a	27	14	< 5
2013			
Cows' milk protein allergy	-	-	-
Cows' milk protein intolerance	4,036	313	389
Severe intestinal malabsorption	73	55	8
Fat malabsorption	50	90	8
Severe diarrhoea in infant	54	< 5	8
Other indications ^a	32	14	6
2014			
Cows' milk protein allergy	110	8	15
Cows' milk protein intolerance	3,902	320	402
Severe intestinal malabsorption	36	65	< 5
Fat malabsorption	40	91	6
Severe diarrhoea in infant	14	< 5	< 5
Other indications ^a	24	7	< 5
2015 (to June 2015)			
Cows' milk protein allergy	50	5	9

Year and Restriction	Under 2 years (up to 23 months)	2 years or older	Age unknown
Cows' milk protein intolerance	1,769	185	340
Severe intestinal malabsorption	15	36	5
Fat malabsorption	10	62	10
Severe diarrhoea in infant	5	< 5	< 5
Other indications ^a	8	< 5	< 5

Source: DHS Authority Approvals Database, extracted June 2015 (data complete to end June 2015)

^a Chylous ascites, chylothorax, cystic fibrosis, enterokinase deficiency and DVA authorities for uses outside R/PBS listings.

Table 7: Approvals for AA formulae by restriction and age

Year and Restriction	Under 2 years (up to 23 months)	2 years and older	Age unknown
2011			
Cows' milk protein intolerance and enteropathy	9,199	1,750	463
Severe intestinal malabsorption ^a	66	141	5
2012			
Cows' milk protein allergy and anaphylaxis	295	65	5
Cows' milk protein intolerance and enteropathy	8,021	1,619	443
Severe intestinal malabsorption ^a	51	149	< 5
2013			
Cows' milk protein allergy and anaphylaxis	565	86	8
Cows' milk protein intolerance and enteropathy	5,531	1,313	273
Severe intestinal malabsorption ^a	141	149	157
2014			
Cows' milk protein allergy and anaphylaxis	925	107	34
Cows' milk protein intolerance and enteropathy	5,620	1,273	284
Severe intestinal malabsorption ^a	14	127	< 5
2015 (to June 2015)			
Cows' milk protein allergy and anaphylaxis	352	52	35
Cows' milk protein intolerance and enteropathy	2,582	650	315
Severe intestinal malabsorption ^a	7	65	< 5

Source: DHS Authority Approvals Database extracted July 2015 (data complete to end June 2015)

^a Includes DVA authorities for uses outside R/PBS listings.

In the period from 2011 to 2015, 15-18% of all authority approvals for AA formulae have been for cows' milk intolerance, enteropathy and allergy (including anaphylaxis) for children aged 2 years or older. During the same period, 6-8% of all authority approvals for PH formulae were for cows' milk protein intolerance, enteropathy or allergy for were

children aged 2 years or older. The total number of authority approvals for cows' milk protein intolerance, enteropathy or allergy is substantially higher for AA formulae than for PH formulae.

Tables 8 and 9 present the expenditure for PH and AA formulae for children aged 2 years of age and older. This data is from prescription dispensing data and does not include details on the restriction for which the patient was approved. As such, the data contain details on expenditure for all restrictions.

Table 8: PH formulae costs for patients aged 2 years and older (all restrictions)

Year	Age 2 years and older ^a	% of total PH expenditure	Age 3 years and older	% of total PH expenditure
2011	\$239,871	19%	\$156,549	13%
2012	\$263,366	19%	\$174,077	12%
2013	\$277,091	16%	\$195,324	11%
2014	\$310,792	19%	\$214,374	13%

Source: DHS Supplied Prescriptions Database, extracted July 2015

^a Includes children aged 3 years and older as well as children aged 2-3 years.

Table 9: AA formulae costs for patients aged 2 years and older (all restrictions)

Year	Age 2 years and older ^a	% of total AA expenditure	Age 3 years and older	% of total AA expenditure
2011	\$4,746,733	27%	\$2,880,822	16%
2012	\$4,699,195	28%	\$2,925,766	18%
2013	\$4,082,980	31%	\$2,680,095	20%
2014	\$3,975,068	30%	\$2,577,734	19%

Source: DHS Supplied Prescriptions Database, extracted July 2015

^a Includes children aged 3 years and older as well as children aged 2-3years.

The proportion of AA expenditure for patients aged 2 years and older has consistently been higher than PH formulae.

Prescriptions by condition

Table 10 presents the number of nutritional product prescriptions supplied each year from 2011 to 2014.

Table 10: Prescriptions for nutritional products

Condition	2011	2012	2013	2014	% Growth 2011 to 2014
Cows' milk intolerance or allergy - AA	45,821	43,058	33,033	33,995	-26%
Cows' milk intolerance or allergy - PH	13,274	15,132	17,426	17,053	28%
Chronic renal failure	263	293	283	318	21%
Eosinophilic oesophagitis – AA	90	294	682	683	659%
Glycogen storage disease	55	81	84	88	60%
Homocystinuria	100	121	148	165	65%
Hypercalcaemia in children	64	90	140	135	111%
Inborn errors of protein metabolism	1,659	1,804	1,938	2,216	34%
Ketogenic diet	490	490	532	681	39%
Lactose intolerance	16,576	16,946	16,149	15,013	-9%
Maple syrup urine disease	507	556	571	518	2%
Medium chain triglycerides	1,895	1,986	1,904	2,199	16%
Organic acidaemias	163	175	173	178	9%
Peroxisomal biogenesis disorders	-	-	-	19	
Phenylketonuria	6,563	7,139	7,730	7,856	20%
Restrictive therapeutic diet	324	382	320	285	-12%
Tyrosinaemia	167	189	167	151	-10%
Urea cycle disorders and Gyrate atrophy	779	960	1,121	1,236	59%
Total cows' milk protein enteropathy or allergy	59,095	58,190	50,459	51,048	-14%
Total excluding cows' milk intolerance	29,695	31,506	31,942	31,741	7%
Total	88,790	89,696	82,401	82,789	-7%

Source: DHS Supplied Prescriptions Database, extracted June 2015

Overall, there has been a decrease in the number of nutritional product prescriptions. There have been increases in prescriptions for some of the less frequently used product groups. There has only been a 7% growth in the number of prescriptions for conditions other than cows' milk protein intolerance and allergy from 2011 to 2014.

Supplies to area Aboriginal Health Services (AHSs) do not have data on prescriptions. Table 11 presents the data on the number of packs supplied by condition.

Table 11: Nutritional product packs supplied to AHSs

Condition	2011	2012	2013	2014
Cows' milk intolerance or allergy - AA	10	23	5	-
Cows' milk intolerance or allergy - PH	26	< 5	< 5	6
Eosinophilic oesophagitis	< 5	< 5	-	-
Inborn errors of protein metabolism	-	-	< 5	-
Ketogenic diet	< 5	-	-	-
Lactose intolerance	644	776	335	289
Medium chain triglycerides	-	-	< 5	-

Source: Remote Aboriginal Health Services Section 100 PBS Supply Data, extracted August 2015

Only small numbers of packs of nutritional products are supplied through AHSs. Products for lactose intolerance account for the majority of packs supplied to AHSs.

Analysis of expenditure

Table 12 presents the cost to Government of nutritional product supplied each year from 2011 to 2014. This data also includes supply to AHSs.

Table 12: Expenditure for nutritional products

Condition	2011	2012	2013	2014	% Growth 2011 to 2014
Cows' milk intolerance or allergy - AA	\$17,832,174	\$16,694,345	\$13,073,194	\$13,306,366	-25%
Cows' milk intolerance or allergy - PH	\$1,234,327	\$1,413,001	\$1,711,149	\$1,655,635	34%
Chronic renal failure	\$270,545	\$302,612	\$304,986	\$413,921	53%
Eosinophilic oesophagitis	\$66,187	\$169,864	\$335,187	\$384,042	480%
Glycogen storage disease	\$36,961	\$55,833	\$60,410	\$65,548	77%
Homocystinuria	\$255,297	\$309,970	\$382,005	\$461,072	81%
Hypercalcaemia in children	\$23,196	\$31,815	\$48,671	\$47,200	103%
Inborn errors of protein metabolism	\$489,423	\$527,865	\$578,711	\$660,765	35%
Ketogenic diet	\$442,430	\$460,823	\$486,934	\$560,104	27%
Lactose intolerance	\$1,438,951	\$1,459,001	\$1,390,215	\$1,354,582	-6%
Maple syrup urine disease	\$909,472	\$980,882	\$1,078,792	\$1,056,787	16%
Medium chain triglycerides	\$413,092	\$430,797	\$413,987	\$500,096	21%
Organic acidaemias	\$268,162	\$309,632	\$325,876	\$342,359	28%
Peroxisomal biogenesis	-	-	-	\$2,018	N/A

Condition	2011	2012	2013	2014	% Growth 2011 to 2014
disorders					
Phenylketonuria	\$8,806,267	\$9,703,522	\$10,698,349	\$10,944,394	24%
Restrictive therapeutic diet	\$107,884	\$122,883	\$96,389	\$93,326	-13%
Tyrosinaemia	\$336,720	\$376,390	\$368,392	\$383,904	14%
Urea cycle disorders and Gyrate atrophy	\$560,702	\$621,389	\$739,024	\$812,625	45%
Total cows' milk protein enteropathy or allergy	\$19,066,500	\$18,107,347	\$14,784,344	\$14,962,001	-22%
Total excluding cows' milk intolerance	\$14,425,288	\$15,863,279	\$17,307,928	\$18,082,742	25%
Total	\$33,491,788	\$33,970,625	\$32,092,272	\$33,044,744	-1%

Source: DHS Supplied Prescriptions Database, extracted June 2015. Remote Aboriginal Health Services Section 100 PBS Supply Data, extracted August 2015

Overall, the total cost of nutritional products has not increased since 2011. Between 2011 and 2014, there has been a 25% increase in the cost for products for conditions other than cows' milk intolerance or allergy. Supply to AHSs accounted for less than 0.5% of costs.

Discussion

See DUSC consideration for the DUSC's views.

There has been a clear decrease in the number of patients using AA formulae on the PBS following the July 2012 changes to the restrictions relating to cows' milk protein intolerance/enteropathy. This appears to be mainly due to a decrease in the number of new and total patients aged up to one year of age using AA formulae. At the same time, the number of patients starting treatment with PH formulae increased, increasing the total number of patients supplied PH formulae. Most of the increase in PH formulae use occurred in patients up to one year of age. These changes have led to a decrease in PBS expenditure for cows' milk protein intolerance, enteropathy and allergy from over \$19 million in 2011 to less than \$15 million in 2014.

The PBAC review of the restrictions for the PH and AA formulae stemmed from concern that AA formula was being prescribed in the first instance for cows' milk protein intolerance or allergy instead of trialling patients on a soy protein or a PH formula prior to initiating an AA formula. The previous DUSC review of nutritional products in October 2011 also concluded that only a minority of patients with cows' milk protein intolerance or allergy trial PBS listed PH prior to commencing an AA formula. The results of this review indicate that there has been a change in prescribing practice for PBS listed PH and AA formulae as a result of the changes to the restrictions that were effective from July 2012. The decrease in the number of patients starting treatment with an AA formula and decrease in the total number of patients on an AA coupled with the increase use of PH formula since the

restriction changes were implemented indicate that more patients may be trialling a PH formula before starting an AA formula, as recommended by guidelines.

There appears to be a reasonably high level of use of AA formulae in patients aged two years and older. The number of patients aged 2 years and older starting AA formula is low, with fewer than 50 patients starting treatment each quarter. However, there are almost 900 patients aged 2 years and older supplied AA formulae each quarter. This is in contrast to PH formulae, which has fewer than 300 patients aged 2 years and older supplied each quarter. It appears that patients starting AA formula for cows' milk protein enteropathy are using it for long periods of time. The National Health and Medical Research Council (NHMRC) Infant Feeding Guidelines state that from 12 months of age, children should be consuming foods consistent with the Australian Dietary Guidelines. Special complementary foods or milks are not required for healthy children. Calcium-enriched plant-based milk may be used in children over 12 months of age.³ Additionally, a Danish cohort study has found 77% of children with cows' milk protein allergy or intolerance recover by 2 years of age.⁴ The cost of AA formulae for children aged two years and older is approximately \$4 million each year and accounts for 30% of the total PBS expenditure for AA formulae. A small amount of the use of AA formulae may be due to use for enteral feeding that may be outside PBS restrictions.

An analysis assessing the use of PH formulae prior to AA formulae was not undertaken. PBS data may only show part of the use of PH formula in Australia for cows' milk intolerance, enteropathy or allergy. PH formulae, such as Karicare Aptamil Pepti-Junior Gold, are available from pharmacies without a prescription for less than \$16 for each 450g container.^{5,6} This is comparable to the cost of standard infant formula. As a result it is likely that PH formula is purchased privately as a first or second line treatment option. Hence there may be more patients following the recommended treatment pathway for cows' milk protein intolerance or allergy of a non-severe nature of a PH formula prior to initiation of an AA formula than indicated by the number of patients starting a PBS PH formula.

The use of nutritional products for conditions other than cows' milk protein enteropathy and allergy is growing. From 2011 to 2014, the number of prescriptions for these products increased at 2% per year while expenditure grew at 8% per year. This may reflect patients with metabolic disorders growing older and requiring larger volumes of nutritional products.

DUSC consideration

There has been a substantial decrease in the utilisation of AA formulae for cows' milk protein intolerance and allergy following the July 2012 restriction changes. Between 2011 and 2014, the number of patients supplied AA formulae decreased by 31% and has since stabilised. At the same time the number of patients supplied PH formulae increased 24%.

The DUSC considered that the changes to the PBS restrictions effective July 2012 have been successful in their intent and that current PBS use of AA and PH formulae appears to be more in line with clinical guidelines than PBS use prior to the restriction changes. The DUSC considered that the increased use of PH formulae and concurrent decrease in use of AA formulae since the July 2012 restriction changes indicate that more prescribers are following the clinical guidelines which recommend the use of PH formula in infants with cows' milk protein allergy prior to an AA formula, except in infants who have had an anaphylactic reaction to cows' milk protein, where AA formula is the first choice of formula.

The DUSC considered that the use of PH formula in the Australian population may be higher than the PBS utilisation given that PH formula may be purchased from pharmacies without a prescription at a similar cost per container as cows' milk formula. However, the DUSC further noted that the PBS listings for PH formulae allow for a maximum quantity of eight containers and hence the cost to the patient for the maximum PBS quantity is much less than the cost of purchasing the equivalent quantity without a PBS prescription both for general and concessional patients.

The DUSC further noted that given the much higher cost of the AA formulae in comparison to the protein hydrolysate formulae, the changes in PBS utilisation of these formulae since the July 2012 restriction changes has resulted in a 22% reduction (approximately \$4 million reduction) in total PBS expenditure on products for the treatment of cows' milk protein intolerance and allergy in 2014 compared to 2011.

- There is a large group of children supplied AA formulae who are aged 2 years and older. Almost 900 patients aged 2 years and older are supplied AA formulae each quarter. In 2014, this represented over 25% of patients supplied AA formulae. This is in contrast to PH formulae which have fewer than 300 patients aged 2 years and older supplied each quarter, representing less than 13% of PH patients in 2014. In 2014, this represented 30% and 19% of total expenditure for AA and PH formulae respectively.

The DUSC noted the reasonably high utilisation of AA formulae in patients aged over 24 months. The DUSC also noted that patients appear to stay on AA formula longer than protein hydrolysate formula.

The DUSC noted that the Secretariat had sought advice from the PBAC's Nutritional Products Working Party (NPWP) and the Australasian Society of Clinical Immunology and Allergy (ASCI). The ASCIA and the majority of the NPWP members were unable to provide comment prior to the DUSC meeting (comment was received from one NPWP member).

The DUSC noted that any advice received from these organisations would be included with this report for the PBAC's consideration if received in time for inclusion in the PBAC agenda and in particular looked forward to any reasons these organisations may be able to suggest for the reasonably high utilisation of AA formulae in patients aged over 24 months. The DUSC however noted comment from a NPWP member that the high use of AA formulae in the greater than two years age group may be due to a lack of knowledge about how to wean children off AA formulae onto nutritionally adequate milk/soy free diets.

The DUSC noted that Nutricia Australia suggested that one of the reasons for the higher utilisation of AA formulae in patients over the age of 24 months is for use in eosinophilic oesophagitis for which AA formulae is listed on the PBS but for which PH formulae is not. The DUSC however noted that the data in this report on the use of AA formulae for cows' milk protein intolerance and allergy excludes use for eosinophilic oesophagitis (these listings have separate item codes).

The DUSC also noted that Nutricia Australia noted that a sub-set of children with severe forms of food allergy may require the use of an AA based formula for longer. The sponsor gave the example of infants with multiple food protein allergies, noting that whilst most develop tolerance between 18 to 24 months of age, a small sub-set of children will still require an AA formula by 3 years of age.

In the report discussion the finding of a Danish cohort study that 77% of children with cows' milk protein allergy or intolerance recover by 2 years of age was referenced. Nutricia Australia considered that the Danish study prevalence rates cannot be applied to the Australian population for the reason that the Danish cohort included patients with cows' milk protein intolerance. The sponsor considered that AA formulae is only prescribed for cows' milk protein allergy and not cows' milk protein intolerance. The DUSC however disagreed, noting that AA formulae are PBS listed for cows' milk protein intolerance (as combined intolerance to cows' milk protein, soy protein and protein hydrolysate formulae) and hence considered that AA formulae is prescribed for cows' milk protein intolerance in Australia.

The report referenced the National Health and Medical Research Council (NHMRC) Infant Feeding Guidelines which state that from 12 months of age, children should be consuming foods consistent with the Australian Dietary Guidelines. Special complementary foods or milks are not required for healthy children. Calcium-enriched plant-based milk may be used in children over 12 months of age. Nutricia Australia noted that these guidelines are for healthy children and that children receiving AA formulae may have a severe allergic condition.

The report noted that a small amount of the use of AA formulae may be due to use for enteral feeding that may be outside PBS restrictions. Nutricia Australia considered that use for enteral feeding would be within the PBS indications. The DUSC noted that if use was on an outpatient basis it may be within the PBS restrictions.

- The DUSC noted that Infant formula products are the most widely used nutritional products on the PBS, accounting for almost half of PBS expenditure on nutritional products in 2014.

The DUSC noted the comment from a NPWP member regarding the annual cost to the PBS of lactose free products of approximately \$1.5 million in the context of these products costing a similar amount to standard infant formula when purchased without a prescription. The DUSC however noted that patients may receive a maximum quantity of five containers of lactose free formula on a PBS prescription for which the patient co-payment (both for general and concessional patients) would be much less than the cost of five containers purchased without a prescription.

- The use of nutritional products for metabolic conditions or other conditions requiring strict dietary management is growing. From 2011 to 2014, the number of prescriptions for these products increased 7% while expenditure grew 25%.

The DUSC noted comment from a NPWP member that increased use of products for many metabolic conditions is likely due to increased awareness and diagnosis of these conditions.

Actions undertaken by the DUSC Secretariat

Prior to consideration by the DUSC, a copy of the report was provided to the sponsors of the products, the NPWP and ASCIA for comment.

DUSC actions

The DUSC requested that the report be provided to the PBAC.

The DUSC requested that any advice received from the PBAC's Nutritional Products Working Party and the Australasian Society of Clinical Immunology and Allergy also be provided to the PBAC. At the time of the PBAC meeting comment from ASCIA had not been received, nor further comment from the NPWP.

References

1. Kemp AS, Hill DJ, Allen KJ, Anderson K, Davidson GP, Day AS, et al. Guidelines for the use of infant formulas to treat cows milk protein allergy: an Australian consensus panel opinion. *Med J Aust.* 2008;188:109-12.
2. Dieticians Association of Australia. Enteral Feeding Manual for Adults in Health Care Facilities 2015 [cited 2015 14 August]. Available from: <<http://daa.asn.au/wp-content/uploads/2015/03/Enteral-nutrition-manual-January-2015.pdf>>.
3. National Health and Medical Research Council Infant Feeding Guidelines. Canberra: National Health and Medical Research Council; 2012.
4. Host A, Halcken S, Jacobsen HP, Christensen AE, Herskind AM, Plesner K. Clinical course of cow's milk protein allergy/intolerance and atopic diseases in childhood. *Pediatr Allergy Immunol.* 2002;13 Suppl 15:23-8.
5. Superpharmacy. Karicare Aptamil Gold Pepti Junior Formula 450G [cited 2015 19 August]. Available from: <<https://www.superpharmacy.com.au/products/view/5892>>.
6. Discount Pharmacy Group. Karicare Aptamil Pepti-Junior Gold 450g [cited 2015 19 August]. Available from: <http://www.canberradiscountpharmacy.com.au/productdetail.aspx?name=Karicare-Aptamil-Pepti_Junior-Gold-450g#undefined1>.

Context for analysis

The DUSC is a Sub Committee of the Pharmaceutical Benefits Advisory Committee (PBAC). The DUSC assesses estimates on projected usage and financial cost of medicines.

The DUSC also analyses data on actual use of medicines, including the utilisation of PBS listed medicines, and provides advice to the PBAC on these matters. This may include outlining how the current utilisation of PBS medicines compares with the use as recommended by the PBAC.

The DUSC operates in accordance with the quality use of medicines objective of the National Medicines Policy and considers that the DUSC utilisation analyses will assist consumers and health professionals to better understand the costs, benefits and risks of medicines.

The utilisation analysis report was provided to the pharmaceutical sponsors of each drug and comments on the report were provided to DUSC prior to its consideration of the analysis.

Sponsors' comments

Abbott Australasia Pty Ltd, Aspen Pharmacare Australia Pty Limited, Cortex Health Pty Ltd, Nestle Australia Ltd, Nutricia Australia Pty Limited, Sharpe Laboratories Pty Ltd, Vitaflo Australia Pty Limited. The sponsors had no comment.

Disclaimer

The information provided in this report does not constitute medical advice and is not intended to take the place of professional medical advice or care. It is not intended to define what constitutes reasonable, appropriate or best care for any individual for any given health issue. The information should not be used as a substitute for the judgement and skill of a medical practitioner.

The Department of Health (DoH) has made all reasonable efforts to ensure that information provided in this report is accurate. The information provided in this report was up-to-date when it was considered by the Drug Utilisation Sub-committee of the Pharmaceutical Benefits Advisory Committee. The context for that information may have changed since publication.

To the extent provided by law, DoH makes no warranties or representations as to accuracy or completeness of information contained in this report.

To the fullest extent permitted by law, neither the DoH nor any DoH employee is liable for any liability, loss, claim, damage, expense, injury or personal injury (including death), whether direct or indirect (including consequential loss and loss of profits) and however incurred (including in tort), caused or contributed to by any person's use or misuse of the information available from this report or contained on any third party website referred to in this report.

Appendix 1: PBS listings of Nutritional Products

Condition, product and brand	DPMQ
Chronic renal failure	
whey protein formula supplemented with amino acids, long chain polyunsaturated fatty acids, vitamins and minerals, low in protein, phosphate, potassium and lactose	
Renastart	\$1432.71
whey protein formula supplemented with amino acids, vitamins and minerals, and low in protein, phosphate, potassium and lactose	
Kindergen	\$1,029.17
Cows' milk intolerance or allergy - amino acid formulae	
amino acid synthetic formula	
EleCare	\$347.17
Neocate Advance	\$347.17
Neocate Advance Vanilla	\$347.17
amino acid synthetic formula with long chain polyunsaturated fatty acids with or without medium chain triglycerides	
Alfamino	\$353.89
EleCare LCP	\$353.89
Neocate Gold	\$353.89
Neocate LCP	\$353.89
Cows' milk intolerance or allergy - protein hydrolysate formulae	
protein hydrolysate formula with medium chain triglycerides	
Alfare	\$160.93
Karicare Aptamil Pepti-Junior Gold	\$104.45
Eosinophilic oesophagitis	
amino acid synthetic formula	
EleCare	\$347.17
Neocate Advance Vanilla	\$347.17
amino acid synthetic formula with long chain polyunsaturated fatty acids	
Neocate Gold	\$353.89
Glycogen storage disease	
amylopectin modified long chain	
Glycosade	\$727.61
Homocystinuria	
amino acid formula with fat, carbohydrate, vitamins, minerals and trace elements	
HCU Anamix junior LQ	\$2,508.49
amino acid formula with vitamins and minerals without methionine	
HCU Anamix infant	\$743.97
HCU cooler 10	\$2,048.37
HCU cooler 15	\$3,098.89
HCU cooler 20	\$4,082.89
HCU express 15	\$3,098.89
HCU gel	\$2,048.37

HCU Lophlex LQ 20	\$3,098.85
XMET Maxamaid	\$1,720.37
XMET Maxamum	\$2,705.25
cystine with carbohydrate	
Cystine 500	\$500.41
Hypercalcaemia in children	
milk powder synthetic low calcium	
Locasol	\$367.41
Inborn errors of protein metabolism	
carbohydrate, fat, vitamins, minerals and trace elements	
Energivit	\$304.21
carbohydrates, fat, vitamins, minerals, trace elements and supplemented with arachidonic acid and docosahexaenoic acid	
basecal 100	\$234.25
basecal 200	\$458.13
triglycerides long chain with glucose polymer	
ProZero (protein free milk substitute)	\$290.01
Sno-Pro (low protein milk substitute)	\$178.99
triglycerides medium chain and long chain with glucose polymer	
Duocal	\$281.57
Ketogenic diet	
high fat formula with vitamins, minerals and trace elements and low in protein and carbohydrate	
KetoCal 3:1	\$1,001.97
KetoCal 4:1	\$1,001.97
KetoCal 4:1 LQ	\$953.28
milk protein and fat formula with vitamins and minerals carbohydrate free	
Carbohydrate Free Mixture	\$627.81
soy protein and fat formula with vitamins and minerals carbohydrate free	
RCF	\$648.93
triglycerides long chain	
carbzero	\$285.83
triglycerides medium chain	
betaquik	\$369.53
Lactose intolerance	
S-26 LF	\$107.18
Karicare Aptamil Gold De-Lact	\$91.33
Digestelact	\$70.77
Maple syrup urine disease	
amino acid formula with vitamins and minerals without valine, leucine and isoleucine	
MSUD AID III	\$2,672.49
MSUD Anamix infant	\$743.97
MSUD Anamix Junior	\$1,735.45
MSUD Anamix Junior LQ	\$2,508.49

MSUD cooler 10	\$2,048.37
MSUD cooler 15	\$3,098.89
MSUD cooler 20	\$4,082.89
MSUD express 15	\$3,098.89
MSUD express 20	\$4,094.65
MSUD gel	\$2,048.37
MSUD Lophlex LQ 20	\$3,098.85
MSUD Maxamaid	\$1,720.37
MSUD Maxamum	\$2,705.25
amino acid formula without valine, leucine and isoleucine	
MSUD amino5 (amino acid supplement)	\$3,098.85
isoleucine with carbohydrate	
Isoleucine 1000	\$549.41
Isoleucine 50	\$500.41
valine with carbohydrate	
Valine 1000	\$549.41
Valine 50	\$500.41
Medium chain triglycerides	
triglycerides medium chain	
Liquigen	\$200.45
MCT Oil	\$51.89
triglycerides medium chain formula	
Lipistart	\$428.85
MCT Pro-Cal	\$239.61
Monogen	\$407.33
Peptamen Junior	\$844.13
Organic acidaemias	
amino acid formula with vitamins and minerals without lysine and low in tryptophan	
GA express 15	\$3,154.93
GA gel	\$2,048.37
GA1 Anamix infant	\$743.97
XLYS, LOW TRY Maxamaid	\$1,720.37
amino acid formula with vitamins and minerals without methionine, threonine and low in isoleucine	
MMA/PA Anamix infant	\$743.97
MMA/PA cooler 15	\$3,098.89
MMA/PA express 15	\$3,098.89
MMA/PA gel	\$2,048.37
XMTVI Maxamaid	\$1,720.37
XMTVI Maxamum	\$2,705.25
glycine with carbohydrate	
Glycine500	\$500.41
Peroxisomal biogenesis disorders	
arachidonic acid and docosaheptaenoic acid with carbohydrate	

keyomega	\$356.81
docosahexaenoic acid with carbohydrate	
docomega	\$356.81
Phenylketonuria	
amino acid formula with vitamins and minerals without phenylalanine	
add-ins	\$1,581.24
Easiphen	\$1,267.03
Lophlex	\$1,494.09
PKU Air 15	\$1,493.01
PKU Air 20	\$1,988.01
PKU Anamix Junior	\$862.01
PKU Anamix Junior LQ	\$1,225.25
PKU Cooler 10	\$999.21
PKU Cooler 15	\$1,493.01
PKU Cooler 20	\$1,988.01
PKU express 15	\$1,493.81
PKU express 20	\$1,988.01
PKU gel	\$1,022.13
PKU Lophlex LQ 10	\$1,022.87
PKU Lophlex LQ 20	\$1,494.09
PKU Lophlex Sensation 20	\$1,786.74
PKU squeezie	\$1,022.13
XP Maxamaid	\$854.29
XP Maxamum	\$1,304.69
amino acid formula with vitamins, minerals and long chain polyunsaturated fatty acids without phenylalanine	
PKU Anamix infant	\$680.85
amino acid formula without phenylalanine	
Phlexy-10	\$1,231.57
Phlexy-10 Drink Mix	\$1,410.92
glycomacropeptide and essential amino acids	
Camino Pro Restore	\$1,225.53
glycomacropeptide and essential amino acids with vitamins and minerals	
Camino Pro Bettermilk	\$1,427.09
Camino Pro Complete	\$837.41
PKU Glytactin RTD 10	\$1,042.29
PKU Glytactin RTD 15	\$1,523.25
tyrosine with carbohydrate	
Tyrosine 1000	\$500.41
Restrictive therapeutic diet	
vitamins, minerals and trace elements with carbohydrate	
FruitiVits	\$284.91
Paediatric Seravit	\$376.41
Tyrosinaemia	

amino acid formula with fat, carbohydrate, vitamins, minerals and trace elements without phenylalanine and tyrosine, and supplemented with docosahexaenoic acid	
TYR Anamix junior LQ	\$2,508.49
amino acid formula with vitamins and minerals without phenylalanine and tyrosine	
TYR Anamix infant	\$743.97
TYR Anamix Junior	\$1,735.45
TYR cooler 10	\$2,048.37
TYR cooler 15	\$3,098.89
TYR cooler 20	\$4,082.89
TYR express 15	\$3,098.89
TYR gel	\$2,048.37
TYR Lophlex LQ 20	\$3,098.85
XPhen, Tyr Maxamaid	\$1,720.37
XPhen, Tyr Maxamum	\$2,705.25
phenylalanine with carbohydrate	
Phenylalanine 50	\$500.41
Urea cycle disorders and Gyrate atrophy	
arginine with carbohydrate	
Arginine 2000	\$745.41
Arginine 500	\$500.41
Arginine 5000	\$987.97
citrulline with carbohydrate	
Citrulline 1000	\$500.41
essential amino acids formula	
Essential Amino Acid Mix	\$1,158.63
essential amino acids formula with minerals and vitamin C	
Dialamine	\$614.03
essential amino acids formula with vitamins and minerals	
EAA Supplement	\$1,462.41

Source: August 2015 PBS Schedule. DPMQ = Dispensed price for maximum quantity.

Note: Some drug names have been shortened from how they appear on the Schedule.

Appendix 2: New PBS listings of Nutritional Products

Listing date	Product (Brand)	Condition	PBAC recommendation
Apr-12	Neocate Advance Vanilla	Cows' milk intolerance or allergy - AA	The PBAC (November 2011) recommended the PBS as an Authority Required benefit under the same listing conditions and the same price as the currently listed Neocate products
Jul-12	HCU Lophlex LQ 20, MSUD Lophlex LQ 20 TYR Lophlex LQ 20	Homocystinuria, Maple syrup urine Tyrosinaemia disease, respectively	The PBAC (March 2012) recommended the three products at the price requested which as at an equivalent price per gram of protein compared to the respective comparator products.
Jul-12	Neocate Advance Vanilla and Neocate Gold	Eosinophilic oesophagitis	The PBAC recommended listing Neocate LCP+MCT and Neocate Advance Vanilla as Authority Required benefits for the same eosinophilic oesophagitis indication as for EleCare. The PBAC recommended listing at the price requested, which is the same as EleCare for eosinophilic oesophagitis.
Aug-12	MMA/PA cooler 15	Organic acidemias	The PBAC (March 2012) recommended listing at the price requested, which was at an equivalent price per gram of protein compared to the comparator products.
Aug-12	Lipistart	Medium chain triglycerides	The PBAC (March 2012) recommended the listing of LipiStart as a Restricted benefit for the same indications as the comparator.
Aug-12	MSUD express 20 PKU express 20	Maple syrup urine disease Phenylketonuria	PBAC recommended the listing of the two products at an equivalent price per gram of protein compared to MSUD express 15 and PKU express 20 respectively. These products are an additional strength providing 20 mg of protein.
Aug-13	Camino Pro Complete Camino Pro Bettermilk Camino Pro Restore	Phenylketonuria	The PBAC (July 2012) recommended the listing of the products at an equivalent price per gram of protein as the comparator products.
Aug-13	HCU cooler 10 HCU cooler 20 MSUD cooler 10 MSUD cooler 20 TYR cooler 10 TYR cooler 20	Homocystinuria Maple syrup urine disease Tyrosinaemia	The PBAC (March 2013) recommended the listing of the additional pack sizes of these Cooler products and observed that the price would be consistent with current PBS listed Cooler 15 products.

Listing date	Product (Brand)	Condition	PBAC recommendation
Aug-13	KetoCal 3:1	Ketogenic diet	The PBAC (March 2013) recommended listing of KetoCal 3:1 at the price proposed in the submission as a restricted benefit with the same restrictions as for the 4:1 formulation (which does not include reference to age). The submission stated that currently, for patients requiring the 3:1 ketogenic diet, a modular feed is prepared, which is difficult and time consuming. The PBAC also noted listing KetoCal 3:1 on the PBS would not increase ketogenic diet product use, and cost to the PBS. The price of KetoCal 3:1 was accepted to be the same as for KetoCal 4:1.
Nov-13	PKU Lophlex Sensation 20	Phenylketonuria	The PBAC (July 2013) recommended listing PKU Lophlex Sensation 20 as a Restricted Benefit for the management of phenylketonuria on a cost-minimisation basis compared to PKU Lophlex LQ 20 and PKU Cooler 20, at an equivalent price per gram of protein. The PBAC noted the NPWP's advice that PKU Lophlex Sensation 20 is different from the existing products PKU Lophlex LQ 20 and PKU Cooler 20 as it is semi-solid and contains sugar from natural fruit juices (from concentrate) and fat (including docosahexaenoic acid), whilst the current PKU Lophlex products are oral liquids.
Dec-13	Alfamino	Cows' milk intolerance or allergy - AA	The PBAC (July 2013) recommended listing Alfamino as an Authority required benefit for the same indications as those applying to Neocate Gold, on a cost-minimisation basis compared to Neocate Gold and at an equivalent price per gram of protein.
Dec-13	Karicare Aptamil Gold De-Lact	Lactose intolerance	The PBAC (July 2013) recommended listing Karicare Aptamil Gold De-Lact at the same price as that applying to Karicare Aptamil De-Lact and under the same listing circumstances as Karicare Aptamil De-Lact. The upgraded formula, known as Karicare Aptamil Gold De-Lact, is intended to replace the existing Karicare Aptamil De-Lact.
Dec-13	Renastart (cans)	Chronic renal failure	The PBAC recommended listing RenaStart packaged in a can as an Authority Required benefit with a maximum quantity of 4 and 5 repeats, at an equivalent price per gram of powder as RenaStart packaged in sachets, and under the same listing circumstances as RenaStart sachets. RenaStart was first PBS listed on 1 March 2009.
Mar-14	Betaquik	Ketogenic diet	The PBAC recommended the listing of BetaQuik as an Authority Required benefit for the indications requested. Currently available MCT preparations are not well tolerated, and that uptake of BetaQuik may be larger than that predicted in the submission due to improved palatability and ease of use. The NPWP considered that it was likely that the listing of BetaQuik may grow the market for MCT preparations, leading to increased overall cost to the PBS. The PBAC agreed with the NPWP that this was acceptable as increased utilisation may be a reflection of improved patient acceptance and compliance, and this may lead to improved clinical outcomes.

Listing date	Product (Brand)	Condition	PBAC recommendation
Mar-14	Basecal 100 Basecal 200	Inborn errors of protein metabolism	The PBAC (November 2013) recommended the listing of BaseCal100 and BaseCal200 on the PBS as a Restricted benefit for patients with proven inborn errors of metabolism who are unable to meet their energy requirements with permitted food and formulae. The PBAC noted that the proposed price of BaseCal 100 and BaseCal 200 was based on the same price per 100 kcal as Energivit®, and that listing was not expected to be at additional cost to the PBS.
Mar-14	Docomega Keyomega	Peroxisomal biogenesis disorders	The PBAC (November 2013) noted that the revised restriction limiting use to patients with peroxisomal biogenesis disorders reduced the number of eligible patients, and cost to the PBS compared to the previous submissions. The PBAC agreed with the NPWP that there was potential for leakage outside of the revised restriction criteria, and similarly agreed with the NPWP that an Authority Required listing would be appropriate to minimise the risk of this leakage.
Mar-14	carbzero	Ketogenic diet	The PBAC (November 2013) recommended listing for patients requiring a long chain triglycerides (LCT) supplement for dietary management with the ketogenic diet. The PBAC considered it likely that CarbZero would replace grocery items which are not PBS listed, rather than KetoCal as the submission suggested, and it was unlikely that the listing of CarbZero would be cost neutral to the PBS. This was acceptable to the NPWP as increased utilisation may be a reflection of improved patient acceptance and compliance with LCT supplementation which may lead to improved clinical outcomes.
Jun-14	Arginine 5000	Urea cycle disorders	The PBAC (November 2013) recommended the listing of Arginine 5000 as a Restricted Benefit for urea cycle disorders. The PBAC noted that whilst the strengths of arginine sachets currently available on the PBS (500 mg and 2000 mg) are suitable for most paediatric patients, the larger 5000 mg pack size would be appropriate and more convenient for patients who require higher doses of arginine based on their body weight. The cost of Arginine 5000 would be offset by the savings associated with reduced use of Arginine 2000.
Nov-14	MSUD amino5	Maple syrup urine disease	The PBAC (July 2014) recommended the listing of MSUD amino5 as a Restricted Benefit for maple syrup urine disease at the same price per gram of protein as MSUD Aid III.
Nov-14	Peptamen Junior	Medium chain triglycerides	The PBAC (July 2014) noted that the NPWP supported the listing of Peptamen Junior® with the same restriction wording as that of the comparator, Monogen. The PBAC recommend the listing of Peptamen Junior as advised. The PBAC also recommended that the restriction for Peptamen Junior should include the same administrative notes as currently apply to the listings of Monogen and Lipistart.

Listing date	Product (Brand)	Condition	PBAC recommendation
Nov-14	FruitiVits	Restrictive therapeutic diet	The PBAC (July 2014) recommended the listing. Listing for FruitiVits® was requested at the same price per gram of key nutrients as the main comparator, Paediatric Seravit®. The PBAC noted that the NPWP recommended listing of FruitiVits as an Authority Required benefit for the dietary management of conditions requiring a highly restrictive therapeutic diet. The NPWP recommended that the restriction should be consistent with the current restriction for Paediatric Seravit.
Dec-14	KetoCal 4:1 LQ	Ketogenic diet	The PBAC (March 2014) recommended the listing of KetoCal 4:1 LQ as a Restricted Benefit for patients requiring a ketogenic diet, for the treatment of intractable childhood epilepsy, glucose transporter protein deficiency and pyruvate dehydrogenase deficiency
Dec-14	Sno-Pro	Inborn errors of protein metabolism	The PBAC (July 2014) recommended listing with the same restriction wording as currently applies to the comparator ProZero. The NPWP advised that the current maximum quantity for ProZero is too high. It was reported that wastage is an issue with the current PBS availability of ProZero, with product going out of date prior to it being used. It was noted that ProZero does not appear to be being given to achieve 30% of dietary energy requirements, and that smaller amounts are being used. Given this, the NPWP considered that a lesser maximum quantity of 2 boxes (x 27 x 200 mL cartons) for Sno-Pro would be more appropriate.
Dec-14	Glycine500	Organic acidaemias	The PBAC (July 2014) recommended listing for isovaleric acidaemia. The proposed price of Glycine500® is comparable with the price of other individual amino acid supplements with carbohydrate listed on the PBS (Phenylalanine 50, Valine 50 and Isoleucine 1000). The submission requested identical listing conditions (price, quantity and number of repeats) to these currently available products.
Jul-15	PKU Glytactin RTD 10 PKU Glytactin RTD 15	Phenylketonuria	The PBAC (March 2015) recommended the listing of PKU Glytactin RTD as a Restricted Benefit for the treatment of phenylketonuria on a cost-minimisation basis with Camino Pro Bettermilk at the same price per gram of protein unit.
Aug-15	PKU Air 15 PKU Air 20	Phenylketonuria	The PBAC (March 2015) recommended the listing of PKU Air® as a Restricted Benefit for the management of phenylketonuria on a cost-minimisation basis with the existing PKU Cooler listings at the same price per gram of protein. The PBAC deferred making a recommendation regarding PKU Air at its November 2014 meeting due to incomplete information provided in the submission.

Listing date	Product (Brand)	Condition	PBAC recommendation
Aug-15	Nutrini Peptisorb	Medium chain triglycerides	<p>The PBAC (March 2015) recommended listing Nutrini Peptisorb as a Restricted Benefit for the dietary management of conditions requiring a source of medium chain triglycerides on a cost-minimisation basis against Peptamen Junior with the same price per gram of energy equivalence between Nutrini Peptisorb and Papatmen Junior. The submission also sought listing for malabsorption due to radioenteritis, chemotherapy treatment or bone marrow transplant. The PBAC considered the submission's estimates for use and financial implications to the PBS were likely to be significantly underestimated for this listing population. Additionally, the PBAC was also concerned that listing for this patient population would create a risk of inappropriate use in a patient population which did not necessarily have fat malabsorption, which in turn could contribute to an increase in obesity in children. The PBAC noted that submissions seeking the addition of a new indication/s on the PBS would usually require a major submission.</p>

LCP = Long chain polyunsaturated fatty acids, MCT = Medium chain triglycerides, NPWP = Nutritional Products Working Party, LCT = long chain triglycerides