

6.22 URSODEOXYCHOLIC ACID

Capsule 250 mg

Tablet 500 mg

Ursofalk®

Dr Falk Pharma Australia Pty Ltd

1 Purpose of Submission

- 1.1 The Category 4 submission requested to change the maximum number of repeats for the PBS listings of ursodeoxycholic acid (Ursofalk®) 250 mg capsule and 500 mg tablet forms from 2 repeats to 4 repeats.

2 Background

- 2.1 The submission requested an increase to the maximum number of repeats from 2 to 4, which it claimed would provide for at least 6-months' supply for most patients based on standard dosing and the average male and female body weights of Australian patients. The submission claimed this would reduce the administrative burden on prescribers and the frequency of obtaining a prescription for patients.
- 2.2 Ursodeoxycholic acid is available on the PBS for the treatment of primary biliary cholangitis (PBC), which was previously referred to as primary biliary cirrhosis, as Authority Required STREAMLINED listings in the following forms and strengths:
- 250 mg capsule (100 pack) with a maximum quantity of 200 capsules and maximum of 2 repeats (multiple brands including Ursofalk)
 - 500 mg tablet (100 pack) with a maximum quantity of 100 tablets and maximum of 2 repeats (one brand only, Ursofalk).
- 2.3 The submission noted PBC is an autoimmune disease of the liver marked by the gradual destruction and eventual loss of the epithelial cells lining the small intrahepatic bile ducts requiring chronic, long-term treatment.
- 2.4 The submission claimed ursodeoxycholic acid is the first-line treatment of choice for patients with PBC.

Registration status

- 2.5 Ursofalk 250 mg capsule blister pack was registered in the Australian Register of Therapeutic Goods (ARTG) by the Therapeutic Goods Administration (TGA) on 24 May 1999 for the treatment of chronic cholestatic liver diseases.
- 2.6 Ursofalk 500 mg tablet blister pack was registered in the ARTG on 6 October 2016 for the treatment of chronic cholestatic liver diseases.

Previous PBAC consideration

- 2.7 The PBAC recommended the 250 mg strength capsules for PBS listing at its June 2000 meeting (paragraph 6.1, Ursofalk, Public Summary Document (PSD), March 2017 PBAC meeting).
- 2.8 In March 2017 the PBAC recommended the Authority Required (STREAMLINED) listing of ursodeoxycholic acid 500 mg tablets for the treatment of primary biliary cirrhosis (paragraph 6.1, Ursofalk, PSD, March 2017 PBAC Meeting).

For more detail on PBAC’s view, see section 6 PBAC outcome

3 Requested listing

- 3.1 The requested listing is shown in the table below. Suggested additions are in italics and deletions are in strikethrough.

Table 1: Requested PBS listing

MEDICINAL PRODUCT medicinal product pack		PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
URSODEOXYCHOLIC ACID						
ursodeoxycholic acid capsule, 250 mg, 100		8448P	2	200	2 4	Ursofalk
ursodeoxycholic acid tablet, 500mg, 100		11180K	1	100	2 4	
Restriction Summary / Treatment of Concept:						
Concept ID		Category / Program: GENERAL – General Schedule (GE)				
		Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners				
		Restriction type: <input checked="" type="checkbox"/> Authority Required (Streamlined)				
Prescribing rule level		Administrative Advice: Continuing Therapy Only: For prescribing by nurse practitioners as continuing therapy only, where the treatment of, and prescribing of medicine for, a patient has been initiated by a medical practitioner. Further information can be found in the Explanatory Notes for Nurse Practitioners.				
		Administrative Advice: Not for use in the treatment of sclerosing cholangitis or cholelithiasis.				
		Indication: Primary biliary cholangitis (previously known as Primary biliary cirrhosis)				

For more detail on PBAC’s view, see section 6 PBAC outcome

4 Comparator

- 4.1 The submission did not nominate a comparator. This was appropriate as the request was for an increase in number of repeats of the existing listings only.

For more detail on PBAC’s view, see section 6 PBAC outcome

5 Consideration of the evidence

Sponsor hearing

- 5.1 There was no hearing for this item.

Consumer comments

- 5.2 The PBAC noted and welcomed the input from health care professionals (3) via the Consumer Comments facility on the PBS website. The comments described that increasing the number of repeats of ursodeoxycholic acid prescriptions will reduce specialist visits and increase the capacity of relevant specialists and clinics. The input also noted that the treatment does not require regular safety assessments and considered that patients will contact their health professionals if their disease progresses.

Clinical trials

- 5.3 The submission did not present any clinical trials to support the application. The submission analysed the quantities of medicine required for treatment based on the mg/kg dosing regimen approved by the TGA and the average body weight of each sex based on Australian Institute of Health and Welfare data (71.8 kg females and 87 kg males), the analysis presented in Tables 2 & 3 show the days of supply for both the existing and proposed listings for females and males respectively.
- 5.4 The existing listings for the 250 mg form provide for between 120 and 150 days' supply at the upper and lower ends of the dose range for females, while the proposed listing would provide 200 to 250 days' supply. The 500 mg form listing provides for the same amounts (Table 2). The Secretariat noted the approach of rounding calculations up, such as estimating use of 2.5 x 500 mg (1250 mg total) tablets for males where the intended dose is 1044 mg, may not reflect use in practice, where rounding down may also be considered by clinicians.
- 5.5 The existing listings for 250 mg form provide for 100 to 120 days' supply for males at the upper and lower ends of the dose range, while the proposed listing would provide 166 to 200 days' supply. The 500 mg form listing provides for the same amounts (Table 3).

Clinical claim

- 5.6 Based on recommended weight-based dosage ranges, the current listings for ursodeoxycholic acid provides PBC patients with only 3 to 5 months' treatment per prescription at maximum quantity and repeats (depending on dose and weight of the individual).
- 5.7 Increasing the number of repeats would allow female patients on the upper and lower dose range and male patients on the lower dose range to have access to over 6 months of supply per prescription. The PBAC is asked to advise if this is appropriate.

Table 1: Ursofalk PBS quantities of existing and proposed PBS listings for females based on average body weight

	Existing PBS Listings		Proposed PBS Listings	
	Upper range	Lower range	Upper range	Lower range
UDCA dose (mg/kg per day)	16	12	16	12
Dose per day (mg per day) based on 71.8 kg average body weight	1148.8	861.6	1148.8	861.6
No. of 500 mg tablets per day (rounded to nearest 0.5)	2.5	2	2.5	2
No. of 250 mg capsules per day (rounded to nearest whole number)	5	4	5	4
PBS item 11180K (UDCA 500 mg tablets)				
Max qty units per dispensing	100		100	
Max repeats	2		4	
Total qty units	300		500	
Days per dispensing	40	50	40	50
Days per prescription (incl. repeats)	120	150	200	250
PBS item 8448P (UDCA 250 mg capsules)				
Max qty units per dispensing	200		200	
Max repeats	2		4	
Total qty units	600		1000	
Days per dispensing	40	50	40	50
Days per prescription (incl. repeats)	120	150	200	250

Source: "Ursofalk dosing_Nov22.xls" spreadsheet (Attachment 2) for calculations; Table 2 and 3 of main submission
UDCA = ursodeoxycholic acid

Table 3: Ursofalk PBS quantities of existing and proposed PBS listings for males based on average boy weight

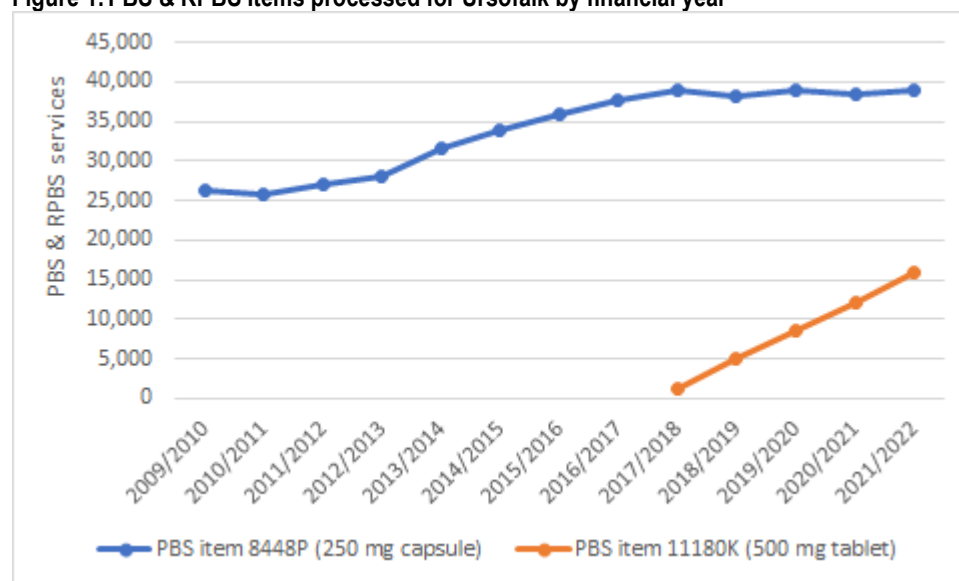
	Existing PBS Listings		Proposed PBS Listings	
	Upper range	Lower range	Upper range	Lower range
UDCA dose (mg/kg per day)	16	12	16	12
Dose per day (mg per day) based on 87 kg average body weight	1392	1044	1392	1044
No. of 500 mg tablets per day (rounded to nearest 0.5)	3	2.5	3	2.5
No. of 250 mg capsules per day (rounded to nearest whole number)	6	5	6	5
PBS item 11180K (UDCA 500 mg tablets)				
Max qty units per dispensing	100		100	
Max repeats	2		4	
Total qty units	300		500	
Days per dispensing	33.33	40	33.33	40
Days per prescription (incl. repeats)	100	120	166	200
PBS item 8448P (UDCA 250 mg capsules)				
Max qty units per dispensing	200		200	
Max repeats	2		4	
Total qty units	600		1000	
Days per dispensing	33.33	40	33.33	40
Days per prescription (incl. repeats)	100	120	166	200

Source: "Ursofalk dosing_Nov22.xls" spreadsheet (Attachment 2) for calculations

UDCA = ursodeoxycholic acid

- 5.8 The submission claimed the number of PBS/RPBS services for the 250 mg strength capsules has plateaued since availability of the 500 mg strength tablets in 2017 (Figure 1).

Figure 1: PBS & RPBS Items processed for Ursofalk by financial year



Source: submission main body

- 5.9 The submission claimed that the implementation of the proposed increase in maximum repeats for these listings could reduce the risk of an interruption in supply of the medicine to patients and reduce the number of consultation visits required to obtain prescriptions.
- 5.10 The PBAC considered that the claim of non-inferior comparative effectiveness was reasonable.

Economic analysis

- 5.11 The submission did not include an economic analysis. The submission asserted that the proposed change will not impact the cost-effectiveness.

Estimated PBS usage and financial implications

- 5.12 The submission asserted that the proposed change will not impact the population or utilisation of the medicine and therefore will not have a financial impact on the PBS. The PBAC advised this was appropriate.
- 5.13 As a Category 4 submission neither the economic analysis nor the financial estimates analysis have been independently evaluated.

For more detail on PBAC's view, see section 6 PBAC outcome

6 PBAC Outcome

- 6.1 The PBAC recommended a change to the listings of ursodeoxycholic acid (Ursofalk®) 250 mg capsule and 500 mg tablet forms on the PBS to increase the maximum number of repeats for the PBS listings from 2 repeats to 4 repeats.
- 6.2 The PBAC noted the change would provide most patients on standard dosing at least

- 6 months' supply per prescription, improving patient access and reducing administrative burden for patients and prescribers.
- 6.3 The PBAC noted that the increase of repeats for certain patients may allow a supply greater than 6 months. However, on balance, the PBAC considered that the improved access would be of greater benefit than any potential risks, which would be managed by clinicians at the time of determining patient dosage and writing of the prescription.
- 6.4 The PBAC advised that the recommended changes should be flowed on to other brands of ursodeoxycholic acid.
- 6.5 The PBAC advised that the proposed changes were not expected to change utilisation or result in a financial impact to Government.
- 6.6 The PBAC noted the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met for this recommendation.
- 6.7 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

7 Recommended listing

- 7.1 Amend number of repeats as follows:

MEDICINAL PRODUCT medicinal product pack		PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
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	Administrative Advice: Not for use in the treatment of sclerosing cholangitis or cholelithiasis.					
Indication: Primary biliary cholangitis (previously known as Primary biliary cirrhosis)						

These restrictions may be subject to further review. Should there be any changes made to the restriction the sponsor will be informed.

8 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

9 Sponsor's Comment

The sponsor welcomes the positive recommendation for this prescribing change and the benefit it provides to patients and prescribing clinicians.