CONSULTATION

PHARMAC
Pharmaceutical Management Agency

**3 May 2013**

# Proposal to widen access to ursodeoxycholic acid

PHARMAC is seeking feedback on a proposal to:

- widen access to ursodeoxycholic acid to include four additional indications in both community and DHB hospitals from 1 July 2013; and
- amend the existing criteria by separating the criteria for patients with cholestasis associated with pregnancy and cirrhosis and reducing the bilirubin level relating to decompensated cirrhosis from 170 µmol/L to 100 µmol/L.

In summary, if this proposal were to be implemented in full, the existing access criteria would be widened to also include funded access to ursodeoxycholic acid for patients with:

- Alagille syndrome;
- Progressive familial intrahepatic cholestasis (PFIC);
- Chronic severe drug induced cholestatic liver injury; and
- Total parenteral nutrition induced cholestasis (TPN-IC) in paediatric patients.

In addition, if this proposal were to be implemented in full, it would result in amendments to the existing criteria by separating the criteria for patients with cholestasis associated with pregnancy and cirrhosis and reducing the bilirubin level relating to decompensated cirrhosis from 170 µmol/L to 100 µmol/L.

**Feedback sought**

PHARMAC welcomes feedback on this proposal. To provide feedback, please submit it in writing by **Friday, 17 May 2013** to:


Natalie Davis
Therapeutic Group Manager
PHARMAC
PO Box 10 254
Wellington 6143

Email: natalie.davis@pharmac.govt.nz

Fax: 04 460 4995


All feedback received before the closing date will be considered by PHARMAC's Board (or Chief Executive acting under delegated authority) prior to making a decision on this proposal.

We will not treat any part of your feedback as confidential unless you specifically request that we do. If you would like us to withhold any commercially sensitive, confidential proprietary, or personal information included in your submission, please clearly state this in your submission and identify the relevant sections of your submission that you would like withheld.

Feedback we receive is subject to the Official Information Act 1982 (OIA) and we will consider any request to have information withheld in accordance with our obligations under the OIA.




Level 9, 40 Mercer Street, PO Box 10-254, Wellington 6143, New Zealand
Phone: 64 4 460 4990 - Fax: 64 4 460 4995 - www.pharmac.govt.nz

**Details of the proposal**

Ursodeoxycholic acid (Ursosan 250 mg capsule) is currently listed in Section B and in Part II of Section H of the Pharmaceutical Schedule at a price and subsidy of $71.50 per 100 capsules (ex-manufacturer, excl. GST). Special Authority criteria currently apply to all funded prescribing of ursodeoxycholic acid in Section B. It is proposed that these restrictions be amended and it is further proposed that the amended restrictions also apply as indication restrictions in Part II of Section H of the Pharmaceutical Schedule from 1 July 2013.

We propose that the following amendments to the criteria apply to the listings of ursodeoxycholic acid in Section B and Part II of Section H from 1 July 2013 (additions in **bold** and deletions in ~~strikethrough~~):

**Initial application – (Alagille syndrome or progressive familial intrahepatic cholestasis) - from any relevant practitioner. Approvals valid without further renewal unless notified for applications meeting the following criteria:**
**Either:**

1. **Patient has been diagnosed with Alagille syndrome**
2. **Patient has progressive familial intrahepatic cholestasis**

**Initial application – (Chronic severe drug induced cholestatic liver injury) - from any relevant practitioner. Approvals valid for 3 months for applications meeting the following criteria:**
**Both:**

1. **Patient has chronic severe drug induced cholestatic liver injury; and**
2. **Treatment with UDCA may prevent hospital admission or reduce duration of stay**

**Initial application – (Cirrhosis) - from any relevant practitioner. Approvals valid for 6 months for applications meeting the following criteria:**
**Both:**

1. **Primary biliary cirrhosis confirmed by antimitochondrial antibody titre (AMA) > 1:80, and raised cholestatic liver enzymes with or without raised serum IgM or, if AMA is negative, by liver biopsy; and**
2. **Patient not requiring a liver transplant (bilirubin > ~~170~~ 100 umol/l; decompensated cirrhosis)**

**Note: Liver biopsy is not usually required for diagnosis but is helpful to stage the disease**

Initial application – (Pregnancy~~/Cirrhosis~~) - from any relevant practitioner. Approvals valid for 6 months where the
~~Either:~~
patient diagnosed with cholestasis of pregnancy; ~~or~~
~~1. Both:~~

- ~~1.1. Primary biliary cirrhosis confirmed by antimitochondrial antibody titre (AMA) > 1:80, and raised cholestatic liver enzymes with or without raised serum IgM or, if AMA is negative, by liver biopsy; and~~
- ~~1.2. Patient not requiring a liver transplant (bilirubin > 170 **100** umol/l; decompensated cirrhosis)~~

~~Note: Liver biopsy is not usually required for diagnosis but is helpful to stage the disease.~~

Initial application – (Haematological transplant) - from any relevant practitioner. Approvals valid for 6 months for applications meeting the following criteria:

Both:

1. Patient at risk of veno-occlusive disease or has hepatic impairment and is undergoing conditioning treatment prior to allogenic stem cell or bone marrow transplantation, and
2. Treatment for up to 13 weeks.

**Initial application – (Total parenteral nutrition induced cholestasis) from any relevant practitioner. Approvals valid for 6 months for applications meeting the following criteria:**

**Both:**

1. **Paediatric patient has developed abnormal liver function as indicated on testing which is likely to be induced by TPN; and**
2. **Liver function has not improved with modifying the TPN composition.**

**Renewal (Chronic severe drug induced cholestatic liver injury) from any relevant practitioner. Approvals valid for 6 months where the patient continues to benefit from treatment.**

Renewal – (Pregnancy/cirrhosis) - from any relevant practitioner. Approvals valid for 2 years where the treatment remains appropriate and the patient is benefiting from treatment.

**Renewal - (Total parenteral nutrition induced cholestasis) from any relevant practitioner. Approvals valid for 6 months where a paediatric patient continues to require TPN and who is benefiting from treatment, defined as a sustained improvement in bilirubin levels.**

Note: Ursodeoxycholic acid is not an appropriate therapy for patients requiring a liver transplant (bilirubin > ~~170~~ **100** µmol/l; decompensated cirrhosis). These patients should be referred to an appropriate transplant centre. Treatment failure – doubling of serum bilirubin levels, absence of a significant decrease in ALP or ALT and AST, development of varices, ascites or encephalopathy, marked worsening of pruritus or fatigue, histological progression by two stages, or to cirrhosis, need for transplantation.

## Background

In April 2012, the Gastrointestinal Subcommittee reviewed a proposal from PHARMAC staff to widen access to ursodeoxycholic acid (UDCA) for drug induced liver disease (DILI), Total Parenteral Nutrition (TPN) induced cholestasis, Alagille syndrome, cystic fibrosis related cholestasis, progressive familial intrahepatic cholestasis (PFIC), non-alcoholic steatohepatitis and for chemo-prophylaxis of colon cancer in patients with inflammatory bowel disease. The minutes relating to this discussion can be found at www.pharmac.govt.nz/2012/08/31/2012-04-13%20Gastrointestinal%20Subcommittee%20minutes%20web%20version.pdf

In summary, the Subcommittee recommended that UDCA be funded for the treatment of Alagille syndrome, progressive familial intrahepatic cholestasis and chronic drug induced liver injury subject to Special Authority criteria with a medium priority and the other indications were recommended to be declined. The Subcommittee recommended that the current criteria applying to ursodeoxycholic acid for the level of bilirubin constituting decompensated cirrhosis be amended with a medium priority.

The Gastrointestinal Subcommittee reviewed further evidence for the use of UDCA for the treatment of TPN induced cholestasis at its December 2012 meeting and recommended funding with a medium priority for paediatric patients with TPN-IC however it recommended to decline funding for adults with this condition. At its December 2012 meeting, the Subcommittee deferred its recommendation for patients with cystic fibrosis related cholestasis pending the receipt of further evidence and advice.