Ursodeoxycholic acid

for treating primary biliary cirrhosis

Technology Guidance from the MOH Drug Advisory Committee

Guidance recommendations

The Ministry of Health's Drug Advisory Committee has recommended:

- ✓ Ursodeoxycholic acid 250 mg capsule, 500 mg tablet and 50 mg/ml suspension for treating primary biliary cirrhosis in patients without decompensated hepatic cirrhosis.

Subsidy status

Ursodeoxycholic acid 250 mg capsule, 500 mg tablet and 50 mg/ml suspension are recommended for inclusion on the MOH Standard Drug List (SDL).

Ursodeoxycholic acid 50 mg/ml suspension does not have regulatory approval with the Health Sciences Authority (HSA). The responsibility of prescribing an unregistered product to patients lies with the treating clinician. Before treatment is started, it is important to consider the availability of other suitable registered alternatives and inform the patient or their carer that the product is unregistered.

Updated on 1 September 2020

Factors considered to inform the recommendations for subsidy

Technology evaluation

1.1 The MOH Drug Advisory Committee ("the Committee") considered the evidence presented for the technology evaluation of ursodeoxycholic acid (UDCA) (250 mg capsule and 500 mg tablet formulations) for treating primary biliary cirrhosis in December 2018. The Agency for Care Effectiveness conducted the evaluation in consultation with clinical experts from public healthcare institutions. Published clinical and economic evidence for UDCA was considered in line with the registered indication.

1.2 The evidence was used to inform the Committee's deliberations around four core decision-making criteria:

- Clinical need of patients and nature of the condition;
- Clinical effectiveness and safety of the technology;
- Cost-effectiveness (value for money) – the incremental benefit and cost of the technology compared to existing alternatives; and
- Estimated annual technology cost and the number of patients likely to benefit from the technology.

1.3 Additional factors, including social and value judgments, may also inform the Committee's subsidy considerations.

1.4 In March 2020, the Committee considered a request from the public healthcare institutions to include UDCA 50 mg/ml suspension preparation on SDL for children.

Clinical need

2.1 In local practice, UDCA is used as first-line treatment for primary biliary cirrhosis in accordance with international clinical practice guidelines, and is the only drug registered for this use in Singapore. Treatment is typically lifelong, or until remission, or liver transplantation. The Committee acknowledged the high clinical need to subsidise UDCA to address a therapeutic gap in the MOH List of Subsidised Drugs.

Clinical effectiveness and safety

3.1 The Committee reviewed published clinical studies which showed that UDCA was clinically effective in improving liver biochemistries, delaying histological progression of primary biliary cirrhosis, reducing the need for liver transplantation, and improving survival free from liver transplantation, compared to placebo or best supportive care without UDCA. In terms of safety profile, UDCA was considered generally well-tolerated, with minimal side effects.

Cost-effectiveness

4.1 The Committee considered the cost-effectiveness of UDCA based on published overseas economic evaluations (in the absence of local studies). They noted that UDCA was dominant compared to placebo or best supportive care without UDCA, as it provided better health outcomes and gains in life expectancy with concomitant cost savings. The Committee considered the overseas results were generalisable to the Singapore context, noting the costs of UDCA used were comparable to local drug acquisition costs.

Estimated annual technology cost

5.1 Following value-based pricing discussions, the manufacturer offered a discount for UDCA 500 mg tablet—but not for the 250 mg capsule—in an effort to drive uptake of the 500 mg preparation, and reduce pill burden for patients. The Committee acknowledged approximately 90% of UDCA use is for treating primary biliary cirrhosis, and agreed a SDL listing would be appropriate considering the low risk of misuse in clinical practice. The Committee estimated around 692 people in Singapore would benefit from government subsidy for UDCA 250 mg capsule and 500 mg tablet if they were listed on SDL. The annual cost impact was estimated to be between SG$500,000 to less than SG$1 million in the first year of listing.

5.2 In March 2020, the Committee noted that the additional annual subvention amount required to list UDCA 50mg/ml suspension on SDL was small.

Additional considerations

6.1 In December 2018, the Committee acknowledged a request from the public healthcare institutions to extend subsidy to UDCA 50 mg/ml suspension preparation for children with biliary atresia and cholestasis associated with long-term parenteral nutrition. Despite the clinical need for this treatment, the Committee noted the Health Sciences Authority (HSA) had not registered this preparation for use in Singapore and cautioned against a SDL listing because its quality had not been verified.

6.2 In March 2020, the Committee considered new criteria to guide decision-making for unregistered therapeutic products. Under these criteria, subsidy may be considered if the unregistered product is:

- An additional strength or dosage formulation of an existing subsidised drug preparation that is required for populations in whom the subsidised preparation is unsuitable;
- Intended to replace an existing subsidised drug preparation which has been permanently discontinued, but was the sole source registered with HSA;
- A drug or formulation/strength that is standard of care for a specific subgroup of patients (e.g. paediatric or geriatric patients) that do not have suitable treatment alternatives; or
- A drug or supplement that is standard of care for a rare disease.

6.3 The Committee noted that the UCDA suspension was standard of care for young children and there were no suitable alternatives available. In view of the evidence available, they agreed that there was sufficient clinical need to list UCDA suspension on SDL.

Recommendation

7.1 Based on available evidence considered in December 2018, the Committee recommended UDCA 250 mg capsule and 500 mg tablet be listed on the SDL for treating primary biliary cirrhosis in line with their registered indication, in view of favourable clinical and cost-effectiveness compared to best supportive care, and the high clinical need to subsidise this treatment to ensure appropriate patient care.

7.2 In March 2020, the Committee recommended UDCA 50 mg/ml suspension be listed on the SDL, in view of the high clinical need to extend subsidy to a preparation that is suitable for children. The Committee advised that clinicians are expected to take full responsibility when prescribing this preparation, and should inform the patient or their carer that it is an unregistered product before treatment is administered.

VERSION HISTORY

Guidance on ursodeoxycholic acid for treating primary biliary cirrhosis

This Version History is provided to track any updates or changes to the guidance following the first publication date. It is not part of the guidance.

1. **Publication of guidance**
   Date of Publication 2 May 2019

2. **Guidance updated to include subsidy of new formulation of UDCA 50 mg/ml suspension**
   Date of Publication 1 Sep 2020

About the Agency

The Agency for Care Effectiveness (ACE) is the national health technology assessment agency in Singapore residing within the Ministry of Health. It conducts evaluations to inform the subsidy of treatments, and produces guidance on the appropriate use of treatments for public hospitals and institutions in Singapore. The guidance is based on the evidence available to the Committee as at 17 December 2018 and 20 March 2020. This guidance is not, and should not be regarded as, a substitute for professional or medical advice. Please seek the advice of a qualified healthcare professional about any medical condition. The responsibility for making decisions appropriate to the circumstances of the individual patient remains with the healthcare professional.

Find out more about ACE at www.ace-hta.gov.sg/about

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