

## Ursodeoxycholic acid for cystic fibrosis-related liver disease

NICE has developed the Cochrane Quality and Productivity topics to help the NHS identify practices that could be significantly reduced or stopped completely, releasing cash and/or resources without negatively affecting the quality of NHS care. Each topic has been derived from a Cochrane systematic review that has concluded that the evidence shows that the practice is harmful or ineffective and should not be used, or that there is insufficient evidence to support widespread use of the practice. Unless otherwise stated, the information is taken with permission from the Cochrane systematic review.

### **NICE summary of Cochrane review conclusions**

Evidence does not support the use of ursodeoxycholic acid (UDCA) for the prevention of cystic fibrosis (CF)-related liver disease. Many of the studies performed to date failed to include important outcomes (for example, number of liver transplants), and showed no significant improvement in the normalisation of any single hepatocellular enzyme, increase in weight or improvement in biliary excretion with the use of UDCA. Therefore at present UDCA cannot be recommended.

### **The 'Implications for practice' section of the Cochrane review stated:**

'Evidence of the effectiveness of UDCA is as yet inconclusive. Routine use of UDCA in people with CF cannot, therefore, be recommended. However, in view of these important preliminary results and because of the lack of any other effective intervention to prevent or treat CF-related liver disease, it is essential that a large multicentre RCT of UDCA in people with CF is undertaken.'

## Details of Cochrane review

### Cochrane review title

Ursodeoxycholic acid for cystic fibrosis-related liver disease

### Citation

[Cheng K, Ashby D, Smyth RL. Ursodeoxycholic acid for cystic fibrosis-related liver disease. Cochrane Database of Systematic Reviews 2014, Issue12. Art. No.: CD000222. DOI: 10.1002/14651858.CD000222.pub3.](#)

### When the review content was assessed as up to date

4 December 2014

### Quality and productivity category

Long-term conditions; medicines use and procurement; productive care

<b>Relevant codes</b>	OPCS N/A	ICD10 E84.8–E84.9, K74.4,	HRG G08, P02, D17, G18–
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## Programme budget:

Respiratory system problems; endocrine, nutritional and metabolic problems; gastrointestinal system problems

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## Evidence

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### Relevance to the NHS

Up to 20% of people with cystic fibrosis develop chronic liver disease. Cystic fibrosis-related liver disease peaks in adolescence. It results from the same chloride channel defect that causes pulmonary dysfunction, and causes thickening and plugging of the bile in the biliary system. The resultant ductular obstruction leads to secondary biliary cirrhosis in the liver. One therapeutic option currently used is ursodeoxycholic acid (UDCA), which improves bile flow by inducing a bicarbonate-rich environment. UDCA has been used in the treatment of gallstones, primary biliary cirrhosis and primary sclerosing cholangitis. Although UDCA is relatively inexpensive compared with other treatments taken by people with cystic fibrosis, it is 1 of many treatments and it is important to determine if it is effective.

Ten trials have been identified, of which three trials involving 118 participants were included; the dose of ursodeoxycholic acid ranged from 10 to 20 mg/kg/day for up to 12 months. The complex design used in 2 trials meant that data could only be analysed for subsets of participants. There was no significant difference in weight change, mean difference -0.90 kg (95% confidence interval -1.94 to 0.14) based on 30 participants from 2 trials. Improvement in biliary excretion was reported in only 1 trial and no significant change after treatment was shown. There were no data available for analysis for long-term outcomes such as death or need for liver transplantation.

The trials appeared well organised and well run, but there was not always enough information to judge them properly. On the whole, it is not thought that factors linked to how the trials were run would influence the results greatly, although there are concerns that in 1 trial the group taking UDCA were generally not as healthy at the start of the trial as the group taking placebo. In another trial there were some people who withdrew and were not included in the final analysis, but no reasons for this were given.

Important long-term outcomes such as death or the need for liver transplant, were only reported in the follow-up of 1 trial and the information did not tell us if the people who died or needed a liver transplant had received UDCA or placebo.

Current research shows that side effects of this treatment are rare, but there is not enough information about using it in the long-term to justify routinely giving it to people with cystic fibrosis. As there is no other treatment to prevent liver disease, more research on UDCA is needed.

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### Relevant NICE guidance and products

No relevant NICE guidance or evidence updates were available at the time of publication (January 2017)

### Other accredited guidance and products

[ursodeoxycholic acid \(Ursofalk®\) All Wales Medicines Strategy Group \(2016\)](#)

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## Potential productivity savings

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### Estimate of current NHS use

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# Cochrane Quality and Productivity topics

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The number of patients with CF is 10,800. Of these, about 6,500 are aged over 16 years and 4,300 under 16 years ([UK Cystic Fibrosis Registry, 2015](#)).

It is not known how many of these patients are children who are receiving UDCA to prevent the development of CF-related liver disease.

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## Level of productivity savings anticipated

Based on a child aged 10 years with an average weight of 25kg, the cost per month of UDCA 500 mg daily is £25.29 ([NHS electronic drug tariff 2016](#)). Therefore, there is a saving of £25.29 per month if UDCA is not used.

Based on an adult with an average weight of 65kg, the cost per month of UDCA 1250mg daily is £63.23 ([NHS electronic drug tariff 2016](#)). Therefore, there is a saving of £63.23 per month if UDCA is not used.

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## Type of saving

These are real cash savings

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## Any costs needed to achieve the savings

No cost to achieve the saving

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## Other information

This saving is likely to benefit NHS provider trusts and community prescribing budgets

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## Potential impact on quality of NHS care

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### Impact on clinical quality

There is no firm evidence that clinical quality would be affected by not offering UDCA for cystic fibrosis-related liver disease

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### Impact on patient safety

Patient safety should not be affected by not offering UDCA for cystic fibrosis-related liver disease. However, the review did not investigate the effect of stopping UDCA once treatment had begun.

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### Impact on patient and carer experience

Not anticipated to have any impact on the patient or carer experience

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## Likely ease of implementation

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### Time taken to implement

Can be achieved quickly (0–3 months)

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### Healthcare sectors affected

Affects 1 department or team

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### Stakeholder support

Likely to achieve good buy-in from key influencers

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# Cochrane Quality and Productivity topics

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## References

[All Wales Medicines Strategy Group \(2016\) ursodeoxycholic acid \(Ursofalk®\)](#)

[Cystic Fibrosis Trust \(2015\) UK Cystic Fibrosis Registry](#)

[NHS business services authority \(2016\) electronic drug tariff](#)