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2025002540

**National Health Care
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**Our reference
2025002540**

Date 27 May 2025
Subject GVS advice for maralixibat (Livmarli®) for treating progressive familial intrahepatic cholestasis

Dear Ms Agema,

The National Health Care Institute is hereby advising you about extending the further conditions in the Medicines Reimbursement System (hereinafter also the "GVS") for using maralixibat (Livmarli®) for treating progressive familial intrahepatic cholestasis. This advisory report was prompted by your request in the letter dated 17 March 2025 (CIBG-25-08008).

The National Health Care Institute recommends amending the additional reimbursement conditions on List 2.

Progressive familial intrahepatic cholestasis (PFIC) is a rare and severe hereditary liver disease. In PFIC, bile does not drain from the liver into the intestines properly. Because the bile is not being excreted properly, certain substances accumulate in the body. This condition can lead to severe complications, such as liver damage or liver cancer, and it can even be fatal in young children or teenagers. People with PFIC may suffer from severe itching. In some cases, the itching is so severe that a liver transplant is needed even before liver function is lost. Maralixibat inhibits the reabsorption of bile acids from the intestines back into the bloodstream, leading to more bile acids being excreted and less accumulation in the body. Patients with PFIC have several treatment options for itching, including ursodeoxycholic acid (UDCA), rifampicin, fibrates and odeixibat. The National Health Care Institute recently issued a positive opinion on odeixibat for the indication PFIC.¹

Therapeutic indication(s)

Maralixibat (Livmarli®) is indicated for the treatment of progressive familial intrahepatic cholestasis (PFIC) in patients aged 3 months and older.

Maralixibat (Livmarli®) is available as a solution containing 9.5 mg/ml maralixibat.

In addition, maralixibat (Livmarli®) is licensed and has already been included in

¹ <https://english.zorginstituutnederland.nl/documents/2023/01/18/gvs-advice-odeixibat-bylvay>

the GVS on List 1A for cholestatic pruritus in patients aged 2 months and older with Alagille syndrome (ALGS), and is subject to the following additional reimbursement conditions on List 2:

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Only for an insured person aged two months or older

1. with severe cholestatic pruritus caused by ALGS,
2. who is receiving treatment for it at a centre of expertise and
3. in whom non-invasive, symptomatic treatment has not produced a sustainable therapeutically satisfactory result.

Treatment should be discontinued if no clinically demonstrable symptomatic treatment benefit can be demonstrated after a maximum of four months of continuous treatment.

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Claim by the marketing authorisation holder

The therapeutic value of maralixibat (Livmarli®) for the treatment of PFIC in patients aged 3 months and older is comparable to odevixibat.

The marketing authorisation holder is therefore requesting that the additional reimbursement conditions of the Healthcare Insurance Regulations should be amended.

Advisory report

The National Health Care Institute recommends amending the further conditions for List 2 for maralixibat as follows:

New conditions for maralixibat:

only for insured persons

1. with severe cholestatic pruritus caused by ALGS, or
2. with genetically confirmed PFIC (except PFIC2 subtype BSEP3);
3. receiving treatment for it at a centre of expertise;
4. and who has not yet started non-invasive, symptomatic treatment, or in whom it has not produced a lasting, therapeutically satisfactory result.

Treatment should be discontinued if no clinically demonstrable symptomatic treatment benefit can be demonstrated after a maximum of four months of continuous treatment.

We have explained the preparation of this advice below.

Assessment outcome

Therapeutic value

The National Health Care Institute concluded that the therapeutic value of maralixibat is comparable to odevixibat for the above indication.

No randomised double-blind studies are available that directly compare maralixibat and odevixibat. Both maralixibat and odevixibat were investigated in randomised, double-blind, placebo-controlled phase III studies.

Based on the pruritus score, maralixibat shows a clinically relevant reduction in itching as compared to placebo. Both maralixibat and odevixibat increase the proportion of patients with a clinically relevant reduction in the pruritus score. It has not been demonstrated for either drug whether they are effective in patients

with a specific type of PFIC, namely PFIC2 subtype BSEP3.

It also remains uncertain whether either drug has a positive effect on quality of life. Regarding unfavourable effects, the two drugs are similar. Based on an indirect comparison, the National Health Care Institute concludes that there are no clinically relevant differences between the two drugs.

The National Health Care Institute therefore concludes that maralixibat, when used for treating progressive familial intrahepatic cholestasis (except for patients with PFIC2 subtype BSEP3), meets the criterion of established medical science and medical practice and has a therapeutic value that is comparable to odeixibat.

Budget impact analysis

Given the comparable therapeutic value and the fact that maralixibat is already clustered with odeixibat on List 1A, the amendment of the additional conditions is budget-neutral. In the budget impact analysis of odeixibat¹, the National Health Care Institute estimated that 16 patients are treated with odeixibat annually. There are no reasons to believe that this number will increase as a result of the introduction of maralixibat.

We trust that this letter will have provided you with the information you need. The assessment report is attached as an annex (pharmacotherapeutic report).

Yours sincerely,

M.J. Janssen
Chair of the Executive Board

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