Notification of discontinuation of a paediatric development which is covered by an agreed PIP Decision[i]

Actives substances(s): Fibroblast growth factor 21 analogue (NNC194-0499; zalfermin)/Semaglutide

Latest Decision number(s): 1) P/0022/2024

Corresponding PIP number(s): 1) EMEA-003401-PIP01-23

If the PIP has been submitted as part of a marketing authorisation application in order to comply with the requirements of Article 7 of the Paediatric Regulation (as a condition of the validation of the respective application) and a marketing authorisation was granted based on this application, then there is a legal obligation to complete that PIP. The same applies if there has been a successful post-authorisation application, where the PIP was included in order to comply with the requirements of Article 8 of the Paediatric Regulation.

Please confirm if any of the above applies:

Yes ☐ No ☒

If yes, it means that based on the Marketing Authorisation obtained at the end of that initial procedure or the successful post-authorisation application, as applicable, you are obliged to complete that PIP. That obligation cannot be cancelled by a unilateral decision, including by withdrawing the MA. Such PIP must be completed, unless it is modified in agreement with the PDCO by removing all outstanding PIP measures or granting a full product-specific waiver instead (upon relevant circumstances in accordance with the Paediatric Regulation). Non-completion of a binding PIP establishes noncompliance with the requirements of the Paediatric Regulation, which the European Medicines Agency has an obligation to report to the European Commission.

Please note that development of the medicinal product above in the following **condition(s)/indication(s)**:

Treatment of non-alcoholic steatohepatitis (NASH)

☒ has been discontinued

for the following reason(s): (tick all that apply)

☒ (possible) lack of efficacy in adults

☐ (possible) lack of efficacy in children

☐ (possible) unsatisfactory safety profile in adults

☐ (possible) unsatisfactory safety profile in children

☐ commercial reasons (please specify:)

☐ manufacturing / quality problems

☐ other regulatory action (please specify:)

☐ other reason (please specify:)

Please add a brief description (max 2000 characters) of the reason(s) for the discontinuation:

Zalfermin (NNC0194-0499) and semaglutide were evaluated in a Phase 2 study to assess the safety and efficacy of three doses of zalfermin in combination with semaglutide versus placebo in the treatment of NASH (Study ID NN9500-4656). The trial, which was completed on 14 March 2025, also included treatment arms for NNC0194-0499 alone, semaglutide alone and cagrilinitide (NNC0174-0833) in combination with semaglutide. The primary endpoint was the improvement in liver fibrosis and no worsening of NASH (Yes/No) from baseline to week 52, with improvement in fibrosis defined as greater than or equal to 1 grade improvement on the NASH CRN fibrosis scale.

No unexpected safety concerns were identified with zalfermin, zalfermin + semaglutide or cagrilintide + semaglutide. The safety and tolerability of these drugs and drug combinations were consistent with prior studies and do not preclude further clinical development.

However, the combination of zalfermin + semaglutide did not meet the primary objective on fibrosis improvement without worsening of NASH. There was no dose response effect of the combination of zalfermin (7.5, 15 or 30 mg) and semaglutide on fibrosis and steatohepatitis. The placebo-adjusted effect of zalfermin monotherapy on fibrosis and steatohepatitis was below or on par with the placebo-adjusted effect of semaglutide. There was no additive effect of zalfermin (7.5, 15 or 30 mg) on fibrosis and steatohepatitis on top of semaglutide. Subgroup analysis (F2/F3 and F4) support primary analyses with consistent results.

Given that the superiority for zalfermin 30 mg + semaglutide vs placebo on the primary endpoint was not confirmed, Novo Nordisk has decided to discontinue the zalfermin + semaglutide program in NASH.

Date: 10 December 2025

Contact for inquiries from interested parties:

Telephone: +45 4444 8888

Email: paediatrics@novonordisk.com

[i] This form will be published to the corresponding decision available on the website of the European Medicines Agency.