To:

Head of Paediatric Medicines
European Medicines Agency

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

Actives substances(s): carotuximab

Invented name: carotuximab

Latest Decision number(s): 1) P/0072/2019 2) P/0383/2017 3) P/ 4) P/

Corresponding PIP number(s): 1) EMEA-002138-PIP01-17-M01 2) EMEA-002138-PIP01-17 3) EMEA- 4) EMEA-

Date of initial marketing authorisation granted: N/A

Date of authorisation of new indication, pharmaceutical form or route of administration: N/A

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

Treatment of soft tissue sarcoma

☒ has been discontinued

☐ has been suspended/put on long-term hold (with possible re-start at a later time)

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:) (e.g. suspension, revocation of M.A.)

☐ other reason (please specify:)

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

I am writing to communicate on the discontinuation of pediatric development covered by an agreed PIP for carotuximab in the treatment of soft tissue sarcoma. TRACON Pharma International Limited intends to discontinue clinical development with carotuximab in oncology based on the interim analysis for Study 105SAR301. Upon review of unblinded safety and efficacy data from more than 120 patients

enrolled at time of the interim analysis, the independent data monitoring committee (IDMC) for Study 105SAR301 recommended termination of further enrollment into the TAPPAS Phase 3 trial based on lack of efficacy of carotuximab in angiosarcoma patients when combined with pazopanib compared to single agent pazopanib treatment. TRACON will abide by the IDMC recommendation and terminate further enrollment of Study 105SAR301 at this time. Patients believed by investigators to be deriving benefit from treatment will be allowed to continue on study. As paediatric patients were not eligible prior to interim analyses, no paediatric patiens have been treated.

Since the start of the clinical program, there have been a total of 24 clinical trials evaluating carotuximab in multiple solid tumor indications as a monotherapy and in combination with vascular endothelial growth factor (VEGF) inhibitors, chemotherapy or immune checkpoint inhibitors. Carotuximab has been evaluated in lung cancer, sarcoma, hepatocellular cancer, gestational trophoblastic neoplasia, renal cell cancer and angiosarcoma. While select patients appear to have benefitted from treatment with carotuximab, randomized clinical trials, including Phase 3 Study 105SAR301, have not demonstrated clinical activity sufficient to support continued clinical development with carotuximab in oncology. As a result, TRACON has decided to terminate further enrollment into all company sponsored trials of carotuximab.

Please note that 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 to the PIP in question:

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.

Name and signature of the PIP contact point:	Signature on file
Date:	24 April 2019
Contact for inquiries from interested parties:	Scott Brown
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