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): vedolizumab

Invented name: Entyvio

Latest Decision number(s): 1) P/0276/2019

Corresponding PIP number(s): 1) EMEA-000645-PIP03-18

Date of initial marketing authorisation granted: 22 May 2014 (ulcerative colitis and Crohn's disease)

Date of authorisation of new indication, pharmaceutical form or route of administration: NA

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

Condition: Prevention of acute graft-versus-host disease (EMEA-000645-PIP03-18) - indication not submitted or approved in adults nor in paediatrics.

☒ 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: Study in adults and adolescents terminated due to difficulties in enrolment )

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

Development of vedolizumab for use in this condition, in both adults and paediatrics, is discontinued, due to difficulties with enrolment in the pivotal Phase 3 study vedolizumab-3035, exacerbated by the COVID-19 pandemic. The Sponsor decided to terminate the study (vedolizumab-3035) early by

stopping enrolment while allowing all enrolled subjects, which included only 1 paediatric subject (1 adolescent), to complete the study as per the protocol. Investigators, Health Authorities, and Ethics Committees were informed of this decision, as appropriate. At end of study, 343 subjects had been enrolled (out of the target 558 ) with a total of 69 (of the protocol-defined total 148) primary endpoint events accrued, substantially impacting the statistical power of the primary efficacy analysis. Study results will be submitted to the Agency under Article 46 of the Paediatric Regulation and will be published in line with applicable legislation.

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.

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| Name and signature of the PIP contact point: | Signature on file |
| Date: | 20 May 2022 |

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| Contact for inquiries from interested parties: | Takeda Pharma A/S |
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