To:

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

Actives substances(s): Maribavir

Invented name:

Latest Decision number(s): 1) P/42/2009 2) P/ 3) P/ 4) P/

Corresponding PIP number(s): 1) EMEA-000353-PIP01-08

2) EMEA- 3) EMEA- 4) EMEA-

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

Cytomegaloviral disease / Prevention of cytomegaloviral disease in patient at risk

☒ 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:

At the time ViroPharma submitted the PIP , ViroPharma was conducting two randomized Phase 3 clinical trials for the prevention of CMV disease in adults: Study 1263-300 (A placebo controlled study to assess the efficacy and safety of prophylactic use of maribavir for the prevention of CMV disease in SCT recipients and Study 1263-301 (A study to assess the efficacy and safety of prophylactic use of maribavir vs oral ganciclovir for the prevention of CMV disease in liver transplant recipients)..

In Study 1263-300, maribavir 100 mg BID failed to reduce the incidence of CMV disease within 6 months post SCT when compared with placebo . Study 1263-301 failed to show non-inferiority of maribavir 100 mg BID compared to ganciclovir for the CMV disease prevention within 6 months post liver transplant.

On 10th and 13th of February 2009, ViroPharma informed the EMA of the Phase 3 prophylaxis trials results. These results were also shared with the PDCO.

Development of maribavir in prevention indication was stopped. Paediatric studies were not initiated and only limited formulation work was undertaken.

Based on the favorable safety profile and treatment effect reported from NPP and EIND with higher doses, Viropharma proposed a CMV treatment development programme in transplant patients and received feedback from the CHMP in a scientific advice meeting in 2010.

Subsequently two Phase 2 dose ranging clinical trials in adults were initiated to assess the safety and anti-CMV activity of maribavir in transplant receipients with CMV infection or disease that are resistant or refractory to treatment with ganciclovir/valganciclovir or foscarnet (Study 1263-202) and in transplant recipients with CMV infections with no CMV organ disease (Study 1263-203). Shire acquired Viropharma in January 2014.

In January 2016 Shire received Scientific Advice on the Phase 3 treatment programme . The Company is plans to initiate two Phase 3 studies based on this feedback and will submit a new PIP upon finalization of the design of the peadiatric development programme in 2016.

Shire has kept the EMA (PDCO) fully informed on the status of the adult development programme and the rationale on inability to initiate the paediatric studies previously proposed. A new PIP/deferral/waiver application will be submitted to reflect the change in indication.

Abbreviations

BID: twice daily

CVM: cytomegalovirus

EIND: Emergency Investigational New Drug

NPP: named patient program

SCT: stem cell transplants

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Date:	21 July 2016

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