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): Lixivaptan

Invented name: (Not applicable)

Latest Decision number(s): 1) P/257/2011 2) P/ 3) P/ 4) P/

Corresponding PIP number(s): 1) EMEA-001078-PIP01-10 2) EMEA- 3) EMEA- 4) EMEA-

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

Treatment of hyponatraemia

☒ 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: Rejection of NDA by FDA, see below for details) (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:

Lixivaptan has initially been developed by Cardiokine, Inc., who also agreed the above mentioned PIP with the EMA/PDCO, for the treatment of symptomatic hypervolemic and euvolemic hyponatremia associated with heart failure and syndrome of inappropriate antidiuretic hormone (SIADH). In January 2012, Cardiokine was acquired by Cornerstone Therapeutics, Inc. and became a subsidiary of Cornerstone. In October 2012, FDA rejected the NDA for lixivaptan for the treatment of hyponatremia. Additional clinical safety and efficacy data, as well as product quality data, were requested in order for FDA to consider approval of lixivaptan. Based on FDA's rejection and the short duration of remaining intellectual property protection for lixivaptan, Cornerstone decided to discontinue the development of lixivaptan for the treatment of hyponatremia.

In September 2013, Chiesi Pharmaceuticals acquired Cornerstone and its subsidiary Cardiokine. In July 2016, Palladio Biosciences acquired Cardiokine, and lixivaptan with it, from Chiesi. Palladio intends to develop lixivaptan for Polycystic Kidney Disease.

Name and signature of the PIP contact point: Signature on file

Date: Munich, 14 Feb 2018

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