Dear Healthcare Professional,

Title: Notification about:

1. **Discontinuation of Integrilin (eptifibatide) 2mg/ml 10ml and 0.75mg/ml 100ml**
2. **Increase in nausea and/or vomiting cases, reported with Integrilin (eptifibatide).**

Key Messages

The purpose of this letter is to inform Healthcare Professionals:

1. INTEGRILIN DISCONTINUATION

- That GlaxoSmithKline (GSK) has made the decision to discontinue Integrilin (eptifibatide) with immediate effect.
- Both formulations of Integrilin (eptifibatide) [2mg/ml 10ml solution for injection and 0.75mg/ml 100ml solution for infusion] are affected.
- Considering the discontinuation of Integrilin (eptifibatide); physicians should consider prescribing a generic eptifibatide, an alternative glycoprotein IIb/IIIa receptor inhibitor, or other suitable anti-thrombotic medications as clinically appropriate.
- This discontinuation decision is not due to safety concerns with the product and is not associated with the increase in nausea and/or vomiting cases with Integrilin (eptifibatide) in a few markets (see below).

2. INCREASE IN NAUSEA AND/OR VOMITING CASES REPORTED WITH INTEGRILIN

- About a recent increase in the number of nausea and/or vomiting cases with Integrilin (eptifibatide) reported in a few markets since 2022.
- Many of these increased cases of nausea and/or vomiting were reported to be observed within a few minutes to hours after administration of Integrilin (eptifibatide). Most of these were non-serious in nature.
- GSK's Safety assessment is that a causal association is not established between Integrilin (eptifibatide) and nausea & vomiting as a pharmacological side effect for the active drug substance eptifibatide.
- If nausea and/or vomiting is observed to be closely associated with Integrilin (eptifibatide) injection/infusion in a patient, then consider switching the patient's Integrilin (eptifibatide) to a generic eptifibatide, an alternate glycoprotein IIb/IIIa receptor inhibitor, or other suitable anti-thrombotic medications, as clinically appropriate.
- All adverse events associated with Integrilin (eptifibatide), including nausea and/or vomiting, should be reported directly to GSK on e-mail: Ru.safety@gsk.com and/or report to Academician of the Ministry of Internal Affairs of the Republic of Armenia E. Expert Center for Medicines and Medical Technologies named after Gabrielyan at www.pharm.am link or call the hotline. Phone numbers (+374 10) 20 05 05 and (+374 96) 22 05 05.

Actions Being Taken by GSK

1. INTEGRILIN DISCONTINUATION

- GSK has made the decision to discontinue Integrilin (eptifibatide) 2mg/ml 10ml solution for injection and Integrilin (eptifibatide) 0.75mg/ml 100ml solution for infusion with immediate effect.
- Due to a supply issue with the active pharmaceutical ingredient in Integrilin (eptifibatide), GSK will not be able to manufacture any further batches of Integrilin (eptifibatide) for at least 18 months. GSK has therefore made the decision to discontinue Integrilin (eptifibatide) with immediate effect, bringing forward a strategic product discontinuation planned for the end of 2024.
- This decision applies to the following regions/markets where GSK has a licence - the EU (centralised licence), Armenia, Russia, Switzerland, Ukraine and the United Kingdom.
- This discontinuation decision is not due to safety concerns with the product and is not associated with the increase in nausea and/or vomiting cases with Integrilin (eptifibatide) reported in a few markets.

2. INCREASE IN NAUSEA AND/OR VOMITING CASES REPORTED WITH INTEGRILIN

- GSK's Manufacturing Quality investigation has found no evidence that drug substance or drug product manufacturing processes have contributed to the reported incidents of nausea/vomiting and confirmed that batches should continue to remain within the approved stability specifications until end of shelf life.
- GSK is continuing to monitor all cases of nausea and/or vomiting and the safety profile of Integrilin (eptifibatide).

Actions Required by Healthcare Professionals

- Healthcare Professionals are advised that:
  Integrilin (eptifibatide) is a glycoprotein IIb/IIIa receptor inhibitor and is indicated for adults with manifestation of severe coronary insufficiency defined as spontaneous and recent chest pain with electrocardiographic abnormalities or biological changes. It is usually given with aspirin and unfractionated heparin.

1. INTEGRILIN DISCONTINUATION

- Due to the discontinuation of Integrilin (eptifibatide), physicians should consider prescribing a generic eptifibatide, an alternative glycoprotein IIb/IIIa receptor inhibitor, or other suitable anti-thrombotic medications, as clinically appropriate.

2. INCREASE IN NAUSEA AND/OR VOMITING CASES REPORTED WITH INTEGRILIN

- GSK recommends the following to Healthcare Professionals:
  - Be aware that an increased number of nausea and/or vomiting cases have been reported with Integrilin (eptifibatide) injection/infusion in a few markets.
  - Identify if cases of nausea and/or vomiting are associated with underlying medical conditions and/or concomitant medications, or with Integrilin (eptifibatide).
  - If nausea and/or vomiting is observed to be closely associated with Integrilin (eptifibatide) injection/infusion in a patient, then consider switching the patient's Integrilin (eptifibatide), to a generic eptifibatide, alternate glycoprotein IIb/IIIa receptor inhibitor, or other suitable anti-thrombotic medications, as clinically appropriate.

- All adverse events associated with Integrilin (eptifibatide) including nausea and/or vomiting should be reported directly to GSK on e-mail: Ru.safety@gsk.com and/or report to Academician of the Ministry of Internal Affairs of the Republic of Armenia E. Expert Center for Medicines and Medical Technologies named after Gabrielyan at www.pharm.am link or call the hotline. Phone numbers (+374 10) 20 05 05 and (+374 96) 22 05 05.

Contact(s) for Further Information or Questions

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