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Urgent Field Safety Notice:

Dimension® clinical chemistry system

Eltrombopag Interference with Dimension® Total Bilirubin (TBI) Flex® reagent cartridge

Dear Sirs,

Our records indicate that your facility may have received the following product:

Table 1: Dimension® Chemistry Products affected:

Assay	Test Code	Catalog Number	Siemens Material Number (SMN)	Lot Number
Total Bilirubin	TBI	DF167	10444957	ALL

Reason for Correction

The purpose of this communication is to inform you of an interference identified with the products indicated in Table 1 above and provide instructions on actions that your laboratory must take.

Siemens Healthcare Diagnostics has become aware that the United Kingdom Medicines and Healthcare products Regulatory Agency published an alert to healthcare professionals informing them that laboratory tests for bilirubin should be monitored for patients who take the drug eltrombopag due to the potential for discordant results. Eltrombopag may be used in the treatment of thrombocytopenia and/or aplastic anemia. Siemens spiking studies have shown a positive bias in Total Bilirubin (TBI) results at a therapeutic concentration of eltrombopag. Interference has not been observed with the Direct Bilirubin (DBI) assay.

Table 2 below reflects eltrombopag Interference with Dimension® Total Bilirubin (TBI) assay based on Siemens internal testing.

Table 2. Eltrombopag Interference with Dimension Total Bilirubin Assay

Analyte	Analyte Concentration mg/dL [µmol/L]	Eltrombopag Concentration µg/mL [µmol/L]	Bias (%)
TBI	0.8 [13.7]	25 [56.5]	89.3
TBI	22 [376]	25 [56.5]	3.5

The “Limitations of the Procedure” section in the Instructions For Use (IFU) for the Dimension TBI assay will be updated to indicate: *Use of this assay is not recommended for patients undergoing treatment with eltrombopag due to the potential for falsely elevated results.*

Information related to eltrombopag provided in this letter supersedes the information in the current Dimension TBI IFU until the IFU is updated. Siemens will communicate once the IFU has been updated.

Risk to Health

For patients taking eltrombopag, the potential exists for the misinterpretation of total bilirubin levels, which may confound investigations for the etiology of hyperbilirubinemia. Potential clinical impact would be mitigated by correlation to clinical symptomology and additional laboratory testing including other markers of liver function (e.g. alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, and/or lactate dehydrogenase).
– Siemens is not recommending a review of previously generated results.

Actions to be Taken by the Customer:

- For patients on eltrombopag therapy, use of Dimension TBI is not recommended.
- Please review this letter with your Medical Director.
- Complete and return the Field Correction Effectiveness Check Form attached to this letter within 30 days.
- If you have received any complaints of illness or adverse events associated with the products listed in Table 1, immediately contact your local Siemens Customer Care Center or your local Siemens technical support representative.

Please retain this letter with your laboratory records and forward this letter to those who may have received this product.

We apologize for the inconvenience this situation may cause. If you have any questions, please contact your Siemens Customer Care Center or your local Siemens Technical Support representative.

Sincerely yours,

Siemens Healthcare Diagnostics GmbH

i.V. Dipl. Ing. Franz Schwarz
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Urgent Field Safety Notice:

ADVIA® Chemistry systems

Eltrombopag Interference with ADVIA® Chemistry Direct Bilirubin (DBIL_2) and Total Bilirubin (TBIL_2) Assays

Dear Sirs,

Our records indicate that your facility may have received the following products:

Table 1. ADVIA Chemistry Systems Affected Product(s)

Assay	Test Code	Siemens Material Number (SMN)	Lot Number
Direct Bilirubin	DBIL_2	10316610 (20 mL) 10341114 (70 mL)	ALL
Total Bilirubin	TBIL_2	10341115 (40 mL) 10341113 (70 mL)	ALL

Reason for Correction

The purpose of this communication is to inform you of an interference identified with the products indicated in Table 1 above and provide instructions on actions that your laboratory must take.

Siemens Healthcare Diagnostics has become aware that the United Kingdom Medicines and Healthcare Products Regulatory Agency published an alert to healthcare professionals informing them that laboratory tests for bilirubin should be monitored for patients who take the drug eltrombopag due to the potential for discordant results. Eltrombopag may be used in the treatment of thrombocytopenia and/or aplastic anemia. Siemens spiking studies have shown a positive bias for Direct Bilirubin (DBIL_2) results of 11.1% at therapeutic eltrombopag concentrations of 25 µg/mL. Bias of <10% was observed for Total Bilirubin (TBIL_2) at therapeutic eltrombopag concentrations of 25 µg/mL.

Table 2 below reflects eltrombopag interference with ADVIA® Direct Bilirubin (DBIL_2) and Total Bilirubin (TBIL_2) assays based on Siemens preliminary internal testing. The Instructions For Use for the ADVIA Chemistry DBIL_2 and TBIL_2 assays will be updated as appropriate, when the investigation is completed. Siemens will communicate once the IFUs have been updated.

Table 2. Eltrombopag Preliminary Interference Data for ADVIA Chemistry Direct Bilirubin and Total Bilirubin assays

Analyte	Analyte Concentration mg/dL [µmol/L]	Eltrombopag Concentration µg/mL [µmol/L]	Bias (%)
Direct Bilirubin	0.9 [15.4]	25 [56.5]	11.1
Direct Bilirubin	5.0 [85.5]	25 [56.5]	*less than or equal to 10%
Total Bilirubin	1.1 [18.8]	25 [56.5]	9.1
Total Bilirubin	23.9 [409]	25 [56.5]	*less than or equal to 10%

*Note: At supraphysiological concentrations of 75 µg/mL [170 µmol/L] of eltrombopag, the observed bias was less than 10%, therefore therapeutic concentrations at 25 µg/mL [56.5 µmol/L] of eltrombopag were not tested.

Risk to Health

The risk to health for the issue described above is negligible. The observed biases for total bilirubin and direct bilirubin at therapeutic concentrations of eltrombopag would not lead to a clinically significant change in patient management. Direct and total bilirubin results are not used in isolation but are correlated with clinical history and presentation as well as with other markers of liver function (e.g. alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, and/or lactate dehydrogenase). Siemens is not recommending a review of previously generated results.

Actions to be Taken by the Customer:

- Review the information in Table 2.
- Please review this letter with your Medical Director.
- Complete and return the Field Correction Effectiveness Check Form attached to this letter within 30 days.
- If you have received any complaints of illness or adverse events associated with the products listed in Table 1, immediately contact your local Siemens Customer Care Center or your local Siemens technical support representative.

Please retain this letter with your laboratory records and forward this letter to those who may have received this product.

We apologize for the inconvenience this situation may cause. If you have any questions, please contact your Siemens Customer Care Center or your local Siemens Technical Support representative.

Sincerely yours,

Siemens Healthcare Diagnostics GmbH

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