English

INTENDED USE AND PRINCIPLE OF THE TEST

DOAC-Stop can be used to efficiently extract all types of Direct Oral Anti-Coagulants (DOACs) including dabigatran, edoxaban, betrixaban, rivaroxaban, apixaban and also argatroban from test plasmas with minimal effect on plasma proteins involved in the clotting mechanism. This product is intended for use as an accessory IVD, to be used by professionals trained in laboratory techniques and/or routine coagulation testing.

Therapeutic uses of DOACs are on the increase but the presence of DOACs in samples are known to interfere with almost all clotting tests to varying degrees. Specific antidotes for individual DOACs are being developed but are not yet widely available for laboratory use. DOAC-Stop is the first general agent available for solving the diagnostic problems associated with DOACs. After treatment with DOAC-Stop, plasma samples can be analysed for underlying coagulation defects such as factor deficiencies, heparin, lupus anticoagulant or other interfering antibodies [1].

CONTENTS OF PRODUCT	Product Code	Pack Size
	HX9904-100	100 tablets
	HX9904-50	50 tablets

MATERIALS REQUIRED BUT NOT PROVIDED

Microfuge tubes, pipette and tips.

LIMITATIONS

DOAC-Stop may extract low molecular weight compounds resembling DOACs from plasmas. Those affecting coagulation (but administered intravenously, not orally) include argatroban, aprotinin, protamine, hirudin analogues, polymyxin and related cationic compounds [2]. DOAC-Stop does not absorb haemoglobin in haemolysed plasma samples.

PRECAUTIONS

DOAC Stop is intended for use with plasma samples suspected to contain DOACs. If test results are unchanged by DOAC Stop and DOACs are still suspected to be present, apply appropriate chromogenic anti factor Xa or anti thrombin assays to obtain specific DOAC results. Contact your distributor or manufacturer for technical support.

Store at room temperature. Keep Dry. Do not use after the expiry date indicated on the label. Treat all clinical material as potentially infectious and dispose in accordance with local operating regulations. For further information, please refer to Safety Data Sheet and Product Information.

INSTRUCTIONS FOR USE

Sample preparation: DOAC-Stop has been developed for use with citrated plasmas. Follow your validated laboratory procedures for preparing test plasma. Apply the citrated plasma in the procedure below to remove any DOAC if present. Please refer to www.haematex.com/eifu for Instructions for Use (IFU) in other EU Member States languages.

Method for DOAC removal from a test plasma:

1.	Add 1.0mL of citrated test plasma to be treated to a plastic centrifuge tube. *Ideally 1.0mL plasma but a range from 0.5 ml to 1.5 ml is acceptable.*
2.	Add 1 DOAC-Stop mini-tab and mix gently until it has dispersed. Mix for a further 5-10 minutes.
3.	Centrifuge down the particulate matter (for example, 5 minutes at 2000g or 1 minute at 7000g in a microfuge). Do not stop centrifuging too quickly.
4.	The supernatant plasma, now depleted of DOACs can be used directly for testing or can be transferred into a separate plastic tube for frozen storage.

READING AND INTERPRETATION

Normal plasma sample average APTT result is approximately 30-40 seconds. APTT test results after treatment shall be 20% less than the result of the reference test.

PERFORMANCE CHARACTERISTICS

DOAC-Stop is classified as a Class A IVD and such, does not possess critical characteristics, does not measure nor detect, and specifically intended for use in vitro diagnostic examination as an accessory. The table below summarizes the scientific data for DOAC-stop, for additional information, contact your distributor for a copy of the Technical Documentation.

Study Data	Summary	References
Removes 95% of DOACs	DOAC-Stop is effective in removing more than 95% of DOACs within minutes, in normal plasma spiked with 500ng/mL of dabigatran, edoxaban, betrixaban, rivaroxaban or apixaban. No effect on the baseline APTTs after 3 hours further incubation.	[1]
Removes 100% of DOACs	In thrombophilia screening tests involving 135 plasma samples, DOAC-Stop effectively removed dabigatran in 40 samples, apixaban in 38, rivaroxaban in 42 and edoxaban in 15 samples. The incidence of false positive lupus anticoagulants fell from approximately 30% to zero.	[3]
Removes >92% of DOACs	DOAC-Stop removed dabigatran by 100%, rivaroxaban by 98% and apixaban by 92.3% ($p<0.05$). After DOAC-Stop screening dRVVT remained prolonged in 34 patients ($p<0.001$) while dRVVT LA1/LA2 was abnormal in 6 patients, with no association with DOAC concentrations at baseline before and after DOAC-Stop. The APTT-LA screening test remained prolonged in five patients, while the APTT LA1/LA2 ratio was normal in those subjects. DOAC-Stop did not influence LA testing in APS patients [10].	[10]
Removes 100% of DOACs in highly viscous plasma samples	In normal plasma samples, the fibrinogen ranges from 150-400mg/100mL. Viscosity may be increased in some plasma samples with elevated fibrinogen or paraprotein levels. In-house studies investigated whether high levels of fibrinogen or paraproteins interfere with the efficient removal of DOACs. Results of bovine fibrinogen spiked samples up to 800mg/100mL did not interfere with the efficient removal of DOACs using DOAC-Stop.	

Interfering substances

No interfering substances observed in viscous, high fibrinogen and hyperlipidemic and plasma samples. Haemoglobin contained in haemolysed plasma samples interfere in photo-optical detection therefore are excluded in routine testing.

INDEMNITY NOTICE

DOAC-Stop is intended to be used with plasma samples containing DOACs. Follow procedures and refer to precautions that may affect the stated or implied claims and performance of this product. Cellabs, Haematex and its agents or distributors are not liable for damages.

VIGILANCE REPORTING

Vigilance Reporting for EU Member states must be reported without delay, as soon as practicable to the EU Representative, WMDE B. V, Bergerweg 18, 6085 AT Horn, The Netherlands, who will act on behalf of Cellabs Pty Ltd, the Competent Authority (CA) of your country and/or Cellabs Pty Ltd, 7/27 Dale Street, Brookvale, NSW, 2100, Australia or through the website: www.cellabs.com.au.

REFERENCES

[1] Exner T, et al. “Simple method for removing DOACs from plasma samples” Throm Res. 2018; 16: 1028-39.
[2] Exner T, et al. “Effect of an activated charcoal product (DOAC Stop™) intended for extracting DOACs on various other APTT-prolonging agents”. Clin Chem Lab Med. 2019; 57: 690-696.
[3] Favresse J, et al. “Evaluation of the DOAC Stop procedure to overcome the effect of DOACs on several thrombophilia screening tests”. TH Open, 2018; 2: e202-e209.
[4] Platton S, Hunt C. “Influence of DOAC Stop on coagulation assays in samples from patients on rivaroxaban or apixaban”. Int J Lab Haematol. 2019; 41: 227-233.
[5] Jacquemin M, et al. “The adsorption of dabigatran is as efficient as addition of Idarucizumab to neutralize the drug in routine coagulation assays. Int J Lab Hematol. 2018; 40: 442-447”.
[6] Favaloro EJ, et al. “Neutralising rivaroxaban-induced interference in laboratory testing for lupus anticoagulants (LA): A comparative study using DOAC Stop and Andaxanet alpha”. Throm Res. 2019; 180:10-19.
[7] Kopatz WF, et al. “Use of DOAC Stop for the elimination of anticoagulants in the thrombin generation assay”. Throm Res. 2018; 170: 97-101.
[8] Exner T, et al “Clotting tests correlate better with DOAC concentrations when expressed as a “Correction Ratio”; results before/after extraction with the DOAC Stop reagent. Throm Res.2019; 179: 69-72.
[9] Exner T, et al “The effect of DOACs on laboratory tests and their removal to limit interference in functional assays. Int J Lab Hematol. 2020; 42 (Suppl.1): 41-48.
[10] Zabcyk M, Kopytek M, Natoska J, Undas A. The effect of DOAC Stop on lupus anticoagulant testing in plasma samples of venous thromboembolism patients receiving oral anticoagulants. Clin Chem Lab Med. 2019; 57: 1374-1381

EXPLANATION OF SYMBOLS

	Consult instructions for use	REF	Catalogue number
IVD	*In Vitro* Diagnostic Medical Device	Σ n	Contains sufficient for number (n) of tests
	Temperature limitation		Date of Manufacturing
	Keep Dry	LOT	Batch code
	Expiry Date	en	Information for use (IFU) version in English
EC REP	EC Representative		Manufacturer
		CE	CE Mark

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