INSTRUCTIONS FOR USE

INTENDED USE

The microINR system measures prothrombin time (PT) expressed in International Normalized Ratio (INR), for monitoring oral anticoagulant therapy with warfarin. The microINR system consists of a meter and chips (test strips) and uses fresh capillary whole blood from a fingerstick.

The microINR system is intended for patient self-testing use as well as for healthcare professionals at Point of Care settings.

The microINR system is intended for use in patients 18 years old or older. Patients must be stable on warfarin medication for at least 6 weeks before starting to use the microINR system.

For self-testing use: The system is intended for properly trained users under specific prescription of a physician.

Caution: The microINR system is not intended for use in patients who are transitioning from heparin treatment to VKA therapy. The microINR system is not intended to be used for screening purposes.

BEFORE USING THE microINR® SYSTEM

Components of the microINR system

microINR Chips (REF)	Σ n	Compatible meters
CHC0025AD	25	microINR (REF: MEC0001AD) microINR Link (REF: MED0001AD)

These instructions for use will guide you on the handling and use of the microINR Chips. Please, read them as well as the instructions for use of the meter completely. Additionally, do not forget to read the instructions for use of the disposable lancets and/or lancing device used to obtain the capillary blood sample.

Keep these instructions for use inside the package of microINR Chips and refer to them if you have any questions about proper operation of the system.

For self-testing use: Users must receive a proper training before starting to use the microINR system.

STORAGE AND STABILITY OF THE microINR® CHIP

Store the chips in a cool and dry place between 36°F to 77°F (2°C to 25°C).

You can store the chips at room temperature. However, keep the chips in the refrigerator if the storage room temperature is above 77ºF or under 36ºF.

Protect them from sunlight and heat.

The chips can be used until the expiration date printed on the pouch and package of the chips. The meter will not accept expired chips.

Do not use the chip if you detect that the chip is defective or its pouch is opened or damaged.

The chips can be used within 15 minutes once the pouch is opened.

Do not manipulate the meter or the chip with wet or dirty hands/gloves.

PREPARING THE NECESSARY MATERIAL

- microINR Chips.
- Meter (not supplied).
- Disposable lancets and/or lancing device (not supplied).
- Means for skin cleaning (not supplied).

COLLECTION AND TESTING BLOOD SAMPLE

1. Clean and warm-up your hand.

2. Take a pouch containing a chip from the package, verify the expiration date and storage conditions, and open it.

3. Hold the chip by the yellow part so that the "microINR" logo can be read correctly. Insert the chip into the meter slot and push it until it stops. Make sure the chip has reached the end and the "microINR" logo can be correctly read.

4. The meter must be placed on a flat and steady surface.

5. Once the chip is inserted, the meter automatically turns on and performs a quality control to check the system's integrity before the sample application.

6. While waiting for the device to be ready, make sure your hand is warm and the fingertip clean.

7. The chip begins to flash and warms up until it reaches the appropriate temperature. Once that temperature is reached:

- the device emits an audible signal (beep tone).
- the drop symbol begins to flash on the display.
- a countdown appears (80 s).
- the chip emits a steady light.

8. Perform the fingerstick once the countdown begins. Place the lancet firmly against the fingertip and activate it. Massage the finger to bring blood to the finger tip and gently press to help form a drop of blood.

9. Make sure to obtain a spherical and properly sized drop, equivalent to a teardrop. Do not press the fingerstick site or let the drop of blood spread on the finger.

10. Apply the drop of blood to the chip immediately by putting it in contact with the chip's entry channel, without resting the finger on the chip.

The meter will emit a beep tone when it detects that the sample volume is enough, the drop symbol will stop flashing and the countdown disappears.

11. After the beep tone, gently remove the finger, trying to leave a small amount of blood at the chip's entry channel. Do not touch the chip or add more blood during the test. Do not shake the meter and prevent accidental falls.

12. The INR result appears in a short time.

13. Dispose the used lancet and chip appropriately.

14. The meter automatically turns off after around 3 minutes of inactivity or by pressing the left button (EXIT) for 3-4 seconds.

15. If you need to repeat the test, perform the fingerstick in a different finger using a new lancet and a new chip.

NOTES FOR A PROPER SAMPLE APPLICATION

- Before lancing the finger, it is convenient to warm hands. There are several techniques that can be used for that purpose such as washing hands with warm water, keeping hands below the waist and massaging the fingertip softly.
- The fingerstick area must be clean, free of contaminants and completely dry.
- Any alcohol (disinfectants, shaving creams, etc.), lotions or sweat on the fingerstick area or the blood sample may cause incorrect results.
- Washing the hands with warm soapy water is recommended. You may also use alcohol to clean the fingerstick area.
- Always dry the area thoroughly to remove any traces of substances that might interfere with the result. Always use a new, clean and dry gauze.
- Do not manipulate the meter or the chip with wet or dirty hands/gloves.
- Any finger can be used for fingersticking.
- Never lance the finger before the countdown has started.
- Sampling technique can affect the result of the test. Do not squeeze or "milk" the fingerstick area as this can alter the coagulation process. Do not let the drop of blood spread on the finger.
- Before placing the sample on the chip, make sure to obtain a spherical and properly sized drop (equivalent to a teardrop), large enough to leave a small amount of blood (remnant) at the entry channel.
- Samples must be applied immediately after collection, since blood clotting does naturally occur upon fingerstick.
- Do not rest the finger on the chip during the application.
- Apply the sample at once. Never re-apply more sample to the chip.
- If you get an error message, follow the steps described on the "Error Guide" section of the meter's instructions for use.
- If you need to repeat the test, perform the fingerstick on a different finger with a new lancet and a new chip.

WORKING PRINCIPLE

The technology used by the microINR system is based on the microfluidics of the microINR Chip:

The chips contain human recombinant thromboplastin as reagent.

The blood sample is applied to the chip through the entry channel and mixed with the reagents contained in the micro-reactors. The coagulation cascade is triggered instantly. When the blood coagulates, a change in blood flow behavior occurs.

The meter captures the position of the sample by means of a Machine Vision System (MVS) and determines the INR result.

CALIBRATION

Each lot of microINR Chips is calibrated against a reference lot of human recombinant thromboplastin traced to the International Reference Thromboplastin Preparation of the World Health Organization.

The calibration parameters needed for the INR equation are encoded in each microINR Chip along with information related to the expiration date. Therefore, every test is automatically and individually calibrated reducing any risk of error.

INTERPRETING THE RESULTS

The results are shown as International Normalized Ratio (INR) units. The microINR system's results range is between 0.8 and 4.5. If you obtain a result out of the measuring range, the display shows ↓ 0.8 (below 0.8) or ↑ 4.5 (above 4.5).

If an error message is displayed, see the "Error Guide" section of the meter instructions for use and follow the indications described.

Some liver diseases, thyroid dysfunction and other diseases or conditions as well as nutritional supplements or changes in dietary habits, can affect the activity of warfarin and the INR results.

For healthcare professionals: If an unexpected result is obtained, repeat the test making sure that the directions described in these instructions for use are strictly followed. If an unexpected result is obtained again, the result must be checked using another method.

Results are unexpected when they do not match the patient's symptoms (i.e., hemorrhages, bruises, etc.).

For self-testing patients: If an INR result is obtained outside the specific therapeutic range defined by your physician, contact your healthcare provider and follow their instructions.

LIMITATIONS OF PROCEDURE IMPORTANT INFORMATION

- The microINR system is intended to be used in Point Of Care settings such as physicians' offices and anticoagulation clinics, as well as home settings. It is not intended to be used in nursing homes, emergency rooms and intensive care units.
- The microINR Chips are intended to be used exclusively with the meters manufactured by iLine Microsystems.
- Patients under treatment with Direct Oral Anticoagulants (DOACs), such as Apixaban, Rivaroxaban or Dabigatran, must not be tested with this system.
- Patients under treatment with Heparin or Fondaparinux must not be tested with this system.
- The performance of the microINR system has not been demonstrated in blood samples with hematocrit values outside the range of 25% to 55%. Hematocrits out of this range may affect test results. The device must not be used in patients with a hematocrit value below 25% or above 55%.
- The presence of anti-phospholipid antibodies (APAs) could be related to falsely elevated INR values. The use of an APA-insensitive laboratory method is recommended if the presence of APAs is known or suspected.
- Patients with total artificial heart (TAH) and left ventricular assist device (LVAD) have not been enrolled in the clinical evaluations performed for the product clearance. Therefore, the device must not be used in these patients.
- The system can only be used with fresh capillary whole blood samples from a fingerstick.
- The minimum sample volume required is 3 µL. Low sample volume applications will cause an error message.
- microINR Chips are for single use only.
- Make sure to store the microINR Chips correctly to avoid inaccurate results.
- Do not use the chip if you detect that the chip is defective or its pouch is opened or damaged. Dispose of the chip and use a new one.
- These chips are for use outside the body only.
- **For self-testing patients:** if you have any question related to these limitations, please contact your healthcare provider.

INTERFERENCES

The following substances have shown no significant effects on the microINR results:

SUBSTANCE	CONCENTRATION
Acetaminophen	Up to 20 mg/dL
Acetazolamide	Up to 60 mg/L
Acetylsalicylic Acid	Up to 83 mg/dL
Atenolol	Up to 10 mg/L
Bilirubin	Up to 40 mg/dL
Citalopram	Up to 0.8 mg/L
Clopidogrel	Up to 24 mg/dL
Daptomycin	Up to 100 µg/mL
Diclofenac	Up to 54 mg/L
Diltiazem	Up to 5.44 mg/L
Hemoglobin	Up to 1000 mg/dL
Losartan	Up to 50 mg/L
Medroxyprogesterone	Up to 0.81 mg/L
Oritavancin	Up to 7 mg/L
Prasugrel	Up to 16 mg/dL
Pravastatin	Up to 0.6 mg/L
Prednisolone	Up to 3 mg/L
Salicylic Acid	Up to 60 mg/dL
Ticagrelor	Up to 1500 ng/mL
Triglycerides	Up to 3270 mg/dL
Venlafaxine	Up to 0.5 mg/L

For self-testing patients: if you have any question related with these interferences, please contact your physician.

QUALITY CONTROLS

The microINR system performs On-Board Quality controls on every test. These quality controls are performed automatically, so there is no need to run extra quality controls. To know more about the microINR Quality Controls see the instructions for use of the meters.

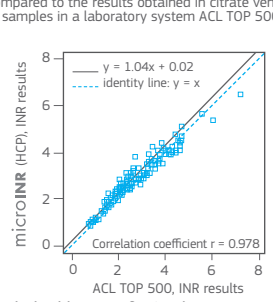
PERFORMANCE CHARACTERISTICS

Sensitivity

The sensitivity of the microINR system to coagulation factors (II, V, VII and X) has been determined by *in vitro* tests. Commercial single factor deficient plasma was mixed with normal pooled plasma and red blood cells at various dilutions. These samples were then tested using nine microINR meters and three microINR Chip lots for each factor sensitivity study. The sensitivity of the microINR system to factors II, V, VII and X was estimated as 28%, 41%, 37% and 45%, respectively.

Accuracy by healthcare professionals

microINR system results with capillary blood from 260 control subjects and patients recruited at three clinical sites were compared to the results obtained in citrate venous plasma samples in a laboratory system ACL TOP 500.



Precision by healthcare professionals

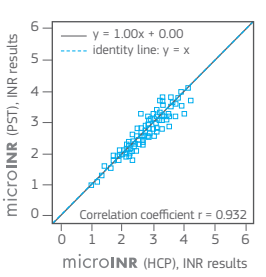
Precision was determined based on duplicate measurements performed on 269 control subjects and patients at three clinical sites.

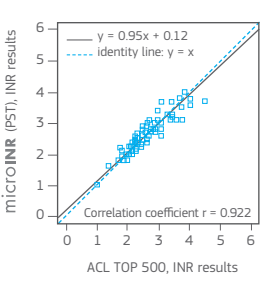
Analysis per INR range	INR < 2.0	2.0 ≤ INR < 3.5	3.5 ≤ INR < 4.5	INR ≥ 4.5
N	91	129	32	17
Mean INR	1.23	2.55	3.79	4.75
SD INR	0.06	0.12	0.21	0.26
CV (%)	5.2	4.6	5.6	5.5

SD: standard deviation. CV: coefficient of variation.

Accuracy by self-testing patients

A Method Comparison Study was conducted at four clinical sites comparing 225 INR test results obtained by self-testing patients (PST) to those obtained by healthcare professionals (HCP) using the microINR system in two visits to the sites. All measurements were done with capillary blood. In addition, the 112 INR test results obtained by the PST at the second visit were compared to the results obtained in citrate venous plasma samples in a laboratory system ACL TOP 500 as reference method. The results indicate that self-testing patients are able to obtain results as accurate as healthcare professionals using the microINR system.





Precision by self-testing patients

The microINR system precision was determined based on duplicate measurements performed at four clinical sites by self-testing patients in the second visit to the site.

	Paired results
N	110
Mean INR	2.61
SD INR	0.13
CV (%)	5.0

SD: standard deviation. CV: coefficient of variation.

Usability

117 self-testing patients participated in the study and filled in a questionnaire about the user-friendliness of the microINR system after two weeks of self-testing. The results summarized in the following table show that the microINR system is easy to use and the labeling of the product is user-friendly. Questions were rated on a scale of 1 (strongly disagree) to 5 (strongly agree) obtaining an overall score of 4.7.

Question	Mean score
The symbols and numbers that appear on the meter screen are easy to read and understand.	4.74
I liked the size of the meter and the meter buttons.	4.71
It is easy to understand when to apply the drop of blood.	4.70
The chip is easy to manipulate.	4.41
The amount of blood sample needed is easy to obtain from a fingerstick.	4.62
I understand how I should store the chips.	4.81
The result is easy to read.	4.92
The meaning of the result is easy to interpret.	4.80
The time it takes for the meter to give a result is not too long.	4.38
The procedure to perform the test is easy to learn.	4.72
Using the meter is easy to learn.	4.74
Turning on the meter is easy.	4.87
Opening the chip package is easy.	4.19
Inserting the chip into the meter is easy.	4.50
I was able to apply blood to the test strip within 80 seconds of lancing the finger.	4.79
It is easy to remove the used chip.	4.80
It is easy to see the results in the memory.	4.85
It is easy to identify the meaning of the error messages in the instructions for use.	4.68
The "EasyGuide" is clear and useful for understanding the operation of the microINR system.	4.73
The instructions for use are clear and useful for understanding the operation of the microINR system.	4.77
Overall score.	4.69

ADDITIONAL INFORMATION

For healthcare professionals: If you need technical help, please contact your local distributor.

For self-testing patients: if you have any question, please contact your healthcare provider.

The instructions for use of the meters contain more information.

Caution: Federal law restricts the device to sale by or on the order of a physician.

This insert is for self-testing patients and for healthcare professionals at Point Of Care settings. This is a CLIA Waived test system. Facilities performing testing must have a CLIA Certificate of Waiver (or higher). Laboratories with a certificate of waiver must follow the manufacturer's instructions for performing a test. All applicable state and local laws must be met.

Any adverse reactions experienced with the use of this product, and/or quality problems should be reported to your healthcare provider (for self-testing patients) or local distributor (for professional users and healthcare providers), to the manufacturer of this device and also to FDA's Med Watch Adverse Event Reporting program online [at www.fda.gov/MEDWatch/report.htm], by phone (1-800-FDA (332)-1088), or by returning the postage-paid FDA form 3500 (which may be downloaded from www.fda.gov/safety/medwatch-fda-safety-information-and-adverse-event-reporting-program/reporting-serious-problems-fda) by mail to (MedWatch, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20852) or fax (1-800-FDA (332)-0178).

LIMITED WARRANTY

iLine Microsystems warrants that this product will meet the specifications stated in the labelling when used in accordance with such labelling and will be free from defects in material and workmanship until the expiration date.

SYMBOLS

	"Manufacturer"
	"Batch code/Lot number"
	"Consult instructions for use"
	"Do not use if package is damaged and consult instructions for use"
	"*In-vitro* diagnostic medical device"
	"Keep away from sunlight"
	"Temperature Limit"
	"Do not re-use"
	"Use-by date"
	"Catalogue number"
	"Contains sufficient for <n> tests"
	"Prescription Use Only"

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