



Monitoring Warfarin Therapy in Lupus Anticoagulant-Positive Patients With the Chromogenic Factor X Assay F10/5767

Lupus Anticoagulants

The lupus anticoagulant (LA) is one part of the antiphospholipid antibody syndrome and may be present in patients with systemic lupus erythematosus, malignancy, HIV infection, other diseases, and even in healthy persons with no manifestation of disease. The presence of a LA may predispose patients to thrombosis (venous or arterial) and subsequently, chronic treatment with warfarin is often indicated. In LA patients, the INR may be falsely elevated by the presence of the LA (varies in different laboratories) and may result in under-treatment with warfarin. To optimally monitor warfarin therapy in such patients, an assay other than the INR is needed.

Chromogenic Factor X (F10)

The vitamin K-dependent clotting factors II, VII, IX, and X suppressed by warfarin are traditionally measured with a clotting test method, e.g., the INR, that may be susceptible to artifact from a LA. To avoid this complication, an alternate method to measure one of these factors is needed. To this end, an automated enzymatic method has been developed that chromogenically measures factor X activity as a percent of normal and completely avoids the LA artifact. By definition, normal pooled plasma has a factor X activity of 100% and all normal patients should have values greater than 70%.

About 10% of patients with a chronic lupus anticoagulant (LA) have falsely elevated INRs and treatment based on this INR could result in undertreatment with warfarin (see reference below). A gold-standard for monitoring warfarin treatment that is not affected by LA is a factor X level measured by a chromogenic, enzymatic assay (F10). This test is performed daily in the Allina Medical Laboratories central laboratory at Abbott Northwestern Hospital. This test is more expensive than an INR but it is important in some patients.

The INR in the Allina Medical Laboratories has been calibrated to international standards. Correlation of the F10 activity with the INR in our laboratory has shown that an INR of 2.5 is equivalent to a F10 activity of about 28% while the INR range of 2.0 - 3.0 corresponds to F10 activity of 20 - 40%. This is consistent with other published work.

Patients on chronic warfarin therapy can have periodic chromogenic F10 activity checked and have their warfarin dose adjusted up or down using the 20-40% therapeutic range, just as we use a 2.0 - 3.0 range for the INR. If the chromogenic factor X activity is below the desired range, the warfarin dose must be **DECREASED**; if it is above, the warfarin dose must be **INCREASED**. This is the opposite response that occurs when using the INR to monitor warfarin so care must be taken to adjust the dose in the appropriate direction.

1. If a LA patient is on a stable dose of warfarin, has an INR between 2-3, and a F10 that approximately matches in the table below, we consider the INR to be accurate and the patient can be monitored with INR only.

2. If a LA patient is on a stable dose of warfarin, has an INR between 2-3, but a F10 that is clearly greater than in the table below, the patient needs to be followed with F10.

It is possible that in a patient with a falsely high INR, after the F10 level is therapeutic and stable between 20-40% an INR could be measured to establish the relationship in that particular patient (e.g., an INR of 4.5 seems to correlate with a F10 of 30%). Thereafter, it might be reasonable to follow the INR targeting the personalized INR goal. However, if the INR becomes unstable forcing a change in the warfarin dose, repeat of the F10 measurement may be necessary to verify stability of the INR/F10 correlation.

CORRELATION OF CHROMOGENIC FACTOR X AND INR IN NON-LA PATIENT

F10	60	50	40	30	20	15	10
INR	1.6	1.8	2.0	2.4	3.3	4.1	5.7

The test is offered 24/7 and can be ordered as F10/5765 "Chromogenic Factor X" and sent to the Allina Medical Laboratories central lab at Abbott Northwestern Hospital. The Chromogenic Factor X assay is more expensive than the INR, but elimination of the LA artifact is so important clinically that the increased cost is well justified.