BioVendor Group®

Human MxA

Precision in medicine: The Role of MxA in Managing Infections and Immune Responses

- Differentiating viral from bacterial infections
- Detection and assessment of active phase of viral infections
- Immune response assessment
- Autoimmune and inflammatory disease activity marker
- Therapeutic monitoring in interferon therapy

BIOVENDOR.GROUP — BRIDGING SCIENCE AND DIAGNOSTICS


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Why to Avoid Overuse of Antibiotics?

Antimicrobial resistance is a global public health challenge, which has been accelerated by the overuse of antibiotics

Increased antimicrobial resistance leads to severe infections, complications, longer hospital stays, and increased mortality.

This issue is particularly prevalent in primary care, where most infections are viral. General practitioners issue about 90% of all antibiotic prescriptions, primarily for respiratory tract infections. Overprescribing antibiotics not only contributes to resistance but also increases the risk of adverse effects and frequent patient re-attendance. Antibiotic overuse issue is not limited to respiratory tract infections in adults; it also significantly impacts vulnerable populations such as newborns.

Effective interventions to reduce antibiotic overuse include improved laboratory tests or reliable rapid point-of-care tests **to reduce diagnostic uncertainty**. Overprescribing antibiotics not only contributes to resistance but also increases the risk of adverse effects and frequent patient re-attendance. In newborns, especially preterm ones, overuse impairs immune system maturation, making them more susceptible to infections and other immune-related conditions. Antibiotics can affect the development and function of T and B cells, crucial for adaptive immunity.

Acute respiratory infections account for 41% of all outpatient antibiotics, with about half being medically unnecessary.[1] Moreover, antibiotic resistance is estimated to cost double compared to antibiotic treatment.[1,2]

Simple, inexpensive tests such as MxA assay that can guide antibiotic prescription in the outpatient setting have been identified as a successful strategy to reduce inappropriate prescription of antibiotics.[3,4,5]

MxA assay can rule out viral infection with up to 95% sensitivity and 94% specificity.[6] As such the assay allows to identify appropriate candidates for antibiotics and reducing errors.[7]

Economic benefits of the MxA test include less outpatient visits, emergency visits, hospitalizations, and reduced costs related to antibiotic resistance.

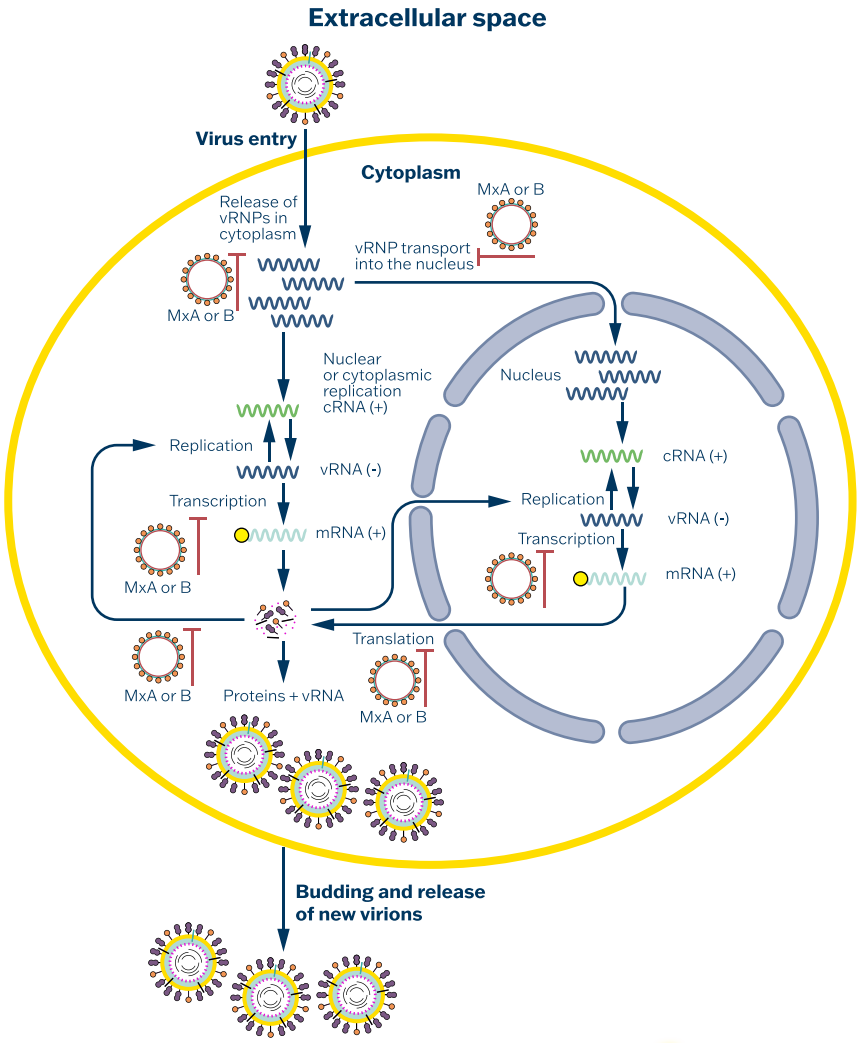
MxA: A Key Player in the Immune Response to Viral Infections

Human MxA protein (Myxovirus resistance protein 1), encoded by the MX1 gene, is a 76-kDa protein composed of 662 amino acid residues and is a member of the dynamin superfamily of large GTPases. The MxA protein plays a crucial role in antiviral defense within cells, providing protection against a broad range of viruses, including influenza, parainfluenza, measles, coxsackie, hepatitis B, and Thogoto viruses.

The viruses are inhibited by MxA protein at an early stage in their life cycle, soon after host cell entry and before genome amplification.

The human MxA protein is accumulated in the cytoplasm and endoplasmic reticulum. The membrane compartment of endoplasmatic reticulum seems to provide an interaction platform that facilitates viral target recognition. MxA appears to detect viral infection by sensing and trapping nucleocapsid structures, and becoming the viral components unavailable for the generation of new virus particles.

The expression of viral MxA protein is induced exclusively and, in a dose-dependent manner, by IFN-alpha and IFN-beta, but not by IFN-gamma, IL-1, TNF-alpha or other cytokines.[8]



Kinetic Features

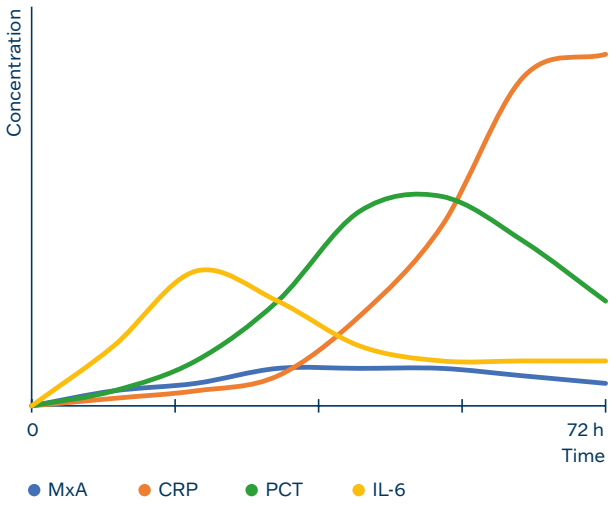
MxA protein may offer advantages as a laboratory marker because of its very low basal concentration, increasing within 1–2 hours of infection and long half-life being approximately 2–3 days.[9]

In mononuclear cells stimulated with high doses of leukocyte IFN-alpha, MxA mRNA levels increased tenfold within 4 hours, and elevated MxA protein levels persists over the next 48 hours.[8,12]

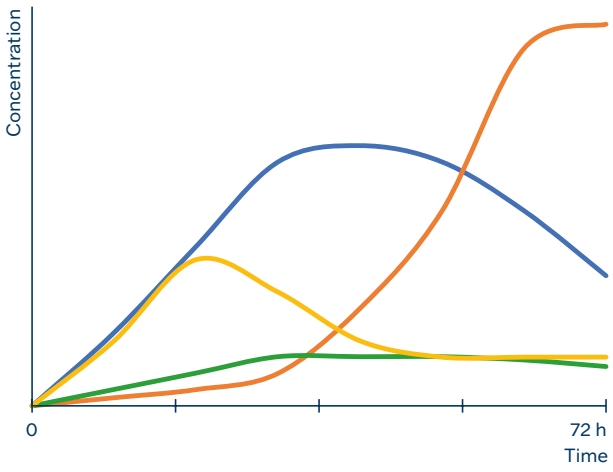
Kinetic Features of CRP, Procalcitonin, IL-6 and MxA

Biomarker	Time-to-induction	Peak	Half-Life	Clinical Relevance
C-Reactive Protein (CRP)	4–6 hours	48 hours	19 hours	Inflammation, Bacterial and viral infections
Procalcitonin	3 hours	12–24 hours	20–24 hours	Bacterial infections
IL-6	1–2 hours	4–24 hours, upon severity or nature of infection	15 hours	Inflammation, Bacterial and viral infections
MxA (Myxovirus resistance protein A)	1–2 hours	16 hours, and remains increased in the presence of increased IFN	2–3 days	Viral infections, including respiratory viruses

Bacterial Infections

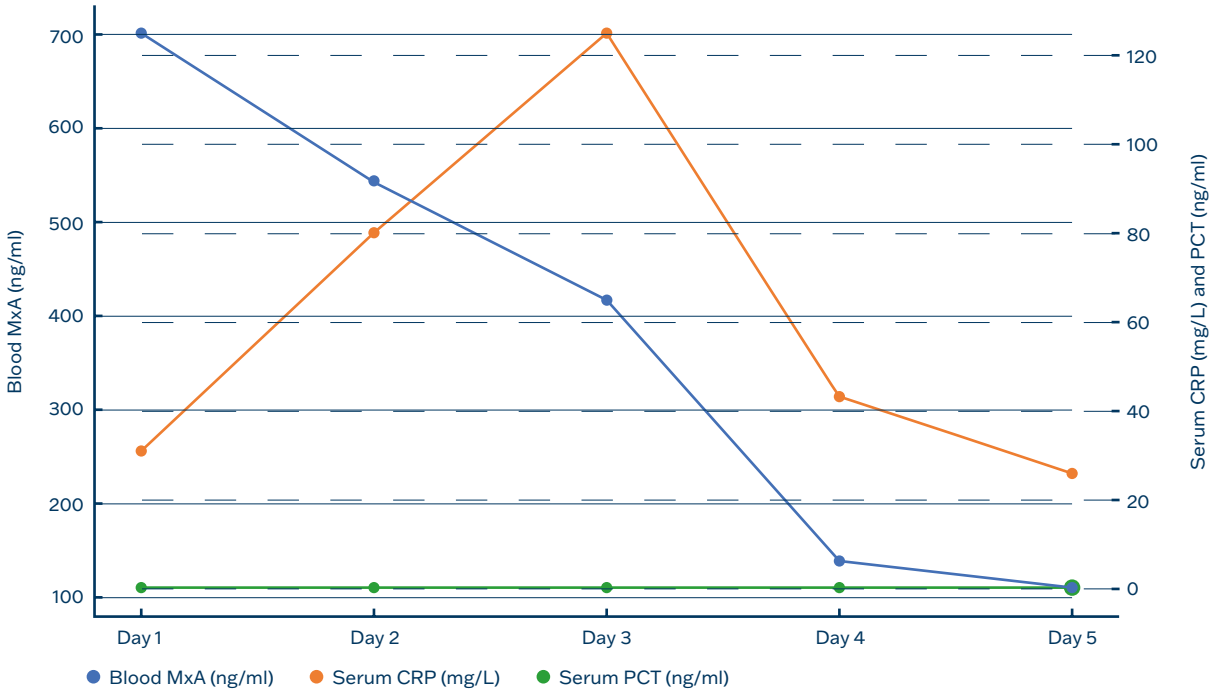


Viral Infections



Case Report

A patient with COVID-19 was admitted to the unit of intensive care with severe viral respiratory tract infection. A substantial improvement in health status was observed during the hospitalization. MxA, CRP and PCT levels were measured during the hospitalization. The severity of the clinical condition was accompanied by high levels of MxA, while a decrease in MxA was observed when the clinical condition improved. CRP levels showed a delayed response compared to MxA and PCT concentrations indicated the absence of bacterial coinfection.



New Insights into Clinical Diagnostics

MxA protein with its low basal concentration and long half-life, offers advantages as a marker for viral infection. Clinical studies have reported on MxA protein in peripheral blood mononuclear cells as a marker distinguishing viral from bacterial disease, and as a reliable marker for type I IFN bioavailability during IFN treatment in patients with multiple sclerosis (MS) according to the recommendation from EMA (European Medicine Agency).

1 **Differentiating viral from bacterial infections**

2 **Detection and assessment of active phase of viral infections**

3 **Immune response assessment**

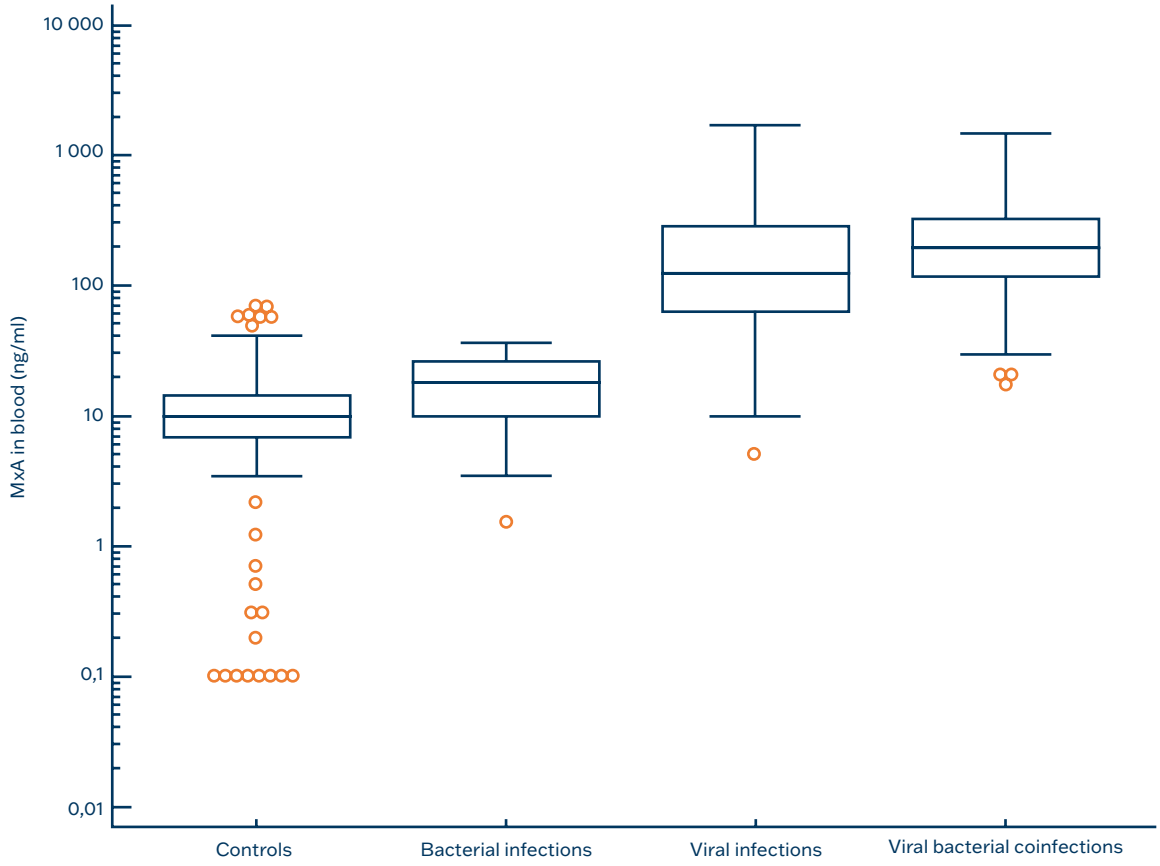
4 **Autoimmune and inflammatory disease activity marker**

5 **Therapeutic monitoring in interferon therapy**

1 Differentiating Viral from Bacterial Infections

Elevated MxA levels are more specific to viral infections and help differentiate viral infections from bacterial infections. MxA is useful in clinical practice to avoid unnecessary antibiotic treatments in viral infections. MxA has been particularly studied in the context of respiratory infections, such as influenza and respiratory syncytial virus (RSV), as its levels rise significantly in these conditions.

The frequency of viral infections is 6–8 times more frequent over bacterial infections in newborns or preterm newborns, and antibiotic treatment is overused substantially. Avoid unnecessary antibiotic treatments substantially reduces risks of immunity damage or later autoimmunity disorders development.



2 Detection and Assessment of Active Phase of Viral Infections

MxA expression is significantly upregulated in peripheral blood mononuclear cells in response to type I interferons (IFN-α/β), which are typically produced in response to viral infections, or directly by viruses. Therefore, measuring MxA levels help identify viral infections, even when the specific virus is not easily detectable.

3 Immune Response Assessment

MxA serves as a marker for assessing the overall immune response capability, particularly in immunodeficiencies or after organ transplantations.

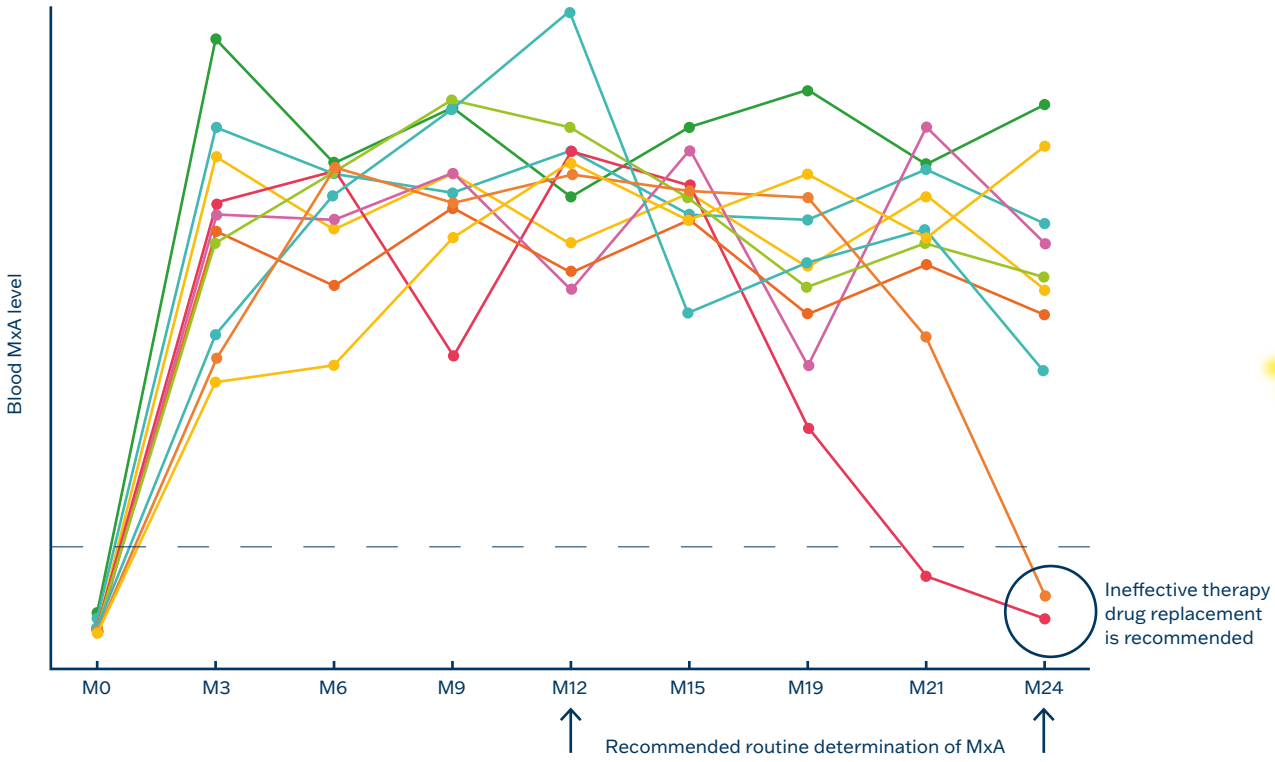
4 Autoimmune and Inflammatory Disease Activity Marker

In diseases such as systemic lupus erythematosus (SLE), which are linked to the pathogenesis of type I interferons, MxA levels reflect disease activity and can monitor disease progression or response to treatment.

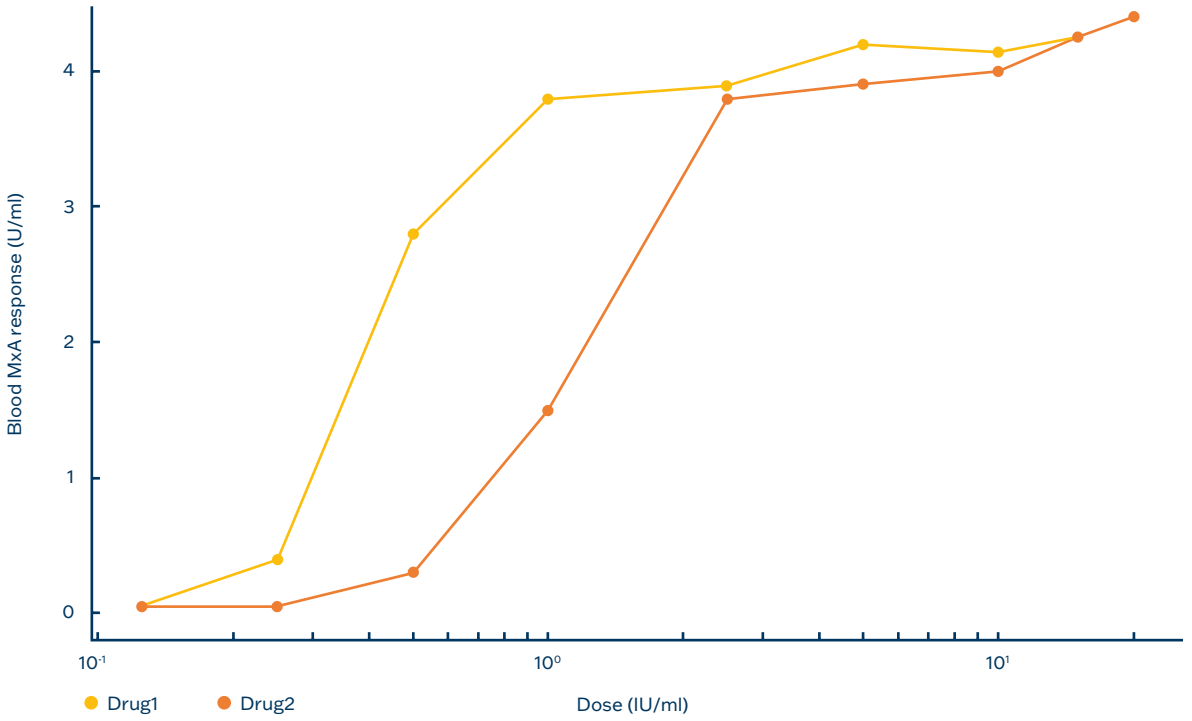
5 Therapeutic Monitoring in Interferon Therapy

In patients receiving interferon therapy, such as those with multiple sclerosis[10] or certain cancers, MxA levels can be monitored to assess the treatment's efficacy. An increase in MxA indicates a response to therapy. 2–40% percent of MS patients develop IFN-beta neutralizing antibodies (NAb) with subsequent attenuation of MxA protein induction. MxA assay can be used for assessment of raised NAb according to the recommendation from EMA (European Medicine Agency).

MxA levels were monitored in 10 patients with multiple sclerosis treated with IFN-1b over 24 months after initiating the therapy. Two patients showed low MxA levels after 24 months, indicating a poor response to IFN, and were advised for the drug replacement.



Evaluation of the biological activity of recombinant IFN beta-1a from two manufacturers using the MxA assay. The comparison indicates that Drug1 is more potent than Drug2, with approximately three times the dose of Drug2 required to achieve the same effect as Drug1.[11]



European Medicines Agency (EMA) Guidelines Suggesting The Use of MxA

The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) released the guideline on clinical requirements for interferon beta (IFN-β) containing medicinal products in 2013: EMA/CHMP/BMWP/652000/2010

Pharmacokinetics
Serum concentrations of IFN-β are very low after the administration of therapeutic dosages and their measurement is technically difficult. Possible methods of detection include a cell-based myxovirus resistance protein A (MxA) induction assay, which measures the biological activity of IFN-β in serum samples, and ELISA assays, which determine the IFN-β protein mass.

Pharmacodynamics
MxA induction can be measured from peripheral blood leukocytes both at the protein and mRNA level; it is currently considered as one of the most sensitive markers of the biological activity of type I interferons and should be one of the selected markers.

Clinical safety
It is recommended that the standardised MxA protein assay or a NAb assay that has been validated against the MxA protein is used for clinical safety of IFN-β (EMEA/CHMP/BWP/580136/2007).

Who Can Benefit from MxA Assay?

Patients

with upper respiratory tract infections

Blood Biobank

for screening donors

Hospitals

for monitoring organ transplant recipients, and preoperative and/or postoperative investigations

Private Medical Care Centres

with travel and tropical medicine department for screening blood-borne tropical viral-origin fevers, such as dengue fever, malaria, or yellow fever

Specialized Healthcare Centres

for conditions Sjögren's Syndrome (applicability of MxA in stratifying patients with primary Sjögren's syndrome according to IFN positivity) and multiple sclerosis (monitoring the efficacy of treatment in patients with multiple sclerosis treated with interferon beta)

Product information

CLIA MxA

CL-MxA050

Assay Format	Size	Regulatory Status
Chemiluminiscence Immunoassay	50 tests	IVD CE

Human MxA POCT

BI005-10

Assay Format	Size	Regulatory Status
Lateral Flow Test	10 tests	IVD CE

Human MxA ELISA

RD194349220R

Assay Format	Size	Regulatory Status
Sandwich ELISA, Biotin-labelled Antibody	96-well	RUO

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