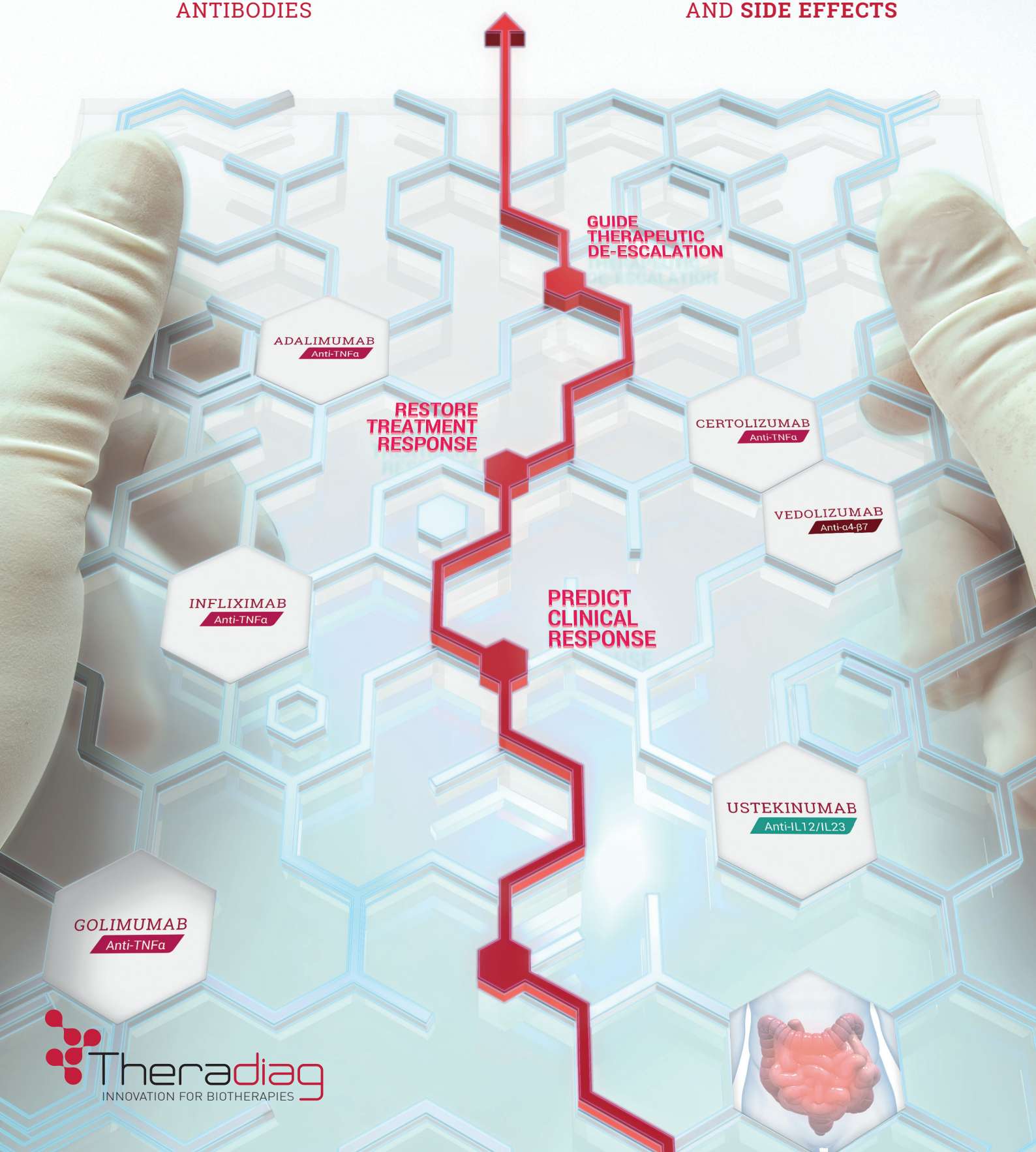
Tracker

THERAPEUTIC DRUG MONITORING IN INFLAMMATORY BOWEL DISEASES

MEASUREMENT OF **BIOLOGICAL DRUG** AND **FREE ANTI-DRUG** ANTIBODIES

EXTEND TREATMENT RESPONSE WHILE **MINIMIZING COSTS** AND **SIDE EFFECTS**



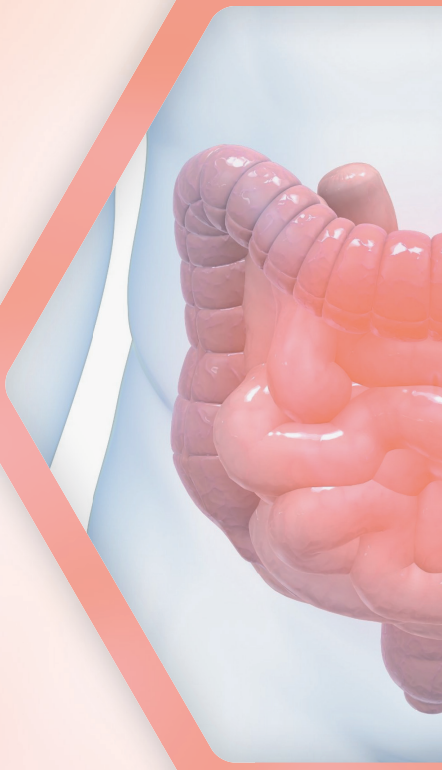
Theradiag
INNOVATION FOR BIOTHERAPIES

Tracker

is your clinical decision-making tool for Inflammatory Bowel Diseases

CLINICALLY RELEVANT

- Numerous publications in peer-reviewed journals
- International decision algorithms validated with Tracker kits



COST-EFFECTIVE

TDM strategy leads to major cost savings (28 to 50%) related to a biologic treatment[24]

- in Ulcerative Colitis (UC) and Crohn's Disease (CD)
- in patients in remission for treatment de-escalation[25]
- in patients with loss of response[26]

ACCURATE

- Accurate quantitative measurement of drugs and anti-drug antibodies
- Detection of free anti-drug antibodies as recommended by international guidelines to fit patient's status
- Performance validated with both Originators and Biosimilars

Therapeutic Drug Monitoring (TDM) strategy leads to major cost savings in IBD patients while maintaining appropriate efficacy[6]

Therapeutic Drug Monitoring (TDM) is a safe method to early measure drug level and detect anti-drug antibodies, guide the therapeutic procedure and optimize treatment efficacy

UNIQUE TDM MENU

- Comprehensive menu in inflammatory diseases and oncology
- CE-IVD validation on serum and plasma samples
- Validation in accordance with the 1st WHO international standards (Infliximab and Adalimumab)
- Validation with Princeps and Biosimilars
- Continuous development on new parameters

CLINICALLY VALIDATED

- Routine use tailored to your clinical practice
- Measurement ranges tailored to induction and maintenance treatment phases

EASY-TO-USE

- Ready-to-use reagents
- Standardized protocols from sample collection to results interpretation
- ELISA format validated on automated platforms (DS2, DSX, Evolis, etc.)
- CLIA format compatible with i-Track10, IDS-iSYS and IDS-i10 random access instruments
- Validated with IMMUNO-TROL INTERNAL CONTROL

Tracker is a solution validated and supported by pharmaceutical companies to adapt patient treatment

THERAPEUTIC DRUG MONITORING TO IMPROVE CLINICAL OUTCOME AND SUPPORT THE PROPER USE OF DRUGS

NEARLY 20-30%

of patients do not respond to an anti-TNFα treatment[1]

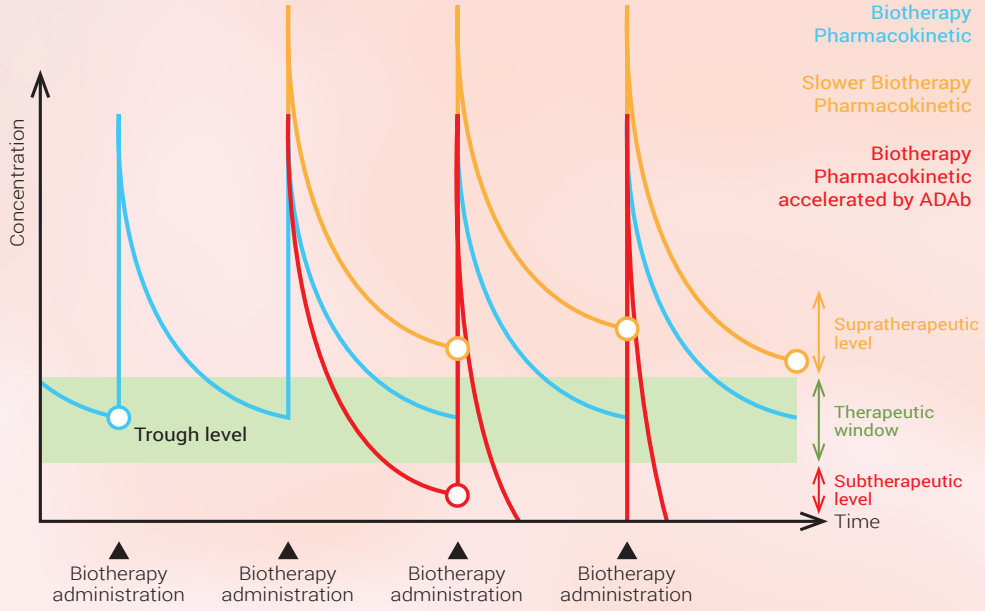
50% OF IBD PATIENTS

experience relapse in disease activity during maintenance therapy[2,3]

Pharmacokinetics and pharmacodynamics of biological therapies are highly variable among patients.

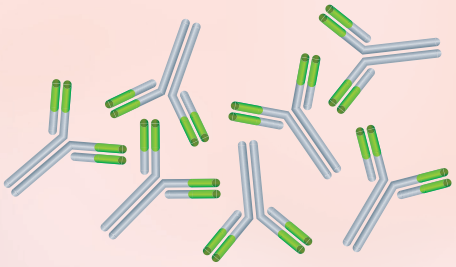
Patients with higher dose of drug or slower pharmacokinetics may have drug trough level above the therapeutic window (supratherapeutic).
Higher trough levels may increase side effects.

Patients with lower dose due to the presence of anti-drug antibodies or with low serum albumin concentration or high baseline CRP concentration may have drug trough levels below the therapeutic window (subtherapeutic), leading to reduced drug efficacy.



Therapeutic Drug Monitoring helps physicians **to make rational treatment decisions during the course of IBD**

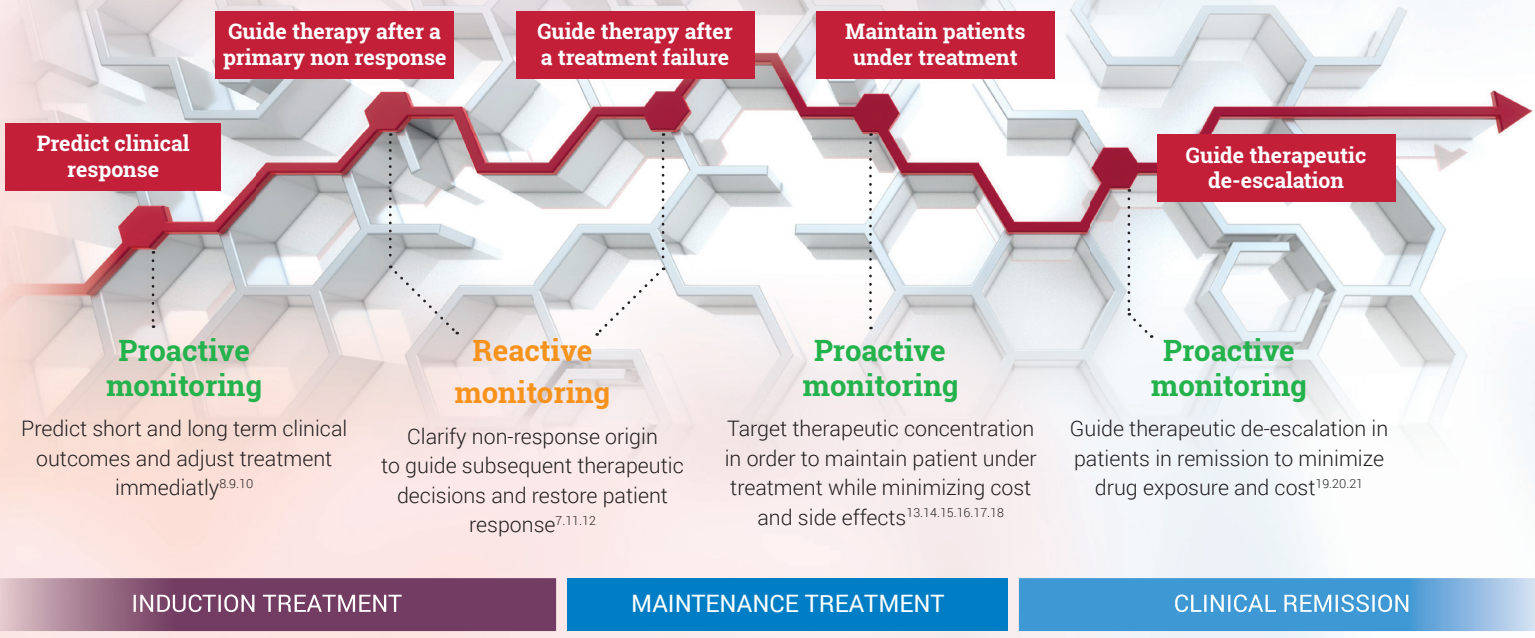
Immunogenicity of Biologics	Crohn's Disease	Ulcerative Colitis
Infliximab & Infliximab Biosimilar (CT-P13)	up to 83%[4]	up to 46%[4]
Adalimumab	up to 35%[4]	up to 5%[4]
Certolizumab Pegol	up to 25%[4]	up to 25%[4]
Vedolizumab	up to 3.7%[4]	up to 3.7%[4]
Ustekinumab	up to 1%[4.27]	up to 1%[4.22]
Golimumab	-	up to 19%[5]



Anti-drug antibodies rates vary widely among biologics regardless of the disease.

Assessment of the immunogenicity of these agents is an important consideration in the treatment decision making process.

WHEN TO PERFORM TDM?



THERAPEUTIC THRESHOLDS

		SUGGESTED DRUG CONCENTRATION THRESHOLD FOR CLINICAL RESPONSE/ REMISSION[23] (µG/ML)	SUGGESTED DRUG CONCENTRATION THRESHOLD FOR MUCOSAL HEALING[23] (µG/ ML)
Infliximab	Induction (week 2)	≥ 20	≥ 25
	Induction (week 6)	≥ 10	N/A
	Postinduction (week 14)	≥ 3	≥ 7
	Maintenance	≥ 3	≥ 7
Adalimumab	Postinduction (week 14)	≥ 5	≥ 7
	Maintenance	≥ 3	≥ 8
Certolizumab Pegol	Postinduction (week 6)	≥ 32	N/A
	Maintenance	≥ 15	N/A
Golimumab	Postinduction (week 6)	≥ 2.5	N/A
	Maintenance	≥ 1	N/A
Vedolizumab	Induction (week 2)	≥ 28	N/A
	Induction (week 6)	≥ 24	N/A
	Postinduction (week 14)	≥ 15	≥ 17
	Maintenance	≥ 12	≥ 14
Ustekinumab	Postinduction (week 8)	≥ 3.5	N/A
	Maintenance	≥ 1	≥ 4.5

N/A, not applicable, due to paucity of data.

These target ranges were those used in landmark studies or international guidelines and do not necessarily translate into general recommendations for individual patients. The target ranges may vary with newly published studies.

WHEN TO COLLECT BLOOD ON PATIENTS?

- Timing of samples collection is key to interpret the result as the drug concentration varies during the interval between two injections
- Drug and anti-drug measurement is recommended to be performed at Trough Concentration (TC), just before the next dose, both during induction and mainenance:
  - Target ranges are defined using TC
  - Free anti-drug antibodies are mostly detectable at TC

INTERPRET DOSING INFORMATION

- Drug levels required to improve clinical outcomes may vary between patients and depend on the desired therapeutic endpoint
- In patients with undetectable drug levels, anti-drug antibody (ADAb) quantification helps to identify how to improve patient response
- In patients with high anti-drug antibodies levels, a switch in-class may be necessary
- In patients with low anti-drug antibodies levels, the addition of an immunosuppressive drug may improve clinical outcomes
- If your patients are good responders with higher drug trough levels, dose decrease may be possible without affecting clinical outcomes

Example of therapeutic decision algorithm in patient with loss of response

	Negative Anti-drug Antibodies	Positive Anti-drug Antibodies
Therapeutic level of Drug	Switch out of therapeutic class	Retest
Subtherapeutic level of Drug	Treatment Optimization	Switch in-class

Measurement of drug concentration and ADAb*

Tracker

Non-responders

Therapeutic or supratherapeutic serum levels

ADAb ⊖

Primary resistance

Switch to another therapeutic class

Subtherapeutic serum levels

ADAb ⊖

Rapid clearance of the drug

Optimization

ADAb ⊕

Secondary resistance

Optimization / switch to another biotherapy + IS

ADAb ⊕⊕⊕

Risk of allergic reactions

Switch to another biotherapy + IS

Good responders

Therapeutic or supratherapeutic serum levels

ADAb ⊖

Right response

Monitoring / reduction of the therapeutic scheme

ADAb ⊕

Risk of resistance

Optimization

Patients monitoring

Tracker

IS = immunosuppressant

* These findings do not constitute a diagnosis in any case. They reflect information available in published peer-reviewed literature and guidelines and should be independently evaluated by the treating clinician and used to complete other clinical and biological information in accordance with clinician's independent medical judgment.

A **COMPLETE SOLUTION** TAILORED TO YOUR MONITORING TESTING NEEDS

i-Tracker

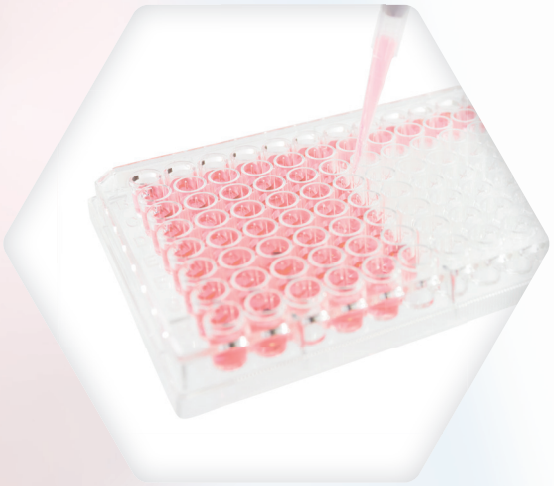
CLIA assays

- Quantitative results for both drug and anti-drug antibodies measurements
- Validated on original drug and biosimilars
- Calibrated against 1st WHO International Standard (Infliximab and Adalimumab)
- Dynamic range adapted to clinical use
- Highly correlated with corresponding LISA TRACKER assays
- Testing protocol is managed by the system
- Ready to use reagents with sample dilutions managed by the system
- Time to first result: 35 mins
- Throughput: 60 tests/hour

LISA TRACKER

ELISA assays

- Quantitative results for both drug and anti-drug antibodies
- Validated on original drug and biosimilars
- Calibrated against 1st WHO International Standard (Infliximab and Adalimumab)
- Dynamic range adapted to clinical use
- Published data
- Standardised protocols for drug and anti-drug antibodies
- Multiple assay formats available to suit testing volume



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ORDERING INFORMATION

i-Tracker

Reference	Designation	Packaging
CTx 002-50/100	i-Tracker Drug	50 / 100 tests
CTx 003-50/100	i-Tracker Anti-Drug	50 / 100 tests

x = Infliximab 100 tests / Adalimumab 100 tests / Vedolizumab 50 tests / Ustekinumab 50 tests / Golimumab 50 tests / Rituximab 50 tests

LISA TRACKER

Reference	Designation	Packaging
LTx 005	LISA TRACKER Duo Drug + ADAb	2 x 48 tests
LTx 002-48	LISA TRACKER Drug	48 tests
LTx 003-48	LISA TRACKER Anti-Drug	48 tests
LTT 004-96	LISA TRACKER TNF	96 tests

x = Infliximab / Adalimumab / Etanercept / Certolizumab Pegol / Golimumab / Rituximab / Secukinumab / Tocilizumab / Bevacizumab / TRastuzumab / Ustekinumab / Vedolizumab

i-Tracker & LISA TRACKER Infliximab are validated on Infliximab princeps Remicade® and Infliximab biosimilars SB2 (Flixabi®), CT-P13 (Remsima® and Inflectra®), Avsola® and Zessly®
i-Tracker & LISA TRACKER Adalimumab are validated on Adalimumab princeps Humira® and Adalimumab biosimilars ABP 501 (Amgevita®), SB5 (Imraldi®) and Idacio®
i-Tracker & LISA TRACKER Rituximab is validated on Rituximab princeps MabThera® and Rituximab biosimilars CT-P10 (Truxima®)

IMMUNO-TROL Internal Quality Control

A range of ready-to-use, internal Quality Control sera, CE marked, dedicated to the pharmacological dosage of biotherapies

For i-Tracker

Reference	Designation	Control
CTx 002-PC	Immuno-Trol Drug: Positive control two levels	2 x 500 µl
CTx 003-PC	Immuno-Trol anti-Drug: Positive control two levels	2 x 1,5 ml

x = Infliximab / Adalimumab / Vedolizumab / Ustekinumab / Golimumab / Rituximab

For LISA TRACKER

Reference	Designation	Control
LTx 002-PC	Immuno-Trol Drug: Positive control two levels	2 x 250 µl
LTx 003-PC	Immuno-Trol anti-Drug: Positive control two levels	2 x 1 ml

x = Infliximab / Adalimumab / Etanercept / Certolizumab Pegol / Golimumab / Rituximab / Secukinumab / Tocilizumab / Bevacizumab / TRastuzumab / Ustekinumab / Vedolizumab

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