



Focus on

Fluoropyrimidines (5-FU / Xeloda[®])

**Prevention of toxicity and treatment
optimisation**





The Eurofins Biomnis Laboratory is committed to offering, day after day, the most innovative tests to support an individualised approach to patient care.

The concept of "personalised medicine" is based on the principle that not all patients suffering from the same disease should necessarily receive the same treatment regimen.

This is particularly true in oncology, where although chemotherapy may very often be necessary, it is not without toxic side effects. Progress in recent years in personalised medicine now enables us to offer tests that can screen patients at high risk of severe toxicity and to adjust dosages accordingly to optimise therapeutic efficacy.

5-FU in oncology

5-fluorouracil (5-FU) and its oral prodrugs, notably capecitabine (Xeloda®), are used in almost 60% of all chemotherapy protocols (colorectal, breast, pancreatic, ENT cancer).

Although generally well tolerated, these substances can cause severe toxicity, mainly in the digestive system, blood cells, the skin and mucosa.

The early severe toxicities of fluoropyrimidines are due, in large part, to the interindividual variability of their metabolism, mainly determined by the activity of dihydropyrimidine dehydrogenase (DPD).

Partial DPD deficiency can result in Grade III-IV toxicity in 20 to 25% of patients treated, which can be fatal in 0.2% of the total patient population.*

Pre-treatment screening for DPD deficiency: a major public health challenge (estimated 120 deaths per year in France)

The multiparametric approach of Eurofins Biomnis

The multiparametric approach includes:

- **Genotyping** (exploration of the 4 most frequent deleterious mutations of the gene responsible for coding DPD):
 - **D949V - rs67376798 - exon 22: 1.8%**;
 - **IVS14+1G>A - DPYD*2 - rs3918290, intron 14: 1.2%**;
 - **I560S - DPYD*13 - rs55886062 - exon 13: 0.3%**;
 - **Del TCAT - DPYD*7 - exon 4: 0.3%**.
- **Phenotyping** (assays of U and UH₂)
 - Pre-treatment plasma assays of endogenous uracil (U) and its metabolite, dihydrouracil (UH₂); determination of the DPD metabolisation index (UH₂/U).
- **Physiopathological characteristics** of patients (age, weight, height, tumour origin, etc.)
- **This data, in combination** with a CE-marked *in vitro* diagnostic medical device (proven algorithm 5-FU^{ODPM Tox™}), enables:
 - ▶ **The prediction of severe, grade III or IV, toxicities: 96%**
 - ▶ **The prediction of lethal toxicities: 100%**
 - ▶ **The proposal of a personalized dose of 5-FU** or capecitabine.



It is important to note that:

- ▶ Genotyping, when used alone, is highly specific but not very sensitive (33%). This means that 67% of screened patients are at risk of severe toxicity.
- ▶ Phenotyping used alone is more sensitive (84%), but still leaves 16% of patients at risk of severe toxicity.
- ▶ The best results are obtained with the Eurofins Biomnis multiparametric approach, which can predict 100% of lethal toxicities and 96% of severe toxicities.

Evaluation of toxicity to fluoropyrimidines: 5-FU^{ODPM Tox™}

Before the initiation of treatment, to avoid severe toxic events

- Experience with more than 20,000 patients: specificity 96%, sensitivity 96%
- It is thus possible to almost completely prevent severe or fatal toxic events.



Practical details

- ▶ 2 tubes of lithium heparin (see associated protocol ref. **K23-24P-INTGB***)
- ▶ **Turnaround time for results: 4 working days.**
- ▶ In the event of a risk of toxicity, a suggested first dose or contraindication to fluoropyrimidines is given in the results report, to support the clinician's prescription.

5-FU dosage adjustment: 5-FU^{ODPM Protocol™}

For duration of treatment, increasing efficacy while reducing toxicity

- PK-guided plasma assay of 5-FU taking into account the results for 5-FU^{ODPM Tox™}
- Enables dose adjustment to maintain 5-FU plasma concentration in the therapeutic range
- **Performance assessed in more than 90,000 courses of treatment to date.**



Practical details

- ▶ Sample to be taken between the 16th and 43rd hour of a 46-hour infusion
- ▶ **Turnaround time for results: 4 working days.**
- ▶ In case of under- or over-dosing, the therapeutic advice on the results report enables adjustment of the dose for the next course of treatment.

Advantages of the Eurofins Biomnis multiparametric approach

The 5-FU^{ODPM Tox™} and 5-FU^{ODPM Protocol™} algorithms are CE marked medical devices which integrate the pharmacogenetic, pharmacological and physiopathological patient data for the following advantages:

- ▶ **5-FU^{ODPM Tox™} detects 96% of patients with partial deficiency and 100% of patients with total deficiencies**
- Preventing fatal toxicities in patients who are “potentially curable” (adjuvant treatments)
- Significant savings to the healthcare system: systematic screening is less expensive than treating toxicity
- PK-guided dose adjustment and treatment monitoring
- Personalising treatment to ensure optimum response
- Improving patient’s quality of life throughout treatment.



References

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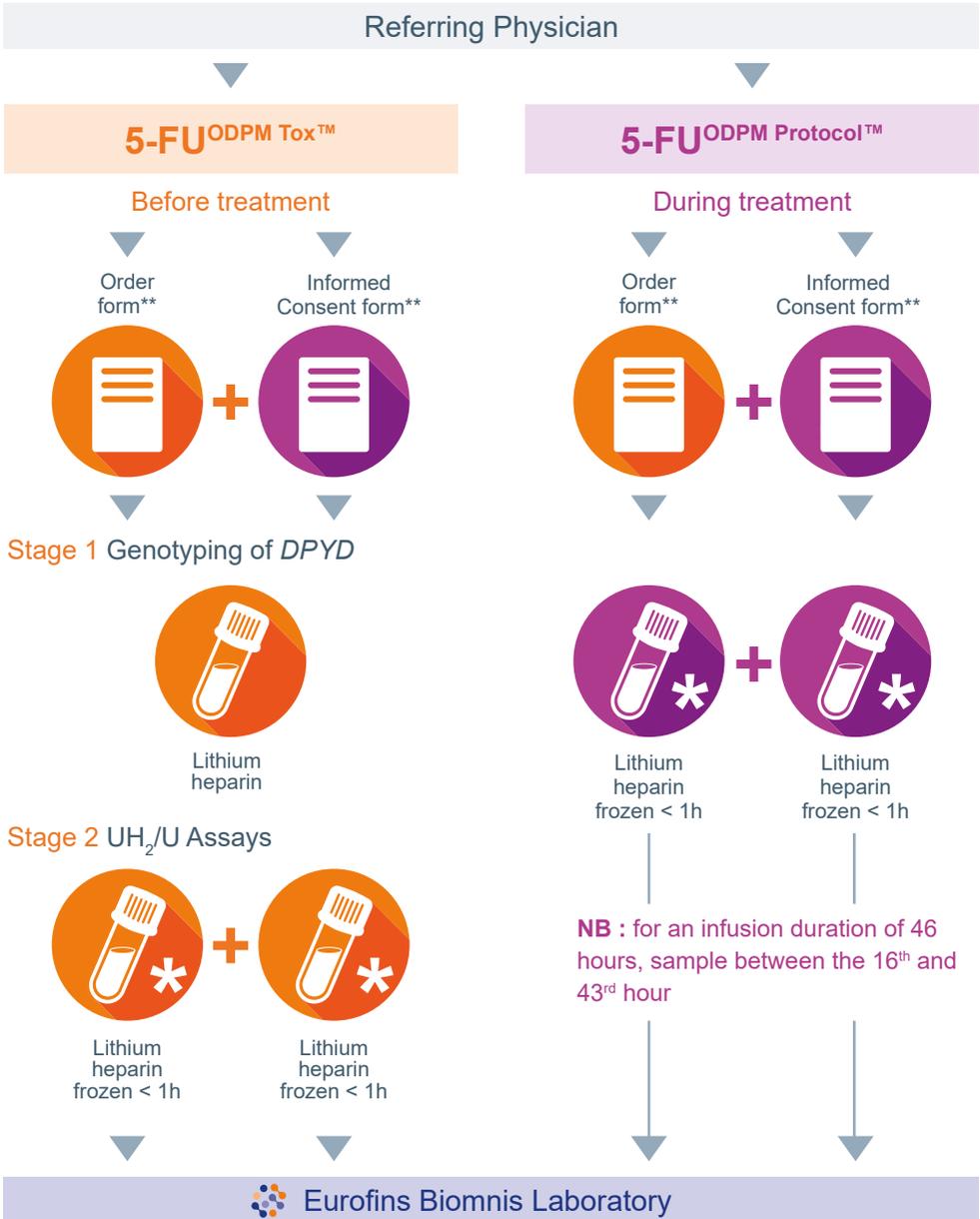
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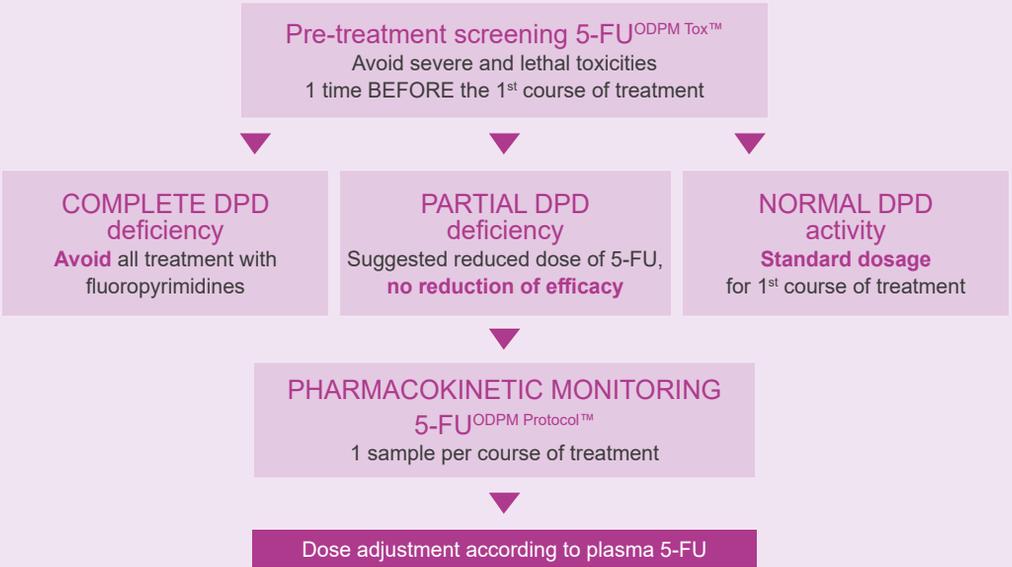
Test prescription



Additional information and the related documents are available from www.eurofins-biomnis.com > Test guide section > Test codes **5FUTO (for the 5FU^{ODPM Tox™} test) and **5FUPR** (for the 5-FU^{ODPM Protocol™} test)



Summary



- ▶ Optimised dosing with no loss of efficacy
- ▶ Improved patient quality of life during treatment
- ▶ Reduction of grade III-IV toxicities
- ▶ NO lethal toxicities

For more information

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