

# LABELLING WITHOUT STRENGTH FOR A PHARMACEUTICAL PREPARATION USED IN A BLINDED DOSAGE ADJUSTMENT OF CLOZAPINE

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## Background

Pharmaceutical preparations labelling must mention the **strength of active ingredient**.

The clinical state of a 17-years-old patient on clozapine for schizophrenia required a **blinded dosage** adjustment to be successful.

## Purpose

Prepare clozapine capsules :

- Of **different strengths**
- Macroscopically **not discernible**

## Materials and Methods

- **Consent** of the patient and his parents
- Feasibility study (Good Preparations Practices) : **crushability** of the tablets
- Micronization with a RETSCH RM 200 mortar apparatus for 4 min, particle size < 3 mm.
- Initial prescription : 1 capsule **165mg in the morning**, 1 capsule **260 mg in the evening** for 15 days
- Preparation :
  - **15 capsules of size 00** (translucent) for the **morning**
  - **15 capsules of size 000** (opaque red) for the **evening**
  - Lactose added if needed
- Dose adjustment criterion : clinical state of the patient



## Results

Obligations for labelling have been fulfilled except for the **strength**, replaced by « **Morning Clozapine** » or « **Evening Clozapine** ».

The clinical evaluation induced a first increase (+12%) of the Morning dose after 5 weeks.

The correct dose was found after 9 weeks with +27% of the daily dose, targeted on the morning, without the patient's fear of the changes. White blood cell counts every 4 weeks were normal.

At the last dose increase, the volume of the powder necessitated to **change the capsules**: from **00** to **000**, **ivory color** (instead of translucent, not available). Nevertheless, these macroscopic changes didn't have nocebo effect.

Blinding required a **double circuit of prescriptions**: those given by the prescriber to the patient mentioning "**morning Capsule: 1, evening Capsule: 1**" to take daily and those which were intended for us, **specifying the strengths**.

Day of preparation	Strength	Size	Color	Label
Day 1	165 mg	00	Translucent	Morning Clozapine
Day 15	260 mg	000	Opaque Red	Evening Clozapine
Day 29				
Day 44	185 mg	00	Translucent	Morning Clozapine
Day 57	260 mg	000	Opaque Red	Evening Clozapine
Day 71	210 mg	000	Translucent	Morning Clozapine
	260 mg	000	Opaque Red	Evening Clozapine

## Conclusions

All items required on the pharmaceutical preparations labelling must be **fulfilled** exhaustively to avoid any **confusion**. However, **exceptionally** and **transiently**, a labelling not mentioning the strength was relevant in helping the prescriber to manage a dosage adjustment and to achieve the desired clinical outcomes.

