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 165 mg 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.

<table>
<thead>
<tr>
<th>Day of preparation</th>
<th>Strength</th>
<th>Size</th>
<th>Color</th>
<th>Label</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>165 mg</td>
<td>00</td>
<td>Translucent</td>
<td>Morning Clozapine</td>
</tr>
<tr>
<td>Day 15</td>
<td>260 mg</td>
<td>000</td>
<td>Opaque Red</td>
<td>Evening Clozapine</td>
</tr>
<tr>
<td>Day 29</td>
<td>260 mg</td>
<td>000</td>
<td>Opaque Red</td>
<td>Evening Clozapine</td>
</tr>
<tr>
<td>Day 44</td>
<td>185 mg</td>
<td>00</td>
<td>Translucent</td>
<td>Morning Clozapine</td>
</tr>
<tr>
<td>Day 57</td>
<td>260 mg</td>
<td>000</td>
<td>Opaque Red</td>
<td>Evening Clozapine</td>
</tr>
<tr>
<td>Day 71</td>
<td>210 mg</td>
<td>000</td>
<td>Translucent</td>
<td>Morning Clozapine</td>
</tr>
<tr>
<td></td>
<td>260 mg</td>
<td>000</td>
<td>Opaque Red</td>
<td>Evening Clozapine</td>
</tr>
</tbody>
</table>

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.