ERr 731® is a nonhormonal therapy to alleviate the uncomfortable symptoms of menopause, including hot flashes.

With more than 30 years of safe, effective use in Europe (backed by decades of postmarketing surveillance data), ERr 731® has been clinically demonstrated, through extensive research, including randomized controlled trials, to safely and effectively reduce menopausal symptoms.

**ERr 731® Research Highlights**

- In a 12-week randomized controlled trial, ERr 731® significantly reduced the number of hot flashes from a median of 12 to 2 daily.
- In the same study, ERr 731® demonstrated an 83% reduction in hot flashes, as well as a significant decrease in anxiety.
- No changes in gynecological findings (e.g., endometrial hyperplasia or abnormalities in breast tissue) and safety parameters were observed in a two-year observational study.
- Postmarketing surveillance found that the incidence of ERr 731®-associated adverse events was very low.

**12-week confirmatory RCT**

112 perimenopausal women

- At 12 weeks, ERr 731® group showed a significant reduction in the number of hot flashes compared to placebo, from a median of 12 to 2—an 83% reduction (Figure 1).
- The Hot-Flash-Weekly-Weighted-Score (HFWWS) was significantly decreased in ERr 731® group (p<0.0001) but not the placebo group.

**6-month observational study (OS) at 70 gynecological practices**

252 peri- and postmenopausal women

- Subjects showed a significant decrease in Menopause Rating Scale (MRS) total score from a mean of 14.5 points at baseline to 6.5 at 6 months (p<0.0001); all 11 individual symptom scores were improved over baseline (Figure 2).
- 90% of women rated the tolerability of ERr 731® “very good” or “good,” and there were no ERr 731®-related AEs.

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**Figure 1**

<table>
<thead>
<tr>
<th>Number of Daily Hot Flashes</th>
<th>Baseline</th>
<th>12 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>ERr 731®</td>
<td>12</td>
<td>2</td>
</tr>
<tr>
<td>Placebo</td>
<td>15</td>
<td>12</td>
</tr>
</tbody>
</table>

**Figure 2**

- Subjects showed a significant decrease in Menopause Rating Scale (MRS) total score from a mean of 14.5 points at baseline to 6.5 at 6 months (p<0.0001); all 11 individual symptom scores were improved over baseline (Figure 2).
- 90% of women rated the tolerability of ERr 731® “very good” or “good,” and there were no ERr 731®-related AEs.
2-year post-RCT observational study (OS)
OS I (48 weeks) consisted of 80 menopausal women; OS II (additional 48 weeks) consisted of 51 women from OS I

  • The mean MRS II total score was reduced from 34.0 at baseline to 5.7 at end of OS II—an 83% reduction (Figure 3)
  • ERr 731® demonstrated a sustained alleviation of menopausal symptoms, and no changes in safety parameters were observed over two years
  • By the end of two years, the endometrial thickness showed a slight decrease in all women
  • No increases in serum progesterone or 17β-estradiol levels were observed, suggesting a lack of a potential hyperproliferative activity of ERr 731® in endometrium or breast

ERr 731® inclusion in JAMA review
  • The Journal of the American Medical Association (JAMA) recently published a systematic review article based on published RCTs of plant-based therapies and reported remedies such as ERr 731® to be associated with improvements in the number of hot flashes

ERr 731®: selective binding of Estrogen Receptor β (ERβ)
  • The clinical benefits of ERr 731® appear to be related to selective binding of ERβ and lack of affinity for ERα (Figure 4)\(^8\)\(^9\)\(^10\)
  • In tissues where both ERα and ERβ are expressed, ERβ may function as a negative regulator of ERα, offering relief of menopausal symptoms as well as protection against inflammation and hyperproliferation\(^11\)\(^12\)

Postmarketing surveillance since 1993
  • Postmarketing surveillance began in Germany (in 1993) and expanded to USA (in 2009), South Africa (in 2011), and Canada (in 2012)
  • Published postmarketing surveillance data, from approximately 153 million doses sold since 1993, suggest ERr 731® is generally safe for consumption

Conclusion
With extensive preclinical and clinical research demonstrating efficacy and safety as well as a decades-long postmarketing surveillance safety record, ERr 731® is a thoroughly tested plant-derived extract that offers an innovative approach to relieving menopausal symptoms, including hot flashes.