# SAFETY EVALUATION

**Extent of Exposure**

Duration: 1-5 days

Dose: 6 capsules daily, in total of 935 mg of fixed combination of 866.4 mg proprietary *Andrographis paniculata* L. Nees. herb standardized native extract , and 68.4mg proprietary *Eleutherococcus senticosus* root native extract, equivalent to 5.8 mg of Herba Andrographidis, and 1.2 g of Radix Eleutherococci.**2**

**Adverse Events (AEs)**

**Summary of adverse events**

The treatment was well tolerated. The only common side effect was a mild pruritus (itchy skin), observed in 10 patients: 6 in the placebo group, and 4 - in the Kan Jang group. Serious adverse events were not observed.

**Display of adverse events**

Adverse events occurring after initiation of study treatments, including events likely to be related to the underlying disease or likely to represent concomitant illness are displayed in summary tables 1 and 2.
No adverse events of allergic reactions like urticaria, angioedema, paresthesia, anaphylactic reactions, rush were observed.

**Analysis of adverse events**

Analysis of adverse events observed in placebo and verum groups (Tables 1 and 22) shows that:

- the types adverse events are the same o in both groups
- the frequency (in % ) is the same o in both groups.

In can be concluded that these events are not related to the treatment..

**Deaths, Other Serious Adverse Events, and Other Significant Adverse Events**

Deaths, other serious adverse events, and other significant adverse deserve special attention have not been observed in this study.

**Clinical Laboratory Evaluation**

The results of blood analysis, table 19, shows normalizing (anti-inflammatory) effect of Kan Jang.

**Vital Signs, Physical Findings, and Other Observations Related to Safety**

Vital signs related to safety do not reveal any evidence of a drug effect.

**Safety Conclusions**

The treatment was well tolerated. The only common side effect was a mild pruritus, observed in 10 patients: 6 in the placebo group, and 4 - in the Kan Jang group. Serious adverse events were not observed.

**Table 1**. Adverse events: treatment emergent signs and symptoms" (TESS) - those not seen at baseline. Number observed and rate with patient identification. Kan Jang group, N=94

| Adverse event | Mild | | Moderate | | Severe | | Total | | Total |
|---|---|---|---|---|---|---|---|---|---|
| | Possibly Related | NR* | Possibly Related | NR | Possibly Related | NR | Possibly Related | NR | R+NR * |
| Pruritus/ itchy skin | | 4(4.2%)<br>N47**<br>N51<br>N46<br>N160 | | | | | | | 4 (4.2%) |

** NR = not related; R – possibly related ** Patient identification number*

**Table 2.** Adverse events: treatment emergent signs and symptoms" (TESS) - those not seen at baseline. Number observed and rate with patient identification. Placebo group, N=85

| Adverse event | Mild | | Moderate | | Severe | | Total | | Total |
|---|---|---|---|---|---|---|---|---|---|
| | Possibly Related | NR* | Possibly Related | NR | Possibly Related | NR | Possibly Related | NR | R+NR |
| Pruritus/ itchy skin | | 6 (7.0%)<br>N7**<br>N77<br>N66<br>N196<br>N36<br>N10 | | | | | | | 6 (7.0%) |

**Table 3.** Overall summary of the treatment-emergent adverse events

| | Group B (Kan Jang) | Group A (Placebo) | Total | Odds ratio, B/A | z statistic | Significance level, *p* value |
|---|---|---|---|---|---|---|
| Number of patients | 94 | 85 | 179 | | | |
| Patients with AE | 4 (4.2%) | 6 (7.1%) | 10 (5.6%) | **0.5852** | **0.807** | **0.4194** |
| Total number of AEs: pruritus/ itchy skin | 4 (4.2%) | 6 (7.1%) | 10 (5.6%) | | | |
| Number of patients with other serious AEs | 0 (0%) | 0 (0%) | 0 (0%) | | | |
| Number of patients withdrawn for AEs | 0 (0%) | 0 (0%) | 0 (0%) | | | |
| Cases of death due to AEs | 0 (0%) | 0 (0%) | 0 (0%) | | | |