Updated March 4, 2002

REUMACON - RHEUMATOID ARTHRITIS (RA)

Trademark:	REUMACON
Active substance:	Semi-synthetic derivatives of two lignan glucosides from the plant Podophyllum emodi
Formulations:	Enteric coated soft gelatin capsules
Indication:	Rheumatoid Arthritis (RA)

Background
Clinicians have started to introduce second-line drugs earlier than was previously recommended in the hope of preventing irreversible tissue damage. In individual patients the short term response to second-line agents varies from no response to complete remission.

REUMACON is a new drug for treating RA-patients. Belonging to the class of disease-modifying anti-rheumatic drugs (DMARDs), *REUMACON* has given positive results in clinical trials and safety studies.

REUMACON is jointly developed by Analytecon SA, Switzerland and Conpharm AB, Sweden.

Project Status
REUMACON has in clinical trials been shown to produce a good clinical effect in patients with severe RA. Already after 2-6 weeks of treatment, both laboratory and clinical parameters show significant improvements. *REUMACON* shows less side-effects than other drugs used for the same category of patients.

The clinical program is ongoing, building a file for registration. The program is managed by Meda AB, Sweden.

Increasing sales of *REUMACON* are recorded already now in all the Nordic countries, where the product is prescribed on a named patient basis. Cumulative sales under this program corresponds to more than 6,500 patient years. More than 1.000 patients with established RA are currently on *REUMACON* treatment in seven (7) countries.This provides experience from practical clinical use of the product.

The price to wholesaler is USD 100 per 100 capsules. This corresponds to USD 6-7 per patient/day.

Summary of Clinical Experience
Today, the clinical documentation comprises eleven (11) open and double-blind studies with a duration of 3-9 months. In addition, eight (8) safety studies (6 prospective and 2 retrospective) with durations up to 36 months. All performed clinical studies comprise more than 300 treatment years.

Efficacy - REUMACON is at least as effective as currently available products
The efficacy of *REUMACON* has been demonstrated to be on par with that of methotrexate, sulphasalazine and azathioprine.

Safety - REUMACON is associated with a lower risk of serious side-effects than competitors
Side-effects of Reumacon have generally been gastro-intestinal in nature and of mild to moderate severity. Clinical data suggest that the risk for effects on vital organs (blood, liver, kidneys) reported for other DMARDs is considerably lower with *REUMACON*. "Regarding safety, *REUMACON* manifested clear advantages over MTX, which was associated both with a greater prevalence of side-effects and with potentially severe adverse events involving the liver and haematopoidic organs". (Manuscript submitted for publication).

Tolerance - Limited presence of annoying side-effects, in combination with good efficacy, allows long duration of treatment
Clinical studies have demonstrated long duration of *REUMACON* treatment, i.e. up to 50% of refractory patients where still on Reumacon treatment in single therapy or in combination therapy with MTX at 36 months after onset.

Onset of action - The clinical effect of REUMACON can be determined within a month
The time required from start of medication till noticeable effect varies from one to six months for different DMARDs. In the case of Reumacon, this time is about one month, which is similar to MTX.

Few contraindications - REUMACON is subject to less medical restrictions than MTX
"An important advantage of *REUMACON* over MTX is the lack of contraindications in terms of previous disease of haematopoietic organs, liver or lungs". (Manuscript submitted for publication).

Effect in "hard to treat" patients - REUMACON has proven useful in patients resistant to other treatment
REUMACON has been extensively prescribed on a named patient basis in Sweden, Finland, and Norway. To qualify for such prescription, the patient must either be a non-responder to treatment with regularly available products or otherwise unsuitable for such treatment. The use of *REUMACON* by patients increases once physicians have started to prescribe it. This increased use is a clear sign that *REUMACON* works for a number of these patients.

Position of REUMACON
REUMACON merits a product position as the first choice for mono-therapy in patients who are candidates for DMARDs. Further, initial data suggest that *REUMACON* and MTX in combination are very effective and well tolerated, and that they may provide treatment for patients who do not respond to mono-therapy.

REUMACON has an attractive clinical profile with a favourable efficacy/safety ratio. It is less risky to use than MTX. However, MTX is very well established and it has distinct advantages of low price and easy administration."Taken together, the findings in this trial suggest that, both from the point of view of efficacy and of safety, *REUMACON* is a useful alternative to MTX in the treatment of active RA". (Manuscript submitted for publication).

REUMACON fits well into present trends towards more aggressive drug therapy in RA.

REUMACON use will be cost-effective, as low toxicity limits the need for follow up visits for safety reasons.