The European Agency for the Evaluation of Medicinal Products
Evaluation of Medicines for Human Use

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WORKING PARTY ON HERBAL MEDICINAL PRODUCTS

FINAL PROPOSAL FOR A CORE DATA SALICIS CORTEX

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Final Proposal for a Core-data on Willow bark

The Working Party on Herbal Medicinal Products proposes the following core-data for *Salicis cortex*.

1. NAME OF THE MEDICINAL PRODUCT

To be specified for the individual finished product.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

i) Willow bark[1]

ii) Extracts[2]

Dry extract (8-14:1), prepared with ethanol 70% V/V
dry or liquid, hydro-alcoholic or aqueous extract
tincture (1:6), prepared with ethanol 50% V/V

3. PHARMACEUTICAL FORM

The pharmaceutical form should be described by the European Pharmacopoeia full standard term.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Herbal medicinal product:
a) for the symptomatic treatment of fever and pain[3]
b) for the symptomatic treatment of mild rheumatic conditions[3]

4.2 Posology and method and duration of administration

Adult daily dose:	dry hydro-alcoholic (8-14:1, ethanol 70%) or aqueous extracts, tinctures or fluid extracts, equivalent to 120 mg – 240 mg total salicin, or 6 - 12 g of powdered drug as a decoction (corresponding to 120 mg - 240 mg total salicin), divided into two doses.
Elderly daily dose:	dose as for adults.

Method of administration
Oral use

Duration of use
No prolonged use without medical advice (see section 4.4 Special warnings and precautions for use).

1 The material complies with the Ph. Eur.
[2] Quantified extract Ph. Eur. (ref 765 on extracts) : content of total salicin to be specified
[3] Decision by majority

4.3 Contra-indications

Not to be used in the third trimester of pregnancy.
Not to be used in patients with known hypersensitivity to salicylates (e.g. asthma, bronchial spasm, rhinitis or chronic urticaria).
The use of willow bark in patients with hypersensitivity to other NSAID's is not recommended as a general precaution.
Use should be avoided in case of asthma because severe reactions (acute bronchospasms) could be induced.

4.4 Special warnings and precautions for use

In children and adolescents below 16 years [product name] should only be used on medical advice and only in cases where other therapies failed to succeed. In a child or adolescent who has become very unwell with severe vomiting, drowsiness or loss of consciousness following a viral infection, Reye's syndrome may be suspected. This is an extremely rare but life threatening disease, which requires immediate medical attendance.

In case of severe liver or renal dysfunction, coagulation disorders, gastric/duodenal ulcer and glucose-6-phosphate dehydrogenase deficiency, the product should only be taken under medical supervision.

If fever persists after 3 days of treatment or exceeds 39°C, a physician should be consulted.

Particular attention should be paid when using [Product's name] in acute conditions of swelling of joints, redness and impaired mobility. If pain or symptoms persist or worsen during the first week of use, a physician should be consulted.

4.5 Interaction with other medicaments and other form of interaction

Willow bark may increase the effects of anticoagulants such as heparin and coumarin derivatives.

4.6 Use in pregnancy and lactation

Because data on the use during the first and second trimester of the pregnancy and during lactation are not available, the use is not recommended as a general precaution. Salicylates cross the placenta and appear in breast milk.
Not to be used in the third trimester of pregnancy.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Allergic reactions such as pruritus, urticaria, asthma and gastrointestinal symptoms may occur.

4.9 Overdose

None reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmaco-therapeutic group: Analgesics and antipyretics
ATC code: N02BG (other analgesics and antipyretics)

Dose-dependent analgesic effects of willow bark dry extract (8-14:1, ethanol 70%) were observed in recent controlled clinical studies in patients with low back pain exacerbations and patients with osteoarthritis.

Antiphlogistic effects of willow bark were studied in vitro (hen's egg chorioallantoic membrane test).

AA- and ADP-induced platelet aggregation was decreased in patients receiving willow bark extract.

Constituents other than salicin may contribute to the overall analgesic effects.

Level of evidence[4]:
Indication a): level IV
Indication b): level I

5.2 Pharmacokinetic properties

Salicylglycosides of willow bark form salicin after hydrolysis. Salicin is degraded by the intestinal flora into saligenin (salicyl alcohol) and glucose. Saligenin is absorbed and oxidized in the blood and liver to salicylic acid.

Intake of quantified willow bark extract (1360 mg, equivalent to 240 mg salicin), resulted in salicylic acid as the major metabolite of salicin detected in the serum (86% of total salicylates), besides salicyluric acid (10%) and gentisic acid (4%). Peak levels were reached within 2 hours after oral administration.
Peak serum levels of salicylic acid were on average 1.2mg/l and the AUC was equivalent to that expected form an intake of 87 mg acetylsalicylic acid.
Renal elimination occurred predominantly as salicyluric acid.

5.3 Preclinical safety data

No data are available on willow bark.

6.0 Date of compilation

February 2004

[4] Points to consider on the evidence of safety and efficacy required for well established herbal medicinal products in bibliographical applications (HMPWP/23/99)

