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*Evaluation of Medicines for Human Use*

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**COMMITTEE ON HERBAL MEDICINAL PRODUCTS (HMPC)**

**DRAFT**

# COMMUNITY HERBAL MONOGRAPH ON *SALIX*, CORTEX

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| **DISCUSSION IN WORKING PARTY ON COMMUNITY MONOGRAPHS AND COMMUNITY LIST (MLWP)** | July 2007<br>September 2007 |
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| **REDISCUSSION IN WORKING PARTY ON COMMUNITY MONOGRAPHS AND COMMUNITY LIST (MLWP)** | |
| **ADOPTION BY HMPC** | |
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| **KEYWORDS** | Herbal medicinal products; HMPC; Community herbal monographs; well-established medicinal use; traditional use; *Salix*; Salicis cortex; willow bark |

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# COMMUNITY HERBAL MONOGRAPH ON *SALIX*, CORTEX

## 1. NAME OF THE MEDICINAL PRODUCT

To be specified for the individual finished product.

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION[1, 2]

| Well-established use | Traditional use |
|---|---|
| With regard to the marketing authorisation application of Article 10(a) of Directive 2001/83/EC as amended | With regard to the registration application of Article 16d(1) of Directive 2001/83/EC as amended |
| *Salix* [various species including *S. purpurea* L., *S. daphnoides* Vill., *S. fragilis* L.] | *Salix* [various species including *S. purpurea* L., *S. daphnoides* Vill., *S. fragilis* L.] |
| i) Herbal substance<br>Not applicable | i) Herbal substance<br>whole or fragmented dried bark |
| ii) Herbal preparation | ii) Herbal preparations |
| Dry extract (8-14:1) ethanol 70% V/V, quantified for total salicin. | Dry hydro-alcoholic or aqueous extracts<br>Liquid extract (1:1 in alcohol 25% V/V )<br>Powdered dried bark<br>The herbal preparation should be quantified for total salicin. |

## 3. PHARMACEUTICAL FORM

| Well-established use | Traditional use |
|---|---|
| Quantified herbal preparation in solid dosage form.<br>The pharmaceutical form should be described by the European Pharmacopoeia full standard term. | Quantified herbal substance or herbal preparation in solid or liquid dosage form.<br>The pharmaceutical form should be described by the European Pharmacopoeia full standard term. |

[1] The material complies with the Ph. Eur. monograph (ref. 01/2005:1583 corrected)
[2] The declaration of the active substance(s) for an individual finished product should be in accordance with relevant herbal quality guidance.

## 4. CLINICAL PARTICULARS

### 4.1. Therapeutic indications

| Well-established use | Traditional use |
|---|---|
| Herbal medicinal product used for the short symptomatic treatment of low back pain. | Traditional herbal medicinal product used for the symptomatic relief of:<br>a) minor articular pain,<br>b) fever associated with common cold,<br>c) headache.<br><br>The product is a traditional herbal medicinal product for use in specified indications exclusively based upon long-standing use. |

### 4.2. Posology and method of administration

| Well-established use | Traditional use |
|---|---|
| **Posology**<br>*Adults, elderly*<br>The daily dose is dry extract (8-14:1) ethanol 70% V/V, equivalent to 240 mg total salicin, divided into two doses.<br><br>Not recommended for use in children and adolescents under 18 years of age (see section 4.4 Special warnings and precautions for use)<br><br>**Duration of use**<br><br>If the pain or symptoms persist during the first week of use of the medicinal product, a doctor or a pharmacist should be consulted.<br><br>Duration should be restricted to a maximum of 4 weeks.<br><br>**Method of administration**<br>Oral use. | **Posology**<br>*Adults, elderly*<br>Dry bark for herbal tea preparation: 1 to 3 g, three to four times daily<br>Dry aqueous extracts (16-20:1, 16-21:1, 8-16:1): 600 mg twice daily<br>Liquid extract (1:1 in 25% ethanol V/V): 1 to 3 ml, three times daily<br>Powdered dry bark: 400 mg three times daily<br><br>The single and the daily dose should not contain equivalent amount of salicin exceeding 120 mg and 240 mg, respectively.<br><br>Not recommended for use in children and adolescents under 18 years of age (see section 4.4 Special warnings and precautions for use)<br><br>**Duration of use**<br><br>Indication a)<br>Duration should be restricted to a maximum of 4 weeks.<br><br>Indication b)<br>A doctor should be consulted after 3 days.<br><br>If the symptoms persist during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.<br><br>**Method of administration**<br>Oral use. |

## 4.3. Contraindications

| Well-established use | Traditional use |
|---|---|
| Hypersensitivity to the active substance.<br>Hypersensitivity to salicylates or to other NSAIDs (e.g. history of angioedema, bronchial spasm, or chronic urticaria in response to salicylates or to other NSAIDs).<br><br>Asthma because severe reactions could be induced.<br><br>Active peptic ulcer disease.<br><br>Third trimester of pregnancy. | Hypersensitivity to the active substance.<br>Hypersensitivity to salicylates or to other NSAIDs (e.g. history of angioedema, bronchial spasm, or chronic urticaria in response to salicylates or to other NSAIDs).<br><br>Asthma because severe reactions could be induced.<br><br>Active peptic ulcer disease.<br><br>Third trimester of pregnancy.<br><br>Children and adolescents below 18 years of age because medical supervision should be sought.<br><br>Severe liver or renal dysfunction, coagulation disorders, gastric/duodenal ulcer and glucose-6-phosphate dehydrogenase deficiency because medical supervision is needed. |

## 4.4. Special warnings and precautions for use

| Well-established use | Traditional use |
|---|---|
| In children and adolescents below 18 years, the product 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, a serious disease may be suspected. This in an extreme rare but life threatening disease, which requires immediate medical attendance.<br><br>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.<br><br>If pain or symptoms worsen during the first week of use, a doctor should be consulted.<br><br>Concomitant use with salicylates and other NSAIDs is not recommended without medical advice. | The product is not intended to be used in case of acute arthritis as this condition requires medical advice.<br><br>If fever exceeds 39°C, persists or is associated with severe headache or if symptoms worsen during the use of the medicinal product, a doctor should be consulted.<br><br>Concomitant use with salicylates and other NSAIDs is not recommended without medical advice. |

### 4.5. Interactions with other medicinal products and other forms of interaction

| Well-established use | Traditional use |
|---|---|
| Willow bark may increase the effects of anticoagulants such as coumarin derivatives. | Willow bark may increase the effects of anticoagulants such as coumarin derivatives. |

### 4.6. Pregnancy and lactation

| Well-established use | Traditional use |
|---|---|
| In absence of sufficient data the use during the first and second trimester of pregnancy and lactation is not recommended. Salicylates cross the placenta and appear in breast milk.<br>Contraindicated in the third trimester of pregnancy. | In absence of sufficient data the use during the first and second trimester of pregnancy and lactation is not recommended. Salicylates cross the placenta and appear in breast milk.<br>Contraindicated in the third trimester of pregnancy. |

### 4.7. Effects on ability to drive and use machines

| Well-established use | Traditional use |
|---|---|
| No studies on the effect on the ability to drive and use machine have been performed. | No studies on the effect on the ability to drive and use machine have been performed. |

### 4.8. Undesirable effects

| Well-established use | Traditional use |
|---|---|
| Allergic reactions such as rash, pruritis, urticaria, asthma, exanthema and gastrointestinal symptoms such as, nausea, vomiting, abdominal pain, diarrhoea, dyspepsia, heartburn, may occur. The frequency is not known.<br><br>If other adverse reactions not mentioned above occur, a doctor or a pharmacist should be consulted. | Allergic reactions such as rash, pruritis, urticaria, asthma, exanthema and gastrointestinal symptoms such as, nausea, vomiting, abdominal pain, dyspepsia, heartburn, diarrhoea may occur. The frequency is not known.<br><br>If other adverse reactions not mentioned above occur, a doctor or a qualified health care practitioner should be consulted. |

### 4.9. Overdose

| Well-established use | Traditional use |
|---|---|
| No case of overdose has been reported. | No case of overdose has been reported. |

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1. Pharmacodynamic properties

| Well-established use | Traditional use |
|---|---|
| Pharmacotherapeutic group: Analgesics and antipyretics<br>ATC code: N02BG (other analgesics and antipyretics)<br><br>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.<br><br>Antiphlogistic effects of willow bark were studied *in vitro* (hen's egg chorioallantoic membrane test).<br><br>AA and ADP-induced platelet aggregation was decreased in patients receiving willow bark extract.<br><br>Constituents other than salicin may contribute to the overall analgesic effects. | Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC as amended.<br><br>AA and ADP-induced platelet aggregation was decreased in patients receiving willow bark extract. |

### 5.2. Pharmacokinetic properties

| Well-established use | Traditional use |
|---|---|
| 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 oxidised in the blood and liver to salicylic acid.<br><br>Intake of quantified willow bark extract (1,360 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 genitisic acid (4%). Peak levels were reached within 2 hours after oral administration.<br>Peak serum levels of salicylic acid were on average 1.2 mg/l and the AUC was equivalent to that expected from an intake of 87 mg acetylsalicylic acid.<br>Renal elimination occurred predominantly as salicyluric acid. | Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC as amended. |

## 5.3. Preclinical safety data

| Well-established use | Traditional use |
|---|---|
| Tests on reproductive toxicity, genotoxicity and carcinogenicity have not been performed. | Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC as amended, unless necessary for the safe use of the product.<br><br>Tests on reproductive toxicity, genotoxicity and carcinogenicity have not been performed. |

## 6. PHARMACEUTICAL PARTICULARS

| Well-established use | Traditional use |
|---|---|
| Not applicable. | Not applicable. |

## 7. DATE OF COMPILATION/LAST REVISION

7 September 2007