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COMMITTEE ON HERBAL MEDICINAL PRODUCTS (HMPC)

FINAL

COMMUNITY HERBAL MONOGRAPH ON *SALIX*, CORTEX

DISCUSSION IN WORKING PARTY ON COMMUNITY MONOGRAPHS AND COMMUNITY LIST (MLWP)	July 2007 September 2007
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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.], whole or fragmented dried bark	*Salix* [various species including *S. purpurea* L., *S. daphnoides* Vill., *S. fragilis* L.], whole or fragmented dried bark
i) Herbal substance Not applicable	i) Herbal substance Not applicable
ii) Herbal preparation	ii) Herbal preparations
Dry extract (8-14:1) extraction solvent ethanol 70% V/V, 15% total salicin[3].	Dry aqueous extracts (16-20:1; 8-16:1, 16:23-1) Liquid extract (1:1), extraction solvent ethanol 25% V/V Tincture (1:5), extraction solvent ethanol 25% v/v Comminuted herbal substance Powdered herbal substance

3. PHARMACEUTICAL FORM

Well-established use	Traditional use
Quantified herbal preparation in solid dosage form. The pharmaceutical form should be described by the European Pharmacopoeia full standard term.	Herbal preparation in solid or liquid dosage form, or as herbal tea for oral use. The pharmaceutical form should be described by the European Pharmacopoeia full standard term.

[1] The material complies with the Ph. Eur. monographs (ref. 01/2005:1583 corrected and 04/2008: 2312)
[2] The declaration of the active substance(s) for an individual finished product should be in accordance with relevant herbal quality guidance.
[3] 15% total salicin represents an average value. The exact range should be established for each finished product on the basis of the manufacturer's specifications in accordance with the relevant herbal quality guidance.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Well-established use	Traditional use
Herbal medicinal product used for the short-term treatment of low back pain.	Traditional herbal medicinal product used for the relief of: a) minor articular pain b) fever associated with common cold c) headache. 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 *Adults, elderly* The daily dose is 1572 mg dry extract (8-14:1) Not recommended for use in children and adolescents under 18 years of age (see section 4.4 'Special warnings and precautions for use') **Duration of use** If the pain or symptoms persist during the first week of use of the medicinal product, a doctor or a pharmacist should be consulted. Duration should be restricted to a maximum of 4 weeks. **Method of administration** Oral use.	**Posology** *Adults, elderly* Dry aqueous extracts (16-20:1, 8-16:1): 600 mg twice daily Dry aqueous extracts (16-23:1): 480 mg twice daily Liquid extract (1:1): 1 to 3 ml, three times daily Tincture (1:5): 15-24 ml per day Comminuted herbal substance for herbal tea preparation: 1 to 3 g, three to four times daily Powdered herbal substance: 260-500 mg three times daily Contraindicated in children and adolescents under 18 years of age (see section 4.3 'Contraindications') **Duration of use** Indication a) Duration should be restricted to a maximum of 4 weeks. Indication b) After three days a doctor should be consulted. Indication c) If headache persists for more than one day or is recurrent, medical advice should be sought.

	If the symptoms persist during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted. **Method of administration** Oral use.

4.3. Contraindications

Well-established use	Traditional use
Hypersensitivity to the active substance.	Hypersensitivity to the active substance.
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).	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).
Asthma.	Asthma.
Active peptic ulcer disease.	Active peptic ulcer disease.
Third trimester of pregnancy (see section 4.6 Pregnancy and lactation).	Third trimester of pregnancy (see section 4.6 Pregnancy and lactation).
Glucose-6-phosphate dehydrogenase deficiency.	Children and adolescents under 18 years of age because medical supervision should be sought. 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. Reye's syndrome is an extremely rare but life threatening condition, which requires immediate medical attention.
	Severe liver or renal dysfunction, coagulation disorders, gastric/duodenal ulcer and glucose-6-phosphate dehydrogenase deficiency.

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. Reye's syndrome is an extremely rare but life threatening condition, which requires immediate medical attention.	The product is not intended to be used in case of acute arthritis as this condition requires medical advice.
In case of severe liver or renal dysfunction, coagulation disorders, and gastric/duodenal ulcer, the product should only be taken under medical supervision.	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.
	Concomitant use with salicylates and other NSAIDs is not recommended without medical advice.

If pain or symptoms worsen during the first week of use, a doctor should be consulted. 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
The use during the first and second trimester of pregnancy and during lactation is not recommended. Salicylates cross the placenta and appear in breast milk. Contraindicated in the third trimester of pregnancy.	The use during the first and second trimester of pregnancy and during lactation is not recommended. Salicylates cross the placenta and appear in breast milk. 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. 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. 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 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. Antiphlogistic effects of willow bark were studied *in vitro* (hen's egg chorioallantoic membrane test, effects on COX-1, COX-2, HLE and 5-LOX, tests on antioxidant effects) and in vivo (rat paw oedema, air pouch, adjuvant-induced arthritis, writhing-test, Randall-Sellito test, brewer's yeast-induced fever reaction). 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.	Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC as amended. 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 into saligenin (salicyl alcohol) and glucose. Saligenin is oxidized in the blood and liver to salicylic acid. 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 gentisic acid (4%). Peak levels were reached within 2 hours after oral administration. 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. 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. 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

14 January 2009