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Committee on Herbal Medicinal Products (HMPC)

Assessment report on *Ribes nigrum* L., folium

Draft – Revision 2

Based on Article 16d(1), Article 16f and Article 16h of Directive 2001/83/EC (traditional use)

Herbal substance(s) (binomial scientific name of the plant, including plant part)		*Ribes nigrum* L., folium
Herbal preparation(s)		a) Comminuted herbal substance b) Powdered herbal substance c) Dry extract (DER 7:1), extraction solvent water
First assessment	Rapporteur	G. Laekeman/A. Vlietinck
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Note: This draft assessment report is published to support the public consultation of the draft European Union herbal monograph on *Ribes nigrum* L., folium. It is a working document, not yet edited, and shall be further developed after the release for consultation of the monograph. Interested parties are welcome to submit comments to the HMPC secretariat, which will be taken into consideration but no 'overview of comments received during the public consultation' will be prepared on comments that will be received on this assessment report. The publication of this draft assessment report has been agreed to facilitate the understanding by Interested Parties of the assessment that has been carried out so far and led to the preparation of the draft monograph.

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1. Introduction

1.1. Description of the herbal substance(s), herbal preparation(s) or combinations thereof

- Herbal substance(s)

In accordance with the European Pharmacopoeia (11th ed., 07/2013:2528), blackcurrant leaf consists of the dried leaves of *Ribes nigrum* L. (blackcurrant leaf). The leaf is simple, lamina is up to 10 cm long and 12 cm wide, with 3 or 5 rounded triangular lobes, dentate or crenate on the margins, with the median lobe being the largest (European Pharmacopoeia 11th ed., 07/2013:2528).

- Herbal preparation(s)

No official quality standard is available for the herbal preparations included in the monograph. The British Pharmacopoeia (Volume III, 2009) describes a syrup obtained from the fresh ripe fruits of *Ribes nigrum* L., together with their pedicels and rachides. It possesses a strong and characteristic odour.

- Relevant constituents for this assessment report

The dried *Ribes nigrum* leaf contains not less than 1% of flavonoids, expressed as isoquercitroside. The material complies with the monograph of the European Pharmacopoeia 11th ed. (2013).

The most important secondary metabolites present in the herbal substance can be subdivided into several groups of phytochemical compounds.

Phenolic substances, belonging to four phenolic groups – flavanols, hydroxycinnamic acids, flavonols, and flavanones, with flavonols being the most abundant. The major flavonols were present as conjugates of myricetin, quercetin, kaempferol, and isorhamnetin (Wyk & Wink, 2005; Gacnik *et al*., 2024). Among the individual flavanols representatives, epicatechin, catechin and procyanidin dimer were identified in *Ribes nigrum* leaves (Gacnik *et al*., 2024).

Some substances can seasonally appear in the glands of leaves of *Ribes nigrum*. Sakuranetin is a methylated flavanone aglycone (4',5-diOH-7-methoxyflavanone). Its biosynthesis may be useful in the protection against parasites like *Botrytis cinerea* Pers. ex Fr. (Atkinson & Blakeman, 1982).

Hydroxycinnamic acid derivatives: chlorogenic acid and chlorogenic acid derivatives (neochlorogenic acid, cryptochlorogenic acid), caffeic acid, gallic acid, ferulic acid, coumaric acid, salycilic acid, gentisinic acid (Staszowska-Karkut & Materska, 2020).

Prodelphinidins (proanthocyanidines) were identified in a methanolic extract of the leaves. They may be responsible for the anti-inflammatory properties of the herbal preparations (Tits *et al*., 1992a, 1992b).

The presence of glycerolipids has been reported. The total fatty acid composition was unusual, because the following unsaturated fatty acids were identified: linolenic acid (alpha-18:3), together with cis-7, 10, 13-hexadecatrienoic acid (16:3) and lower amounts of stearidonic acid (18:4) and gamma-linolenic acid (gamma-18:3). This makes the lipid composition type mixed: typical of 16:3 plants but also partially typical for 18:4 plants (Dobson, 2000).

The essential oil of the leaves of *Ribes nigrum* contains mainly monoterpenic substances like alphapinene, myrcene, p-cymene, limonene, beta-ocimene, beta-phellandrene, linalool, terpinen-4-ol, geraniol, citronellylacetate. Furthermore, the sequiterpenes caryophyllene and humulene were identified, as well as methyl salicylate (Andersson *et al*., 1963).

Maximum content of Ca, Mg, Fe, Al, Cr and K in the blackcurrant leaves is detected in the month of June (Nour *et al*., 2014). Other elements detected in *Ribes nigrum* leaves are P, N, B, Na, Mn and Cu (Staszowska-Karkut & Materska, 2020).

The potassium-sodium ratios in the leaf of *Ribes nigrum* L. and decoctions of the leaves were 128:1 and 242:1 respectively. These ratios are considered as eventually contributing to the diuretic effect (Szentmihályi *et al*., 1998).

1.2. Search and assessment methodology

☒ Scientific/Medical/Toxicological databases

An extensive research using the terms "*Ribes nigrum* + leaf" and or "blackcurrant + leaf" has been carried out in Pubmed, Embase, Web of Science and Cochrane library from September 2016 to June 2025. This search returned 57/64, 50/45, 90/56, and 0/0 bibliographic references, respectively.

☒ Pharmacovigilance databases

☒ data from EudraVigilance

☐ from other sources (e.g., data from VigiBase)

☐ Other

Books

☒ Several books (e.g. PDR for Herbal Medicines, Hagers Handbuch) were also consulted.

Regulatory practice

☒ Old market overview in AR (i.e., check products fulfilling 30/15 years of TU or 10 years of WEU on the market)

☒ Market overview (including pharmacovigilance actions taken in member states)

☒ PSUSA

☒ Feedback from experiences with the monograph during MRP/DCP procedures

☒ Ph. Eur. monograph

☐ Other

Consistency (e.g., scientific decisions taken by HMPC)

☒ Public statements or other decisions taken by HMPC

☒ Consistency with other monographs within the therapeutic area

☐ Other

1.3. Main changes introduced in the second revision

The monograph and the assessment report have been harmonised with other monographs in the same therapeutic area. This includes the indication, contraindication and warning sections. To be in line with the monographs of other herbal substances with a similar scope of diuretic use, the indication was expressed in the same way: "Traditional herbal medicinal product for the relief of symptoms associated with mild urinary tract symptoms in addition to the general recommendation of adequate fluid intake to increase urine volume. The product is a traditional herbal medicinal product for use in certain indications based exclusively on long-term use". Several new references have been added to the assessment report, mainly regarding chemical composition and non-clinical studies.

2. Data on medicinal use

2.1. Information about products on the market

2.1.1. Information about products on the market in the EU/EEA Member States

Information on medicinal products marketed in the EU/EEA

Table 1. Overview of data obtained from marketed medicinal products.

Herbal substance/ preparation	Indication	Posology and method of administration	Regulatory status
Ribes nigrum L., folium Dry extract (extraction solvent water; DER: 7:1)	a) Traditionally used to treat minor articular pain. b) Traditionally used to support renal and digestive elimination systems.	Herbal preparations in solid dosage form: hard capsule Method of administration: oral use Posology: adults only Single dose: 169 mg of extract/hard capsule Daily dose: 169 mg of extract/hard capsule 1 to 3 times daily Duration of use: a) 4 weeks b) 2-3 weeks	France, TUR From 1990 until 2011 it was registered in France as a medicinal product. Currently there are no medicinal products authorised/registered in France containing *Ribes nigrum* L., folium as dry extract as monocomponent.
Ribes nigrum L., folium Powdered herbal substance	a) Traditionally used in the symptomatic treatment of minor painful joint conditions. b) Traditionally used to promote urinary and digestive elimination functions.	Herbal preparations in solid dosage form: hard capsule Method of administration: oral use Posology: adults only Single dose:1 hard capsule contains 340 mg of powder Daily dose:1 hard capsule 3 times daily Max dose: till 5 hard capsules if necessary	TUR use in France since 1987

		Duration of use: a) 4 weeks b) 2-3 weeks	
Ribes nigrum L., folium Powdered herbal substance	a) Traditional herbal medicinal product for relief of minor articular pain. b) Traditional herbal medicinal product to increase the amount of urine to achieve flushing of the urinary tract as an adjuvant in minor urinary complaints.	Herbal preparations in solid dosage form Method of administration: oral use Posology: adults only Single dose: 1 hard capsule contains 340 mg of powder Daily dose: 3 capsules per day, 1020 mg Duration of use: a) and b) 2 to 4 weeks	Spain It was registered by former registration scheme in January 1992. TUR since May 2009, according to article 16 of Directive 2001/83 was granted.
Ribes nigrum L., folium Comminuted herbal substance	Traditionally used as an aid in mild rheumatic complaints.	Herbal preparations for infusion as herbal tea Method of administration: oral use Posology: adults only Single: 2 to 4 g pour with 200mL of boiling water, infuse under cover for 10-15 min. Drink freshly prepared infusion 3 times a day. Duration of use: 4 weeks	TUR use in Poland since 1978

This overview is not exhaustive. It is provided for information only and reflects the situation at the time when it was established.

Information on relevant combination medicinal products marketed in the EU/EEA

Not applicable.

Information on other products marketed in the EU/EEA (where relevant)

Not applicable.

2.1.2. Information on products on the market outside the EU/EEA

Not applicable.

2.2. Information on documented medicinal use and historical data from literature

Indications exclusively in folk medicine for the *Ribes nigrum* leaf are: arthritis, rheumatic complaints, diarrhoea, spasmodic cough as well as it has been traditionally used as an infusion to cure joint complaints (traditionally classified as 'rheumatism') (Wichtl, 1994; Gruenwald *et al*., 2000; Wyk and Wink 2005).

Ribis nigri folium is also described in folk medicine as a diuretic, eliminating uric acid. The preparations mentioned are aqueous decoctions (Hänsel *et al*., 1994).

Rarely preparations of *Ribis nigri* folium were locally applied on wounds (Wichtl, 1994; Gruenwald *et al*., 2000; Kendir *et al*., 2019), as well as the leaves were applied on the head against migraine (Decaux, 1930).

Table 2. Overview of historical data.

Herbal substance/ preparation	**Documented use / Traditional use**	**Posology and method of administration**	**Reference and date of the reference**
Comminuted herbal substance	Traditional diuretic. Leaves are taken in cases of rheumatism and urinary problems	As a tea, 2-4 g of finely chopped leaves taken several times a day	Wyk and Wink, 2005
Comminuted herbal substance	Usage based on tradition in folk medicine: as diuretic, uses for gout, rheumatic complaints, diarrhoea, spasmodic cough.	Single dose: 2-4 g of finely cut dried leaf, pour boiling water over and steep for 5-10 minutes and then strain. 1 cup several times daily.	Wichtl, 1994
Comminuted herbal substance	Usage based on tradition in folk medicine: arthritis, gout and rheumatism, diarrhoea, colic, jaundice and liver ailments, painful micturition, urinary stones, convulsive coughs and whooping cough.	Single dose: 2-4 g of black currant leaves in boiling water (150 mL) for the tea, strain after 15 min. preparation. Daily dosage: 1 cup to be drunk several times a day.	Gruenwald *et al*., 2000
Leaves	To increase the amount of urine. Other usages based on tradition in folk medicine: arthritis,	Single dose: 2-4 g /150 mL in boiling water over and steep for 10 min and then strain.	Hänsel *et al*., 1994

Herbal substance/ preparation	Documented use / Traditional use	Posology and method of administration	Reference and date of the reference
	gout and rheumatism, diarrhoea, colic, jaundice and liver ailments, painful micturition, urinary stones, convulsive coughs and whooping cough.	Daily dosage: 1 cup of freshly prepared infusion to be drunk several times a day. To be taken away from meals.	
Comminuted herbal substance or equivalent preparations Powdered herbal substance Dry extract (7:1, water)	For minor articular pain and minor urinary complaints (as a diuretic)	Dry extract (7:1, water), Single dose: 169 mg per capsule. Daily dosage: 3 capsules daily. Powdered herbal substance Single dose: 340 mg per capsule. Daily dosage: up to 5 capsules daily. Infusion as herbal tea of dried leafs: 2-4 g per cup (150 mL). Daily dosage: 3-4 times daily. Fluid leaf extract (1:1) Single dose: 5 mL Daily dosage: 2 daily	Barnes *et al*., 2007

2.3. Overall conclusions on medicinal use

Table 3. Overview of evidence on period of medicinal use.

Herbal substance/ preparation	Indication	Posology and method of administration	Period of medicinal use
Comminuted herbal substance	Traditionally used as an aid in mild rheumatic complaints	Herbal preparations for infusion as herbal tea	TUR use in Poland since 1978

		Posology: adults only Dose: 2 to 4 g in 200 mL of boiling water, infuse for 10-15 min. Drink freshly prepared infusion 3 times a day. Daily dose: 6-12 g Method of administration: oral use Duration of use: 4 weeks	
Powdered herbal substance	a) Traditionally used in the symptomatic treatment of minor painful joint conditions. b) Traditionally used to promote urinary and digestive elimination functions.	Posology: Single dose: 1 hard capsule contains 340 mg of powder 3 times daily; till 5 hard capsules if necessary Daily dose: 1020-1070 mg Method of administration: oral use Duration of use: a) 4 weeks b) 2-3 weeks	TUR use in France since 1987 (and TUR use in Spain since 2009)
Dry extract (extraction solvent water; DER: 7:1)	a) Traditionally used in the symptomatic treatment of minor painful joint conditions. b) Traditionally used to promote urinary and digestive elimination functions.	Herbal preparations in solid dosage form: hard capsule Posology: adults only Single dose: 169 mg[1] of extract/hard capsule 1 to 3 times daily Daily dose: 170-510 mg Method of administration: oral use	TUR in France in the period 1990-2011; Herbal Medicines, 2013

		Duration of use: a) 4 weeks b) 2-3 weeks	

Clinical safety for preparations that fulfil the criteria of medicinal use throughout a period of at least 30 years, including at least 15 years within the EU/EEA, i.e., traditional medicinal use based on Article 16d(1), Article 16f and Article 16h of of Directive 2001/83/EC is further evaluated in chapter 5 'Clinical Safety/Pharmacovigilance'. The non-clinical safety is evaluated in chapter 3 'Non-clinical data'.

According to the information provided by the National Competent Authorities in the overview of the marketed products (see table 1), medicinal products, containing *Ribes nigrum* L., folium, have been available for 30 years in the markets of France, Poland and Spain therefore fulfilling the criteria of traditional use in EU in accordance with Directive 2004/24/EC.

Herbal tea (2-4 g up to 3 times daily) has been used since 1978 in Poland for minor rheumatic complaints and can be accepted according to the 30 years of use stipulated in Directive 2004/24/EC.

Powdered herbal substance in capsules has been marketed in France (since 1987) and in Spain (since 1992) in different posologies (France: 340 mg up to 5 capsules per day; Spain: 340 mg 3 times daily). The period of use fulfils the 30 years of traditional use as stipulated in Directive 2004/24/EC, therefore, this preparation can be included in the monograph.

A herbal medicinal product containing dry extract (7:1; extraction solvent water) of black currant leaves as the only active substance has been marketed in France from 1990 to 2011 in the form of capsules (169 mg per capsule; posology: up to 3 capsules daily) for the relief of minor articular pain and to support renal and digestive elimination systems. The use of the same herbal preparation with the same posology is also described in books for minor articular pain and as a diuretic (Herbal Medicines, 2013). The dry extract was included in the HMPC monograph after the first revision since it meets the 15-year tradition in Europe, and based on the following justification:

- The extract is made with water, a procedure comparable to herbal tea preparations.
- The drug-extract ratio is 7 to 1 and 169 mg is taken as a single dose up to 3 times a day. One capsule corresponds to 1183 mg of herbal substance. For herbal tea, 2 to 4 g herbal substance is infused; virtually, more material can be extracted by preparing the herbal tea. The number of daily doses is similar for the extract and the infusion.

Thus, this preparation is kept in the monograph after the second revision.

The use of leaves of *Ribes nigrum* in children and adolescents under 18 years of age is not recommended due to lack of data.

Because the HMPC could not find a suitable indication for the traditional use "to support digestive elimination", this use was not included in the monograph.

The following indications for *Ribes nigrum* L., folium are proposed for the EU herbal monograph:

Traditional herbal medicinal product based upon long-standing use

Indication a): Traditional herbal medicinal product for relief of minor articular pain.

Adults and elderly:

- Comminuted herbal substance for infusion as herbal tea preparation

Single dose: 2 to 4 g per cup, 3 times daily.

Daily dose: 6–12 g.

- Dry extract (DER 7:1, water)

Single dose: 170 mg, 1–3 times daily.

Daily dose: 170–510 g.

- Powder in hard capsule

Single dose: 340 mg, 3–5 times daily.

Daily dose: 1020–1700 mg (3–5 hard capsules per day)

Duration of use: 4 weeks

Indication b): Traditional herbal medicinal product for relief of symptoms associated with minor urinary tract complaints in addition to the general recommendation of a sufficient fluid intake to increase the amount of urine

Adults and elderly:

Herbal preparations in solid dosage form: hard capsule

- Dry extract (DER 7:1, water)

Single dose: 170 mg, 1–3 times daily.

Daily dose: 170–510 g.

- Powder in hard capsule,

Single dose: 340 mg, 3–5 times daily

Daily dose: 1020–1700 mg (3–5 hard capsules per day)

Duration of use: 2 weeks

3. Non-Clinical Data

3.1. Overview of available pharmacological data regarding the herbal substance(s), herbal preparation(s) and relevant constituents thereof

3.1.1. Primary pharmacodynamics

Analgesic effects

Ethanolic extracts

In vivo studies:

Mongold *et al*., (1993, only abstract available) reported that a *Ribes nigrum* L., folium extract (500 g dried leaves immersed in 15% ethanol/water in 5 L for 10 days, then filtered and lyophilised) given i.p. induced an analgesic effect in the acetic-induced writhing test in mice (ED_{50} value of 61.5 mg/kg, compared with an ED_{50} value of 132 mg/kg for paracetamol [acetaminophen]), but was not active in the hot-plate stimulus test.

Anti-inflammatory activity

Ethanolic extracts

In vivo studies:

Anti-inflammatory activities with the same extract were observed by Mongold *et al.* in rats*,* (1993) using several *in vivo* models:

- in the carrageenan-induced acute inflammation model *Ribes nigrum* L., at a doses of 50 and 100 mg/kg i.p.demonstrated dose-dependent inhibition of acute inflammatory oedema, and the effect of 100 mg/kg dose was comparable to indomethacin (5 mg/kg, i.p.);
- cotton pellet granuloma, at a dose of 150 mg/kg i.p. the extractreduced granuloma formation of 18.6%, value comparable to that of indometacin 3 mg/kg i.p. (24%);
- Freund adjuvant induced arthritis, the extract at doses of 150 mg/kg and 300 mg/kg i.p.expressed dose-dependent reduction of hind-paw oedema.

A dry extract of *Ribes nigrum* L., folium (maceration of 60 g blackcurrant leaves with 1000 mL of 14% ethanol; 1 mL/kg and 10 mL/kg, p.o.) demonstrated anti-inflammatory activity by the inhibition of carrageenan-induced inflammation compared to reference compounds indomethacin and niflumic acid in acute and chronic studies in Sprague-Dawley rats (Declume *et al.,* 1989).

In vitro studies:

Anti-inflammatory activity of fresh *Ribes nigrum* L., folium dry extract (extraction solution: acetone/water/acetic acid (70:28:2)) was tested on the total myeloperoxidase (MPO, dose 50 ng/mL) released by activated neutrophils measured by an ELISA assay. The higher concentration (1 mg/mL) of *Ribes nigrum* L., folium dry extract gave about 15-20% of inhibition. MPO inhibition was also observed in a Specific Immunological Extraction Followed by Enzymatic Detection assay, *Ribes nigrum* L., folium extract showed a significant dose-dependent inhibition: the lowest a concentration tested, 0.5 µg/mL for leaf dry extract, showed 60% inhibition (Tabart *et al.*, 2012).

Ribes nigrum L., folium extract (containing 60% of proanthocyanidins of the total polyphenol content) increased the CD39-positive endothelial cell fraction in a concentration-dependent manner (for the 2.5 µg/mL it increases up to 10%; for 15 µg/mL up to 33%). It also enhanced endothelial nitric oxide synthase (eNOS) activation. T495 phosphorylation was decreased by 31±6% for the dose of 2.5 µg/mL and 48±6% for 15 µg/mL, whereas S1177 phosphorylation increased by 13±3% for the dose of 2.5 µg/mL and 18±7% for 15 µg/mL compared to untreated cells (Luzak *et al.,* 2014).

The anti-inflammatory effects of an ethanolic extract of *Ribes nigrum* L. leaves (0.125 mg/ml) was investigated on murine BV-2 microglial *Wt* and Acyl-CoA oxidase 1 deficient (*Acox1*$^{-/-}$) cell line models by evaluating the level of nitric oxide (NO) production and the expression of iNOS gene in the absence or the presence of lipopolysaccharide (LPS, 1 µg/ml). The treatment with the extract alone did not have any influence on NO production in both BV-2 cell lines. In both cell lines, the extract reduced the LPS-induced NO level, with a more pronounced effect in the *Acox 1*$^{-/-}$ BV-2 cell line. NO is a signaling molecule involved in acute and chronic inflammation processes in the nervous system as well as on apoptosis. In addition, the extract significantly attenuated the LPS-induced iNOS mRNA level increase in both cell lines. Finally, the extract limited the increased mRNA levels of TNF-α and the IL-1β gene expression induced by LPS, demonstrating a downregulation of pro-inflammatory gene expression (Minasyan *et al*., 2025).

The potential effects of *Ribes nigrum* L. leaves on inflammatory skin disorders was investigated in a model of human keratinocytes (HaCaT) challenged with TNF-α, either alone or in combination with the costimulatory cytokines IFN-γ (5 ng/mL) or IL-4 (100 ng/mL). A dry extract (extract to drug ratio 1:3) obtained from the aqueous extraction of *Ribes nigrum* L. leaves (RNLE) increased IL-10 expression in TNF-α (Tumor Necrosis Factor)-induced human keratinocytes (HaCaT). The extract at 100 µg/ml inhibited TNF-α/IFN-γ- but not TNF-α-induced IL-8 release in HaCaT cells. RNLE (25–50 µg/mL) totally

abrogated TNF-α/IFN-γ-induced IL-6 release in these cells. RNLE (25–50 µg/mL) inhibited both TNF-α- and IFN-γ-induced s-ICAM-1(Intercellular Adhesion Molecule 1) release. Nevertheless, this effect was displayed in a concentration-dependent fashion with a preferential impairment of IFN-γ versus TNF-α challenge. The activity of NF-κB was impaired by a concentration of RNLE a slow as 25 µg/ml underTNF-α/IFN-γ stimulation; on the contrary, the extract was unable to counteract NF-κB activity under TNF-α stimulation. RNLE up to 50 µg/ml was not able to inhibit TNF-α/IL-4-induced IL-6 release in differentiated HaCaT cells, suggesting a marginal impact of RNLE on IL-4 signaling. Finally, in these cells, RNLE 50 µg/ml inhibited TNF-α/IL-4-induced TSLP release, a type-2 cytokine involved in atopic inflammation through the activation of dendritic and ILC2 cells. Quercetin and kaempferol (0.5 and 1 µM) preferentially inhibited IFN-γ-induced sICAM-1 release in HaCaT cells in a concentration-dependent fashion, thus resembling the activity of RNLE (Magnavacca *et al*., 2021).

Isolated constituents

In vitro studies:

The effects of proanthocyanidins (PACs), isolated from blackcurrant leaves on neutrophil accumulation during inflammatory processes were investigated in LT2 cell line originating from human umbilical vein endothelium cells. A proanthocyanidin-enriched fraction was obtained from leaves from *Ribes nigrum* with acetone extraction (70% V/V in water). Purification was done on reversed phase chromatography. A significant inhibition of TNF-α stimulated ICAM-1 expression but not IL-8 and VEGF155 mRNA expression was observed with proanthocyanidins in concentrations from 10 µg/mL to 60 mg/kg (Garbacki *et al.,* 2005).

An *in vitro* decrease of PGE2 production in human Chondrocytes was also observed with prodelphinidines, obtained from the *Ribes nigrum* L., folium, A concentration of 10^{-4}M of gallocatechin and its dimer inhibited the formation of prostaglandins comparable with indomethacin 10^{-5}M: 53%, 57% and 67% respectively. Further, the selectivity on COX-2 inhibition was confirmed (Garbacki *et al.*, 2002).

Ex vivo studies:

An anti-inflammatory activity on isolated rabbit hearts was reported for rutin and isoquercitrin, obtained from the *Ribes nigrum* L., folium (Chanh *et al*., 1986).

In vivo studies:

Anti-inflammatory effects of proanthocyanidins (PACs) were observed in rat's models of carrageenan induced paw oedema and carrageenin-induced pleurisy. Pre-treatment with PACs (10, 30, 60 and 100 mg/kg, i.p.) reduced in a dose time dependent manner paw oedema induced by carrageenin and also inhibited carrageenin-induced pleurisy in rats: particularly reducing lung injury, pleural exudate formation, polymorphonuclear cell infiltration, pleural exudate levels of TNF-α, IL-1β and CINC-1, pleural exudate levels of nitrite/nitrate (NOx). The mechanism of action of the PACs differs from that of indomethacin. Indomethacin treated rats showed that a low the volume of pleural exudate, and a reduced content in leukocytes and in TNF-α, IL-1β, IL-6 and IL-10 but not in NOx (Garbacki *et al.*, 2004).

Garbacki *et al.*, (2005) observed anti-inflammatory activities of proanthocyanidin-enriched fraction (PACS) of *Ribes nigrum* L., folium (the extraction solvent was acetone 70% V/V in water purification by reversed phase chromatography) in Wistar rats with a dose of 10, 30 and 60 mg/kg/per animal. The following effects were observed:

- a dose-dependent inhibition of the carrageen-induced pleurisy by reducing pleural exudate formation and PMNs infiltration;
- leukocyte cell adhesion molecules mobilization was not down-regulated on granulocytes;

- a decrease in the production of endothelial cell adhesion molecules on the lung sections.

Rodelphinidins (5, 10, 40 and 60 mg/kg) isolated from of dried *Ribes nigrum* L., folium extract demonstrated anti-inflammatory activities in a rat carrageenan paw oedema model by reducing paw oedema 18% for 5 mg/kg; 40% -10 mg/kg and 55% - 40 mg/kg, whereas reference compounds indomethacin 4 mg/kg reduced it by 44% and aspirin 200 mg/kg by 47% (Tits *et al.*, 1991).

Diuretic activity

Ethanolic extracts

In vivo studies:

The diuretic and salidiuretic action of *Ribes nigrum* leaves was evaluated *in vivo* and compared to that of furasemide. The intervention consisted of oral administration of a fluid extract (extraction solvent was ethanol; 1:1) of blackcurrant leaf in rats. The diuretic action of an equivalent of 1500 mg dried leaf/kg was comparable to the effect of furosemide at 50 mg/kg. The salidiuretic effect (sodium and potassium) was higher than the effect of furosemide at 20 mg/kg but lower compared to furosemide at 40 mg/kg. (Rácz- Kotilla & Rácz 1977).

Table 4. Overview of the main non-clinical data.

Herbal preparation tested	**Concentration/ Dosage**	**Animal species/ Experimental model**	**Reference**	**Main outcome(s) according to the authors**
Ribes nigrum L., folium extract, extraction solvent: 15% ethanol, lyophilised	Writhing induced by acetic acid.	*In vivo*: Swiss mice Writhing induced by i.p. injected acetic acid solution, *Ribes nigrum* folium extract given as a single i.p. injection before acetic acid injection. Paracetamol used as an active comparator. ED_{50} estimated: the dose of the drug that reduced by 50% the number of mice exhibiting writhing compared to the control animals.	Mongold *et al*., 1993	The analgesic effects demonstrated in Writhing induced by acetic acid test; the lyophilisate showed an ED_{50} of 61.5 mg/kg, paracetamol administered to the control group produced a higher ED_{50} value, equal to 132 mg/kg.
Ribes nigrum L., folium dry extract, extraction solvent: 14% ethanol, lyophilised	Extract 1 mL/kg and 10 mL/kg, p.o. In chronic studies (21 and 28 days oral treatment) *Ribes nigrum* L., folium extract at the dose of 0.33, 1 and 10 mL/kg.	*In vivo*: Plethysmometric measurements in Sprague-Dawley rats – extract was given p.o. 30 minutes before carrageenan injection.	Declume *et al*., 1989	*Ribes nigrum* L., folium extract (1 and 10 mL/kg) dose-dependently (30% and - 54%, respectively) reduced rat paw

				oedema after 4h, compared to indomethacin (for 2.5 mg/kg was 63% and 5 mg/kg - 66%) and niflumic acid (25 mg/kg was 19% reduction and 50 mg/kg was 70%). In chronic studies at the dose of 0.33, 1 and 10 mL/kg the reduction of oedema was 30%, 42.5% and 46%, respectively, for indomethacin (1.66 mg/kg) it was 49% and niflumic acid (12.5 mg/kg) reduction was 53%.
Ribes nigrum L., folium dry extract, extraction solvent: 15% ethanol, lyophilised	a) The carrageenan-induced paw oedema: Ribes extract 50 and 100 mg/kg i.p. or indomethacine (5 mg/kg). b) Cotton pellet granuloma: *Ribes* extract 150 mg/kg i.p. or indomethacine (3 mg/kg), i.p.. c) Freund adjuvant induced arthritis: *Ribes* extract 150 and 300 mg/kg i.p. or indomethacine (3 mg/kg), i.p.	*In vivo*: Wistar rats a) carrageenan-induced acute inflammation; b) cotton pellet granuloma; c) Freund adjuvant induced arthritis *In vivo*: Rats	Mongold *et al*., 1993	The anti-inflammatory activity demonstrated by the inhibition of carrageenan-induced acute inflammation, (paw oedema after 3 hours was reduced 70% by the extract 100 mg/kg and 77% by indomethacin); cotton pellet granuloma (weight of granuloma on day 8 was reduced 18.% by the extract 150 mg/kg and 24% by indomethacin 3 mg/kg); Freund adjuvant induced arthritis (paw volume was reduced by 18.7% for the extract 150 mg/kg, 34.6% by the extract 300 mg/kg and 37.7% by indomethacin 3 mg/kg

Ribes nigrum L., folium liquid extract (Extraction solvent: ethanol; DER 1:1)	Diuretic quotient = 1.56 when 50 mL fluid extract are given in dilution of 3 %/kg body weight.		Rácz-Kotilla & Rácz, 1977	The diuretic effect of an equivalent of 1500 mg/kg dried *Ribes nigrum* L., folium was comparable to the effect of furosemide at the dose of 50 mg/kg; the salidiuretic effect (sodium and potassium) was higher than the effect of furosemide at 20 mg/kg but lower compared to furosemide at 40 mg/kg

Assessor's comment:

Ribes nigrum leaves, mainly as ethanolic extracts, have shown anti-inflammatory activity both in vivo and in vitro; an analgesic effect has been also oberserved, but has not been studied for oral use of Ribes nigrum leaves. Diuretic effect was observed with an ethanolic extract of Ribes nigrum leaves in a very old in vivo study with limited information on the methodology. Studies with preparations included in the monograph are missing. In conclusion, primary PD data available are not relevant in relation to the herbal preparations accepted in the monograph.

3.1.2. Secondary pharmacodynamics

Anthelmintic activity

The development of free-living larvae (*Oesophagostomum dentatum)* was significantly inhibited by *Ribes nigrum* L., folium extract (acetone/water, 3:7) at different concentrations (125, 250, 500 and 1000 µg/mL) (Williams *et al.,* 2014).

Cytotoxic activity

The available *in vitro* studies did not show any cytotoxic effect on normal cells, such as endothelial and microglia cells (Tabart *et al.*, 2012; Ginovyan *et al*., 2022), whilst no studies were available on other CNS cells, cardiomyocites, hepatocytes or bronchial epithelial cells. Cytotoxicity was only observed with an aqueous extract of *Ribes nigrum* leaf on peripheral blood mononuclear cells (CC_{50} of 0.5 ± 0.3 mg/mL); the extract did not affect the proliferative status of human lymphocytes (Haasbach *et al*., 2014).

Antiviral effect

Antiviral activity of a water extract (DER not specified) of *Ribes nigrum* L., folium (0–1 mg/mL) against influenza A virus *in vitro* was observed when the virus was pre-incubated prior to infection or when added directly after infection, however with no antiviral effect when infected cells were treated 2, 4, or 8 h after infection, indicating that the extract blocks a very early step in the virus infection cycle. *In vivo* (the C57BL/6 mouse infection model) study showed that intranasal application of the extract (500 µg) inhibits progeny virus titters in the lung up to 85% after 24 h (Haasbach *et al.*, 2014). Ehrhardt *et al.,* 2013 tested a water extract (DER not specified) of *Ribes nigrum* L., folium against influenza A viruses infections *in vitro* and *in vivo*. The extract inhibited Influenza A virus replication in a

concentration dependent (50, 100 or 200 µg/mL) manner in human alveolar type II epithelial cell line A549 model. The extract did not exert any significant negative effects on cell proliferation or survival, and did not alter transcription or translation processes (Ehrhardt *et al.*, 2013). *Ribes nigrum* L., folium extract (50 and 100 µg/mL) was tested on the A549 cells using MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazoliumbromide] - Cell Proliferation Assay that is based on an enzymatic reaction of the mitochondrial succinic dehydrogenase. The extract did not affect the cell morphology and viability and did not interfere with cellular proliferation and metabolism (Ehrhardt *et al.*, 2013).

In *in vivo* study, BALB/c mice were infected with a sub-lethal dose of influenza virus A/FPV/Bratislava/79 (H7N7). Further animals were exposed to the same extract as *in vitro* studies: 2 bar of aerosolized extract of *Ribes nigrum* L., folium (prepared from the 10 and 15 mg/mL of stock solutions) at the dose of 1.5 mL/per mouse for 10 min twice a day for three (lung titter) or five (body weight) consecutive days twice a day by using the COAALA Mouse Aerosol Application System. The results showed a reduction of virus titters in the lung of infected animals already at the day three of infection (Ehrhardt *et al.*, 2013).

Antihypertensive effect

The model used was the antihypertensive effect on anesthetized cats. Blood pressure was measured manometrically in the carotid artery. The normal blood pressure of the cats was strongly affected by doses of aqueous extract equivalent to of 400 mg dried blackcurrant leaf/kg: the hypotensive factor obtained at a dose of 400 mg/kg body weight is 4.50 and exceeds the values of tolazoline (0.75–1.00 mg/kg body weight). The antihypertensive effect obtained in animals treated with i.v. norepinephrine was also strongest with *Ribes nigrum*. The antihypertensive factor value is 1.82 after administration of 400 mg/kg body weight of liquid extract and is similar to the values obtained after using tolazoline (0.75–1.00 mg/kg body weight) under the same conditions. The duration of the antihypertensive effect (15–20 minutes) is longer than that of the comparator substance (5 minutes) (Rácz-Kotilla & Rácz 1977).

In another study normotensive rats were used. An infusion of blackcurrant leaf (20 g/L) was administered intravenously at a dose equivalent to 360 mg dried leaf per kg. There was a 45% fall in blood pressure, which after 30 minutes was still 30% (Laserre *et al.*, 1983).

Effect on cerebral ischemia and energy production by mitochondria

Antihypoxic activity of an ethanolic extract of blackcurrant leaves was assessed on models of hypobaric, hypercapnic, histotoxic, hematotoxic hypoxia after a course of 14 days oral administration at a dose of 100 mg/kg to ten Balb/c male mice. *Ribes nigrum* had no significant effect on the lifespan of animals under hypobaric hypoxia, hypercapnic hypoxia. In conditions of histotoxic hypoxia, the use of *Ribes nigrum* extract contributed to an increase in the lifespan of mice in comparison with the negative control (NC) group of animals by 166.5%. In modeling hemic hypoxia, the use of the extract contributed to an increase in the life expectancy of animals in relation to the NC group of mice by 116.3%. The anti-ischemic activity was studied in the focal cerebral ischemia model; the extract was administered *per os* after the reproduction of cerebral ischemia for 4 days at a dose of 100 mg/kg to ten Wistar male rats. In the presence of cerebral ischemia, the use of extract of *Ribes nigrum* contributed to a 42.5% decrease in the necrosis zone of the brain tissue in relation to the NC group. Against the background of the use of *Ribes nigrum* extract in rats compared to the NC group of animals, a 2.9 times decrease in serum lactate content was observed, followed by an 1.74 times increase in the serum level of pyruvate and a 1.33 times increase in ATP production in brain tissue respectively (all $p<0.05$).

The introduction of *Ribes nigrum* extract into animals relative to the NC group of rats showed an increase in the general ATP-generating activity *in vitro* in brain tissue, the maximum level of

respiration, respiratory capacity, glycolytic capacity and glycolytic reserve by 2 times, 3.62 times, 2.17 times, 2.97 times and 4.51 times, respectively, while the intensity of glycolysis decreased by 69% (Pozdnyakov *et al.*, 2019).

Anti-obesity effect

The potential anti-obesity effect of blackcurrant extract, specifically its hydro-ethanolic leaf extract (BC-HLE), in comparison to quercetin (QUE). Six groups of six male Wistar rats were randomly assigned to different diets for 12 weeks: Standard, high-fat diet (HFD, 45% fat), HFD + BC-HLE (41 or 50 mg dry matter/kg) and HFD + QUE (0.9 or 50 mg/kg). HFD rats developed a moderate obesity, associated with a gut dysbiosis and a change in their total antioxidant capacity. The increase in body weight gain was prevented only by the low dose of BC-HLE and the high dose of QUE. The impaired glucose tolerance by HFD was attenuated by the low dose of QUE. Hepatic glutathione peroxidase activity was increased in the HFD group and only BC-HLE supplementation counteracted this change. The low BC-HLE dose tended to reduce the HFD-induced gut dysbiosis (Bréger *et al*., 2024).

Wound healing effect

An ointment containing 1% of a dry methanolic extract of powdered *Ribes nigrum* leaves (extraction yield 22.80% w/w) was prepared using the base of an ointment marketed in Turkey, which contains 1% of *Triticum vulgare* Vill. (Poaceae) extract as the active ingredient, which was used as a reference ointment. This base consists of polyethylene glycol, liquid paraffin, cetostearyl alcohol, glycerin and sorbitol. The ointments (0.5 g) were daily applied onto the incised wounds on dorsal parts of SD rats during 10 days and excised wounds on dorsal parts of male Swiss albino mice during 15 days. The healing activity results on incisional wounds showed that *Ribes nigrum* extract significantly increased wound breaking strength after 10 days with the values of 5754±463.6 Pa compared with 2806 ± 146.6 for the reference ointment ($p<0.001$). In parallel with the incisional wound model, significant reduction in the areas were determined for the wounded tissues treated with the ointment prepared from *R. nigrum* (1.67 ± 0.79 mm^2) extract on the 15^{th} day against 8.54 ± 1.82 mm2 for the reference ointment. Histopathological examination results were consistent with the results obtained in excision and incision wound models in terms of ulceration, re-epithelization, proliferation of fibroblasts and collagen, mono/polymorphonuclear cells and angiogenesis. Subsequently, *R. nigrum* extract, which exhibited the highest wound healing effect according to the bioactivity screening studies, was separated into subextracts by fractionation with DCM, EtOAc and BuOH. In wound healing efficacy studies on the subextracts, it was determined that EtOAc subextract was found to exhibit wound healing effect by providing the highest breaking strength (5894.1 ± 415.6 Pa) in the incision wound model against 4609.01 ± 277.9 Pa for the reference ointment. Moreover, EtOAc subextract of *R. nigrum* was found to have significant effect in the excisional wound model with a wound area of 0.17mm^2 on the 15^{th} day in comparison to 2.33 ± 0.82 mm^2 for the base ointment (Kendir *et al*., 2019).

Assessor's comment:

Effects reported but not related to the indications proposed for the Ribes nigrum L. folium in the monograph are antioxidative effects, antimicrobial activity, antiviral activity, effect on energy production by mitochondria, anti-obesity effect, hypoglycaemic effect and wound-healing effect. It is not known if the antihypertensive effect found in cats is (partly) is related to the diuretic effect of Ribes nigrum, leaf.

None of the reported non-clinical pharmacological studies described indicate a cause for safety concern for the Ribes nigrum L., folium.

3.1.3. Safety pharmacology

No data available.

3.1.4. Pharmacodynamic interactions

No data available.

3.1.5. Conclusions

Anti-inflammatory, analgesic, diuretic and antioxidative effects of *Ribes nigrum* L., folium extracts and isolated constituents (flavonoids, proanthocyanidins including prodelphinidines) have been demonstrated in the experimental models *in vitro, ex vivo* and *in vivo*. The preparations tested consisted mainly of alcoholic liquid extracts, which were mostly lyophilised. They were administered per orally as well as intraperitoneally.

Several inflammatory parameters have been reported reversed, especially the formation of oedema and the cellular components as illustrated by reduced exudate, infiltration of polymorph nuclear leukocytes, release of interleukins and cytokines and the formation NO-components.

Apart from the anti-inflammatory activity also an analgesic activity has been demonstrated in the acetic acid induced writhing test with mice. The anti-hypertensive effect might be an indirect indication of diuresis.

Dried ethanolic extract did not show cytotoxicity in non-cancer cells *in vitro*.

Results from relevant non-clinical pharmacology studies on *Ribes nigrum* L. leaves are limited and not required.

3.2. Overview of available pharmacokinetic data regarding the herbal substance(s), herbal preparation(s) and relevant constituents thereof

No data with regard to absorption, distribution, metabolism, elimination and pharmacokinetic interactions with other medicinal products are available.

Assessor's comment:

Specific data on pharmacokinetics and interactions are not available.

3.3. Overview of available toxicological data regarding the herbal substance(s)/herbal preparation(s) and constituents thereof

3.3.1. Single dose toxicity

Intraperitoneal LD_{50} of a lyophilized ethanolic extract of the leaves was 1.09 g/kg, but no toxic effects were observed after oral administration of the extract to rats and mice (Mongold *et al*., 1993, only abstract available).

Assessor's comment:

Single dose toxicity studies with the preparations included in the monograph are not available. No safety concerns are expected based on studies carried out with different preparations of Ribes nigrum L. leaves.

3.3.2. Repeat dose toxicity

Chronic toxicity

Feeding mice with a daily dose of 3 g/kg of dried leaves during 6 months did not reveal any toxicity (Hänsel *et al.*, 1994).

Assessor's comment:

A daily dose of 3 g/kg of dried leaves during 6 months to mice, corresponding to a human equivalent dose of around 12 g, did not reveal any toxicity. No safety concerns are expected based on repeat dose toxicity studies carried out with different preparations of Ribes nigrum L. leaves.

3.3.3. Genotoxicity

Genotoxicity of an ethanolic extract of *R. nigrum* leaf was evaluated using the comet assay on human colon adenocarcinoma cell line HT29. About 10^5 of HT29 cells were seeded in 24-well plates and treated with the plant extracts at different concentrations for 24 h. The mean % DNA in tail was a measure of genotoxic potency of the extract. The damages on nuclei were analyzed with CometScore 2.0.0.38 software. Two independent measurements were performed, in three technical replicates each. *R. nigrum* extract exhibited some genotoxic activity on HT29 cells at 0.5 mg/ml dry weight concentration. According to one-way ANOVA with Dunnett's test, there were not observed significant differences between treated and non-treated cells at the lower tested concentrations of 0.005 and 0.05 mg/ml (Ginovyan *et al*., 2022).

Table 5. Overview of genotoxicity studies.

Type of test/reference	**Test system**	**Herbal substance/ preparation/ isolated compound**	**Concentrations/ Concentration range/ Metabolising system**	**Results positive/negative/ equivocal**
DNA damage in mammalian cells – Comet assay in vitro (Ginovyan et al., 2022)	HT29 cells	Ethanol extract of Ribes nigrum L. leaf	0.005, 0.05 and 0.5 mg/ml	Positive only at the highest concentration

Assessor's comment:

An ethanolic extract of R. nigrum leaf showed some genotoxic activity in an in vitro Comet assay conducted in cultured cancer cells. This results should be considered only as preliminary since no detailed description of the test is reported; in addition, in vitro Comet assay can serve for screening purposes only, thus positive results should be confirmed in further in vivo testing. No genotoxicity tests are available for the preparations included in the monograph.

3.3.4. Carcinogenicity

No data available.

3.3.5. Reproductive and developmental toxicity

No data available.

3.3.6. Local tolerance

No data available.

3.3.7. Other toxicity studies

The haemolytic activity of the water extract (extraction solvent water containing 200 ppm of SO_2) of *Ribes nigrum* L., folium (at the concentrations from the 0,01 up to 0.1 mg/mL) was conducted on fresh, heparinized blood and haemoglobin concentration in the supernatant (expressed as percentage of haemoglobin concentration of totally haemolysed cells) was assumed as the measure of the extent of haemolysis. At between 0.01 and 0.1 mg/ml, the extract did not induce haemolysis but protected erythrocytes against the UVC radiation (Bonarska-Kujawa *et al.*, 2014).

Cyboran *et al.*, (2012) also observed that the polyphenols contained in a water extract of *Ribes nigrum* L., folium, do not induce haemolysis in concentrations of 0.1-0.5 mg/ml. The Cellular Antioxidant Activity of *Ribes nigrum* L., folium (1 g of fresh leaves ground with 1 g of quartz in 10 ml of extraction solution: acetone/water/acetic acid (70:28:2)) was measured using the CAA assay on EAHy926 cells. Leaf extracts had the highest CAA value (12.89 ± 0.77 µmol QE/g of LE).

Assessor's comment:

Studies on potential haemolytic activity of leaves of Ribes nigrum L. did not reveal any safety concern.

3.3.8. Conclusions on toxicological data

Non-clinical information on the safety of *Ribes nigrum* L., folium and relevant preparations is scarce.

As there is no information on reproductive and developmental toxicity, the use during pregnancy and lactation cannot be recommended.

The following text is included in the monograph section 4.6: Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.

The following text is included in the monograph section 5.3: Tests on reproductive toxicity, genotoxicity and carcinogenicity have not been performed.

Due to the lack of adequate data on genotoxicity a list entry cannot be proposed.

3.4. Overall conclusions on non-clinical data

Results from relevant non-clinical pharmacology studies on *Ribes nigrum* L., folium are limited and not required.

Specific data on pharmacokinetics and interactions are not available.

Non-clinical information on the safety of *Ribes nigrum* L., folium is scarce. None of the reported non-clinical pharmacological studies described indicate a cause for safety concern for the *Ribes nigrum* L., folium. Tests on reproductive toxicity, genotoxicity and carcinogenicity have not been performed.

As there is no information on reproductive and developmental toxicity, the use during pregnancy and lactation cannot be recommended.

4. Clinical Data

4.1. Clinical pharmacology

4.1.1. Overview of pharmacodynamic data regarding the herbal substance(s)/preparation(s) including data on relevant constituents

No data available.

4.1.2. Overview of pharmacokinetic data regarding the herbal substance(s)/preparation(s) including data on relevant constituents

No data available.

4.2. Clinical efficacy

4.2.1. Dose response studies

No dose response studies available.

4.2.2. Clinical studies (case studies and clinical trials)

No clinical studies reported.

4.3. Clinical studies in special populations (e.g., elderly and children)

No clinical studies reported.

4.4. Overall conclusions on clinical pharmacology and efficacy

For the *Ribes nigrum* L., folium no data from clinical studies are available therefore, in accordance with Directive 2001/83/EC the well-established use cannot be supported.

5. Clinical Safety/Pharmacovigilance

5.1. Overview of toxicological/safety data from market overview

No data available.

5.2. Patient exposure

No data available.

5.3. Adverse events, serious adverse events and deaths

No data available from literature.

A search in the EudraVigilance database was done on December 2024. It resulted in one hit on *Ribes nigrum* folium and blackcurrant leaf powder. In this case the patient had taken concomitant medicinal

products. Overall, no new safety issues could be identified from reports in the EudraVigilance database up to December 2024.

5.4. Laboratory findings

None reported.

5.5. Safety in special populations and situations

5.5.1. Use in children and adolescents

No data available.

Assessor's comment:

The use in children and adolescents has not been investigated and is not supported by the traditional use. Therefore, the use in children and adolescents under 18 years of age is not recommended

5.5.2. Contraindications

Oedema due to heart failure or renal insufficiency is mentioned as a possible contra-indication without any further specification (Hänsel *et al.*, 1994; Gruenwald *et al*., 2000).

The monograph includes a contraindication for persons with hypersensitivity to the active substance and to other plants of the Asteraceae (Compositae) family.

Assessor's comment:

No clinical data are available to support the contraindication of Ribes nigrum leaf in case of oedema due to heart failure or renal insufficiency. Conditions where reduced fluid intake is advised (e.g. severe cardiac or renal disease) are reported as a warning in line with monograph of other plants with the same therapeutic indication (i.e. for the relief of symptoms associated with minor urinary tract complaints in addition to the general recommendation of a sufficient fluid intake to increase the amount of urine).

5.5.3. Special warnings and precautions for use

No data available. However, to exclude serious diseases and worsening of the complaints the following warnings are proposed for the monograph:

For the indication 'Traditional herbal medicinal product for relief of minor articular pain':

- 'articular pain accompanied by swelling of joints, redness or fever, should also be examined by a doctor'.

For the indication 'Traditional herbal medicinal product used for the relief of symptoms associated with minor urinary tract complaints in addition to the general recommendation of a sufficient fluid intake to increase the amount of urine':

- 'if complaints or symptoms such as fever, dysuria, spasms or blood in the urine occur during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted';

- ‘Because adequate fluid intake is required during treatment *Ribes nigrum* L., folium is not recommended for patients with conditions where reduced fluid intake is advised'.

For both indications:

- The use in children and adolescents under 18 years of age has not been established due to lack of adequate data.

Assessor’s comment:

Section 4.4 of the monograph includes warning and precautions consistent with those of other plants with the same therapeutic indications.

5.5.4. Drug interactions and other forms of interaction

No data available.

5.5.5. Fertility, pregnancy and lactation

No data is available, therefore, use of *Ribes nigrum* L., folium cannot be recommended during pregnancy and lactation.

No fertility data available.

Assessor’s comment:

The following text is included in the monograph section 4.6 ” Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.

Women of childbearing potential should consider using effective contraception during treatment.

No fertility data available”.

5.5.6. Overdose

No data available.

5.5.7. Effects on ability to drive or operate machinery or impairment of mental ability

No data available.

5.5.8. Safety in other special situations

Not available.

5.6. Overall conclusions on clinical safety

For *Ribes nigrum* L., folium there is no clinical safety data available. Also, the use in children or adolescents is not documented in literature.

The available information in the literature and pharmacovigilance data of marketed products do not indicate safety concerns for *Ribes nigrum* L., folium. As a precautionary measure warnings are included in the monograph.

6. Overall conclusions

Well established use monograph

Due to the lack of data from clinical studies, the requirements for well-established use according to Article 10a of Directive 2001/83/EC are considered not fulfilled.

Traditional use monograph

The requirements for traditional medicinal use according to Article 16d(1), Article 16f and Article 16h of Directive 2001/83/EC are considered fulfilled. It has been demonstrated that *Ribes nigrum* L., folium has been in traditional medicinal use throughout a period of at least 30 years, including at least 15 years within the EU/EEA, with an acceptable level of safety for:

Herbal substance/preparation	**Indication**	**Therapeutic area for browse search**	**Posology and method of administration**	**Duration of use**
Comminuted herbal substance	Traditional herbal medicinal product for the relief of minor articular pain.	Pain and inflammation	Single dose: 2 to 4 g of the comminuted herbal substance in 200 ml of boiling water as a herbal infusion 3 times daily. Daily dose: 6-12 g.	Four weeks
Dry extract (DER 7:1), extraction solvent water	1. Traditional herbal medicinal product for the relief of minor articular pain. 2. Traditional herbal medicinal product used for the relief of symptoms associated with minor urinary tract complaints in addition to the general recommendation of a sufficient fluid intake to increase the amount of urine.	1. Pain and inflammation 2. Urinary tract and genital disorders	1. and 2. Single dose: 170 mg of dry extract (7:1, water), 1-3 times daily. Daily dose: 170-510 mg.	1. Four weeks 2. Two weeks

Herbal substance/preparation	Indication	Therapeutic area for browse search	Posology and method of administration	Duration of use
Powdered herbal substance	1. Traditional herbal medicinal product for the relief of minor articular pain. 2. Traditional herbal medicinal product used for the relief of symptoms associated with minor urinary tract complaints in addition to the general recommendation of a sufficient fluid intake to increase the amount of urine.	1. Pain and inflammation 2. Urinary tract and genital disorders	1. and 2. Single dose: 340 mg of powdered herbal substance, 3-5 times daily. Daily dose: 1020-1700 mg.	1. Four weeks 2. Two weeks

The indications are considered suitable for self-medication.

There are no published reports on serious side effects with the herbal substance or herbal preparations thereof.

There are no studies available on possible drug interactions.

No data on fertility, reproductive and developmental toxicity and the usage in children and adolescents is available. Therefore, the use is not recommended in children, adolescents and during pregnancy and lactation.

No constituents with known therapeutic activity or active markers could be identified by the HMPC.

List entry

A European Union list entry is not supported due to lack of data on genotoxicity.

Annex

List of references