20 November 2019
EMA/HMPC/645526/2018
Committee on Herbal Medicinal Products (HMPC)

Addendum to Assessment report on *Quercus robur* L., *Quercus petraea* (Matt.) Liebl., *Quercus pubescens* Willd., cortex

Rapporteur(s)	Ewa Widy-Tyszkiewicz
Peer-reviewer	Jaqueline Wiesner

HMPC decision on review of monograph Quercus cortex adopted on	20 November 2019
Call for scientific data (start and end date)	From 2018-04-15 to 2018-06-30
Discussion in Working Party on European Union monographs and list (MLWP) and Committee on Herbal Medicinal Products (HMPC)	September 2018 November 2019
Adoption by Committee on Herbal Medicinal Products (HMPC)	20 November 2019

Review of new data on *Quercus robur* L., *Quercus petraea* (Matt.) Liebl., *Quercus pubescens* Willd, cortex

Periodic review (from 2010 to 2018)

Scientific data (e.g. non-clinical and clinical safety data, clinical efficacy data)

☒ Pharmacovigilance data (data from EudraVigilance and VigiBase):

The EudraVigilance database was searched on 2018-09-13 using the search term “Quercus robur”, “Quercus petraea”, “Quercus pubescens”. The VigiBase database was searched on 2018-09-13 using the search term “Quercus robur” and “Quercus petrea”

☒ Scientific/Medical/Toxicological databases: (from 2010 to present, search date: 6 September 2018):1336 using the using the Mesh term "Quercus robur", “Quercus petraea” and “Quercus pubescens”.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

Pubmed ("Quercus robur" - 245 hits); (“Quercus petraea” – 150 hits); “Quercus pubescens” – 58 hits, respectively).

Embase: (283, 64, 19 hits, respectively).

Medline complete: (220, 116, 33 hits, respectively).

Cochrane Central Register of Controlled Trials: “Quercus robur” - 2 Clinical trials; “Quercus petraea” – no data; “Quercus pubescens” - 1 Trial matching

ToxNet (102, 28, 14 hits, respectively).

National Toxicology Program ("Quercus robur", “Quercus petraea” and Quercus pubescens) - 1 joint Technical Report on the toxicology and carcinogenesis studies of pyrogallol (dermal studies) 2013.

Regulatory practice

- ☒ Old market overview in AR (i.e. products fulfilling 30/15 years on the market)
- ☒ New market overview – information from MS.
- ☐ Referral
- ☒ 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

Availability of new information (i.e. likely to lead to a relevant change of the monograph)

Scientific data	*Yes*	*No*
New non-clinical safety data likely to lead to a relevant change of the monograph	☐	☒
New clinical safety data likely to lead to a relevant change of the monograph	☐	☒
New data introducing a possibility of a new list entry	☐	☒
New clinical data regarding the paediatric population or the use during pregnancy and lactation likely to lead to a relevant change of the monograph	☐	☒
New clinical studies introducing a possibility for new WEU indication/preparation	☐	☒
Other scientific data likely to lead to a relevant change of the monograph	☐	☒
Regulatory practice	*Yes*	*No*
New herbal substances/preparations with 30/15 years of TU	☐	☒
New herbal substances/preparations with 10 years of WEU	☐	☒
Other regulatory practices likely to lead to a relevant change of the monograph	☐	☒
Referrals likely to lead to a relevant change of the monograph	☐	☒
New / Updated Ph. Eur. monograph likely to lead to a relevant change of the monograph	☐	☒

Consistency	*Yes*	*No*
New or revised public statements or other HMPC decisions likely to lead to a relevant change of the monograph	☐	☒
Relevant inconsistencies with other monographs within the therapeutic area that require a change of the monograph	☐	☒
Other relevant inconsistencies that require a change of the monograph	☐	☒

Summary and conclusions on the review

During the review 1347 new references not yet available during the first/previous assessment were identified.

No references were provided by Interested Parties during the Call for data.

11 references were considered to be relevant for the assessment.

No references justify a revision of the monograph.

Scientific data

No new safety issues have been identified from reports in the EudraVigilance database.

In the scientific literature, a number of new non-clinical studies appeared in the evaluated period on both the cutaneous administration of oak preparations and their systemic administration. These studies concerned antioxidant, anti-inflammatory, antimicrobial, antiparasitic, anticancer, cardioprotective, hepatoprotective and gastroprotective activities of oak bark preparations.

In addition, a NTP study was published in 2013 on pyrogallol about its dermal toxicity. The conclusions of these 3 months to 2 years dermal studies showed that there was no evidence of carcinogenic activity of pyrogallol in male or female rats administered 5, 20 or 75mg/kg. There was equivocal evidence of carcinogenic activity in male mice and some evidence of carcinogenic activity in female mice.

Assessor's comment: There is no information on the presence of free pyrogallol in oak bark. Pyrogallol formed by decarboxylation of gallic acid is among the products derived from the metabolism of gallotannins by human enzymatic pool and gut microbiota in low concentrations not relevant for the assessment. In conclusion, there is no new scientific data of relevance for the content of the monograph.

Regulatory practice

No new medicinal products with *Quercus robur* L., Q*uercus petraea* (Matt.) Liebl., *Quercus pubescens* Willd., cortex, as the single active substance have been reported from the Member States.

References

a) References relevant for the assessment:

Deryabin DG, Anna A. Tolmacheva. Antibacterial and anti-quorum sensing molecular composition derived from Quercus cortex (Oak bark) Extract. *Molecules* 2015; 20:17093-17108

Frédérich M, Marcowycz A, Cieckiewicz E, Mégalizzi V, Angenot L, Kiss R. *In vitro* anticancer potential of tree extracts from the Walloon Region forest. *Planta Med* 2009; 75: 1634–1637

Hubert J, Angelis A, Aligiannis N, Rosalia M, Abedini A, Bakiri A, *et al*. *In vitro* Dermo-Cosmetic evaluation of bark extracts from common temperate trees. *Planta Med*. 2016; 82(15):1351-1358.

Lopez VB, de la Barrena EHG, Sastre J. Relevance of clinical sensitization to Quercus pollen in Spain. *J Allergy Clin Immun* 2016; 137(2):AB122, Abstracts, 400

Lorenz P, Heinrich M, Garcia-Käufer M, Grunewald F, Messerschmidt S, Herrick A, *et al*. Constituents from oak bark (Quercus robur L.) inhibit degranulation and allergic mediator release from basophils and mast cells *in vitro*. *J Ethnopharm* 2016; 194:642–650.

NTP Technical report on the toxicology and carcinogenesis studies of pyrogallol in F344, N rats and B6C3F1/N mice (dermal studies), National Toxicology Program, Research Triangle Park 2013

Panchal SK, Brown L. Cardioprotective and hepatoprotective effects of ellagitannins from European oak bark (Quercus petraea L.) extract in rats. *Eur J Nutr* 2013; 52(1):397-408.

Piwowarski JP, Kiss AK, Kozłowska-Wojciechowska M. Anti-hyaluronidase and anti-elastase activity screening of tannin-rich plant materials used in traditional Polish medicine for external treatment of diseases with inflammatory background. *J Ethnopharmacol* 2011; 137(1):937–941.

Singh P, Rahul MK, Thawani V, Sudhakar P. Anxiolytic effect of chronic administration of gallic acid in rats. *J Appl Pharm Sci* 2013; 3(7):101-104.

Umesalma S, Sudhandiran G. Differential inhibitory effects of the polyphenol ellagic acid on inflammatory mediators NF-κB, iNOS, COX-2, TNF-α, and IL-6 in 1,2-dimethylhydrazine-induced rat colon carcinogenesis. *Basic Clin Pharmacol Toxicol* 2010; 107(2), 650–655.

Weber RW. Allergen of the month – Quercus robur. *Ann Allerg Asthma Immun* 2015; 115(5):A13

b) References that justify the need for the revision of the monograph:

None

Rapporteur's proposal on revision

☐ Revision needed, i.e. new data/findings of relevance for the content of the monograph

☒ No revision needed, i.e. no new data/findings of relevance for the content of the monograph

HMPC decision on revision

☐ Revision needed, i.e. new data/findings of relevance for the content of the monograph

☒ No revision needed, i.e. no new data/findings of relevance for the content of the monograph

HMPC agreed with Rapporteurs position that no monograph revision is needed because no new data of relevance were detected that would change the content of the monograph.

The HMPC decided by consensus not to revise the monograph, assessment report and list of references on Quercus cortex.