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Committee on Herbal Medicinal Products (HMPC)

Addendum to Assessment report on *Grindelia robusta* Nutt., *Grindelia squarrosa* (Pursh) Dunal, *Grindelia humilis* Hook. et Arn., *Grindelia camporum* Greene, herba

Rapporteur(s)	I Chinou
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HMPC decision on review of monograph on <i>Grindelia robusta</i> Nutt., <i>Grindelia squarrosa</i> (Pursh) Dunal, <i>Grindelia humilis</i> Hook. et Arn., <i>Grindelia camporum</i> Greene, herba adopted on 20 November 2012	13 January 2021
Call for scientific data (start and end date)	From 01 March 2021 to 31 May 2021
Adoption by Committee on Herbal Medicinal Products (HMPC)	24 November 2021

Review of new data on *Grindelia robusta* Nutt., *Grindelia squarrosa* (Pursh) Dunal, *Grindelia humilis* Hook. et Arn., *Grindelia camporum* Greene, herba Periodic review (from 2012 to 2021)

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

- Pharmacovigilance data (e.g. data from EudraVigilance, VigiBase, national databases)
- Scientific/Medical/Toxicological databases Scopus, PubMed. Keywords: *Grindelia robusta*, *Grindelia squarrosa*, *Grindelia humilis*, *Grindelia camporum*
- Other

Regulatory practice

- Old market overview in AR (i.e. products fulfilling 30/15 years on the market)
- New market overview (including pharmacovigilance actions taken in member states)

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- 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)

<i>Scientific data</i>	Yes	No
New non-clinical safety data likely to lead to a relevant change of the monograph	<input type="checkbox"/>	<input checked="" type="checkbox"/>
New clinical safety data likely to lead to a relevant change of the monograph	<input type="checkbox"/>	<input checked="" type="checkbox"/>
New data introducing a possibility of a new list entry	<input type="checkbox"/>	<input checked="" type="checkbox"/>
New clinical data regarding the paediatric population or the use during pregnancy and lactation likely to lead to a relevant change of the monograph	<input type="checkbox"/>	<input checked="" type="checkbox"/>
New clinical studies introducing a possibility for new WEU indication/preparation	<input type="checkbox"/>	<input checked="" type="checkbox"/>
Other scientific data likely to lead to a relevant change of the monograph	<input type="checkbox"/>	<input checked="" type="checkbox"/>
<i>Regulatory practice</i>	Yes	No
New herbal substances/preparations with 30/15 years of TU	<input type="checkbox"/>	<input checked="" type="checkbox"/>
New herbal substances/preparations with 10 years of WEU	<input type="checkbox"/>	<input checked="" type="checkbox"/>
Other regulatory practices likely to lead to a relevant change of the monograph	<input type="checkbox"/>	<input checked="" type="checkbox"/>
Referrals likely to lead to a relevant change of the monograph	<input type="checkbox"/>	<input checked="" type="checkbox"/>
New / Updated Ph. Eur. monograph likely to lead to a relevant change of the monograph	<input type="checkbox"/>	<input checked="" type="checkbox"/>
<i>Consistency</i>	Yes	No
New or revised public statements or other HMPC decisions likely to lead to a relevant change of the monograph	<input type="checkbox"/>	<input checked="" type="checkbox"/>
Relevant inconsistencies with other monographs within the therapeutic area that require a change of the monograph	<input type="checkbox"/>	<input checked="" type="checkbox"/>
Other relevant inconsistencies that require a change of the monograph	<input type="checkbox"/>	<input checked="" type="checkbox"/>

Summary and conclusions on the review

According to the request of market overview on monoproducts containing *Grindelia* species (as in the existing EU monograph) (*Grindelia robusta*, *Grindelia squarrosa*, *Grindelia humilis*, *Grindelia camporum*, 17 countries have responded negative.

Especially Germany have responded that in 1976 there had been two herbal teas containing *Grindelia* herba as the only active substance on German market.

One product disappeared from the market in December 1989 because of the written renouncement from the company, the other in December 1992 because no application for the marketing authorisation according to Section 109a in connection with/or Section 105 German Medicinal Products Act was submitted.

While in Spain a combination containing a mixture of *Drosera* (tincture), Ephedrine hydrochloride, Codeine phosphate and *Grindelia* (tincture) cannot be considered as a herbal product.

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

Seven references were considered to be relevant for the assessment, however without changing the existing data/conclusions for the monograph and supporting documents.

- During the review (Scopus, Pub Med) after 2012, 20 references were identified for *Grindelia squarrosa* and four were considered relevant.

Mainly referred in phytochemical studies (Nowak & Rychlińska 2012, Veres *et al.*, 2014, Gierlikowska *et al.*, 2020, Gierlikowska *et al.*, 2021) and *in vitro* anti-inflammatory profile (Gierlikowska *et al.*, 2020, 2021).

- Five references were identified for *Grindelia robusta* after 2012 among which three were considered relevant.

Studying chemical profile (Ferrerres *et al.*, 2014), antioxidant activity (Güneş *et al.*, 2019) as well as one publication describing the constituents and activities of *Grindelia robusta* and making reference to the results of two studies conducted in children on the efficacy of a herbal combination product containing *Grindelia robusta* (Murgia *et al.*, 2021).

For *Grindelia humilis* and *Grindelia camporum* after 2012 no references were identified.

No references justify a revision of the monograph.

Revision is considered not required because there are no new data/findings of relevance for the content of the monograph.

References

a) References relevant for the assessment:

Ferrerres F, Grosso C, Gil-Izquierdo A, Valentão P, Azevedo C, Andrade PB. HPLC-DAD-ESI/MSⁿ analysis of phenolic compounds for quality control of *Grindelia robusta* Nutt. and bioactivities. *J Pharm Biomed Anal* 2014, 94:163 – 172

Gierlikowska B, Gierlikowski W, Bekier K, Skalicka-Woźniak K, Czerwińska ME, Kiss AK. *Inula helenium* and *Grindelia squarrosa* as a source of compounds with anti-inflammatory activity in human neutrophils and cultured human respiratory epithelium. *J Ethnopharmacol* 2020, Vol. 249. Article number 112311

Gierlikowska B, Filipek A, Gierlikowski W, Kania D, Stefańska J, Demkow U, Kiss AK. *Grindelia squarrosa* Extract and Grindelic Acid Modulate Pro-inflammatory Functions of Respiratory Epithelium and Human Macrophages. *Frontiers Pharmacol* 2021, Vol. 11. Article number 534111

Güneş A, Kordali Ş, Turan M, Usanmaz Bozhüyük A. Determination of antioxidant enzyme activity and phenolic contents of some species of the Asteraceae family from medicinal plants. *Industrial Crops and Products* 2019, 137:208 – 213

Murgia V, Ciprandi G, Votto M, De Filippo M, Tosca MA, Marseglia GL. Natural remedies for acute post-viral cough in children. *Allerg Immunopathol* 2021, 49(3):173 – 184

Nowak S, Rychlińska I. Phenolic acids in the flowers and leaves of *Grindelia robusta* Nutt. and *Grindelia squarrosa* Dun. (Asteraceae). *Acta Polon Pharm - Drug Res* 2012, 69(4):693 – 698

Veres K, Roza O, Laczkó-Zöldb E, Hohmann J. Chemical composition of essential oils of *Grindelia squarrosa* and *G. hirsutula*. *Nat Prod Commun* 2014, 9(4):573 – 574

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

The HMPC agreed not to revise the monograph, assessment report and list of references on *Grindelia robusta* Nutt., *Grindelia squarrosa* (Pursh) Dunal, *Grindelia humilis* Hook. et Arn., *Grindelia camporum* Greene, herba by consensus.