CHPA Complaints Panel Final Determination 01/21 (Part 2)

Meeting held on February 8, 2022

iNova Pharmaceuticals Pty Ltd ("iNova")
v.
Care Pharmaceuticals Pty Ltd ("Care")

Little Coughs Ivy Leaf (Hedera helix) range

Procedural history

1. iNova initiated this complaint formally by letter dated August 13, 2021. Care responded formally by letter dated August 27, 2021 and iNova referred the complaint to CHPA on September 8, 2021. iNova complained that Care has breached sections 4.1 and 5.1.4 of the ASMI/CHPA Code of Practice ("the Code") in relation to the promotion of its Little Coughs™ Ivy Leaf (Hedera helix) range ("Little Coughs") for use in children under 2 years of age.

2. At its meeting on October 12, 2021, the Panel deferred its consideration of the substance of the Section 4.1 Complaint. The Panel found Care to be in breach of section 5.1.4 of the Code in failing to comply with iNova's request that Care provide to it, in relation to Care's Little Coughs range:

> "the evidence which you hold to substantiate the use of Hedera helix in the quantities and extract ratios used in each of your formulations for dosing in the 6 months – 2 years range".

3. The Panel found the breach to be a Minor breach, having no safety implications.

4. In response to the Panel's draft determination in relation to the section 5.1.4 complaint, Care stated:

> "By way of clarification, there is no single article which Care relies upon in respect to its evidence to support that Hedera helix can be safely provided to the 6 month to 2 year patient population. Care paid for the expertise of a third party to collate and analyse various information to reach a view. Accordingly, as stated…such information is propriety [sic] in nature and confidential to Care."

5. The Panel determined that Section 5.1.4 of the Code requires members who choose to make claims based on confidential, proprietary information to provide that information without delay upon request.

6. Pursuant to Section 10.2.1 of the Code, the Panel directed Care to provide to iNova, within 5 working days of receiving the Panel's Final decision in relation to Section 5.1.4, the evidence held by Care to support the safety of Care's Little Coughs products when supplied to children in the 6 months – 2 years age range at the dosages specified by Care, using the relevant ingredient, quantity and extract ratios.

7. Care appealed to the Arbiter from the Panel's decision on the section 5.1.4 complaint. On December 7, 2021, the Arbiter rejected Care's appeal and confirmed the Panel's

direction to Care pursuant to Section 10.2.1 of the Code. The Arbiter found Care's breach of section 5.1.4 to be a Severe breach, having safety implications, and imposed a fine of $25,000.

8. In response to the Arbiter's direction, by letter dated December 15, 2021, Care provided to iNova, with a copy to CHPA, a list of 47 references on which it relies to support its claims, together with submissions. By letter dated December 17, 2021, iNova notified CHPA that it wished to pursue its Section 4.1 complaint and made submissions. On January 20, 2022, Care provided further submissions to the Panel in response to iNova's letter of December 17, 2021. All of these submissions have been taken into account by the Panel. In particular, the Panel notes iNova's submission in its initial letter to Care dated 13 August 2021:

> "*Whilst there is some evidence available to support Hedera helix-based products in this age group, it should be noted that this has been obtained from studies using products which contain specific proprietary ingredients in their formulation and does not appear to align with the extract ratios/quantities in Little Coughs products.*"

The Section 4.1 complaint

9. The issues to be determined by the Panel in relation to iNova's Section 4.1 complaint are whether the references provided by Care to iNova pursuant to the direction of the Arbiter in relation to the Section 5.1.4 complaint support the efficacy and safety of Care's Little Coughs products when supplied to children in the 6 months – 2 years age range at the dosages specified by Care, using the relevant ingredient, quantity and extract ratios and, if not, whether Care is in breach of Section 4.1 of the Code, which provides:

> **"***Members shall not engage in any unfair* or unconscionable conduct or commercial practice*". "Unfair" is defined in Section 2 as "*not equitable or honest or impartial or according to the Constitution*".

10. The front labels of Care's Little Coughs products include the statements "6 months +" and "For the soothing relief of coughs and chesty congestion". The rear labels contain "Warnings" including, in fine print:

> "Consult your healthcare professional:
> *before using in children under 2 years of age…"

and "Directions for Use" including, also in fine print:

> "Shake well before use
> Use the enclosed dosing syringe to withdraw an accurate dose…

Age	How much	How often
6 months – under 2 years	2.5ml	Once a day"

11. The Panel notes that the statement "*6 months* +" is one of the most prominent features of the front label of Care's Little Coughs products, while the warning "*Consult your healthcare professional: *before using in children under 2 years of age*" appears in fine print on the back label, where it is less likely to be read by consumers before purchase. The Panel accepts Care's contention that those words are important because they

qualify the suitability of use for children aged under 2 years and make clear that if a parent/consumer is intending to use the product on a child aged under 2 years then they should first consult a healthcare professional. However, as mentioned in paragraph 9 above, the issue to be determined is whether the evidence on which Care relies supports the efficacy and safety of its Little Coughs products in children under 2 years.

12. The Panel accepts Care's contention that although the European Union herbal monograph on *Hedera helix* L., folium, [Care reference 1] published by the European Medicines Agency ("the Monograph"), is not binding in Australia, it is a useful document when considering claims that can be made. The Monograph determined the use of *Hedera helix* in children under 2 years of age to be contraindicated due to the risk of respiratory congestion and rising bronchiolitis in infants as a result of the functional features of their air passages and thoracic cavity (small calibre bronchi, immature bronchial surfaces that limit the lung's capacity to remove mucus flow).

13. The EMA Assessment report on Hedera Helix [Care reference 13] considered clinical studies in children (Section 4.3). The Assessment cited 17 of the references included in Care's list, Nos. [43], [44], [38], [37], [41], [42], [20], [23], [31], [24], [25], [33], [35], [36], [45], [27] and [19]. At page 75 the Assessment noted the following in terms of dosage for children (emphasis added):

> **"The daily dosages used in children are in high ranges**. Ethanol-containing ivy preparations are used in daily dosages of maximally 420 mg (over 12 years). Ethanol-free preparations are used in daily dosages of maximally 1 g (over 12 years).
>
> ethanol-containing ivy preparations:
> In accordance with the above listed study results and the literature, for all ethanol-containing ivy preparations, the following maximum daily dosages for children are proposed:
>
> 2-5 years: 150 mg 6-12 years: 210 mg
>
> ethanol-free ivy preparations:
> No study indicates that dosages higher than 656 mg herbal substance are necessary for efficacy in adults.
>
> It is proposed that the group of 6-12 years old children should be given maximum 2/3 of daily dosage of the group of children over 12 years and adults. The group of 2-5 years old children should take maximal 1/3 of the daily dosage of children over 12 years and adults. In summary, the best benefit/risk ratio is a low dose administration. The recommended dosages for children are derived from studies. For the safety of the use in children see also chapter 5.5. **The following maximum daily dosages are recommended:**
>
> **2-5 years: 219 mg herbal substance 6-12 years: 437 mg herbal substance**
>
> **The use in children under 2 years is contraindicated due to possible aggravation of respiratory symptoms.** See also chapter 5.5."

14. The Assessment report lists higher dosages than used in Care's products and contraindicates use of *Hedera helix* in children under 2 years without noting the dosages in studies for this age group.

15. Care contends that, because the contraindication for children under 2 years of age in the Monograph is not specific for *Hedera helix* and is, instead, a more general contraindication for the use of mucolytics in this population, it is not relevant for Care's product range given the availability of supportive studies indicating the safety and efficacy of *Hedera helix* in this population. However, as set out below, the Panel considers that the references on which Care relies do not support the safety and use of Care's Little Coughs products in children between the age of 6 months to 2 years.

16. The TGA's *Guidelines on the evidence required to support indications for listed complementary medicines V3.0 January 2019* [Care's reference 2] (Evidence Guidelines) provide at p.11:

> "As the sponsor of a listed medicine, you must hold evidence to support all the indications you make for your medicine at the time you list the medicine in the ARTG. The evidence you hold must adequately support all indications and demonstrate all claims made for the medicine are true, valid and not misleading. You must keep that evidence for the whole time the medicine remains listed and provide it to the TGA if requested to do so [as provided by subsection 26A(2)(j) and 28(6) of the Act]."

17. Many of the references provided by Care are unsuitable for use as evidence to support a claim for a listed medicine, for the following reasons:

    (i) many are in a different language and neither iNova nor the Panel were provided with translations (such as [41], [42], [43], [44], [45]);

    (ii) many related to a serious disease, condition, ailment or defect (such as [16], [17], [29], [39]). The Evidence Guidelines state:

> "In general, data obtained from studies with participants who have serious diseases, conditions or ailments cannot be extrapolated to a healthy population and, as such, are not relevant evidence to support an indication for a listed medicine." (p 37).

    (iii) many do not relate to the relevant age group. While some include children in the studies, it is often the case that the children are older (5+ or older). The Evidence Guidelines state:

> "When an indication is directed towards a specific subgroup of the population (for example: elderly or pregnant women), it needs to be supported by evidence derived from the same subgroup of the population. The results from studies of target specific subgroups are not relevant to the general population." (p 37).

    (iv) the Evidence Guidelines enable the justification of differences between the study and target population, stating:

> "When you use clinical studies that employ specific study population groups (for example: subjects with a disease) rather than the target population group for your indication (for example: the general healthy population), you should

provide an evidence-based justification. This process should consider biological factors as well as environmental and behavioural factors including the influence of health practitioner intervention which may differ between healthy and unhealthy populations." (p 37).

Care has not provided this justification.

(v) many of the papers used a dosage of the active ingredient which was higher than that used in Care's products (such as [26], [29], [38]). The Evidence Guidelines state:

"In general, active ingredients may be considered as sufficiently identical if there are no relevant differences in the method of preparation and if the medicine has the same intended purpose, dosage and the same route of administration… When evidence relates to an herb or herbal substance, the species (and subspecies where applicable), plant part and route of administration should be identical to that described in the evidence. The method of preparation and processing, the equivalent dry weight and the dose of active component described in the evidence should be consistent with that in the medicine." (p 19).

(vi) Despite these serious deficiencies in evidence, the Panel has reviewed a selection of papers to which Care provided references, to ascertain their relevance to the claims made by Care. The following studies cannot be used to justify the claims made by Care, for these reasons:

- **E Arnold et al, Herbal interventions for chronic asthma in adults and children (Cochrane Review) 2008, *The Cochrane Library*, Issue 1** [Care's reference 40]: concluded that reporting in the studies was poor and that '*On the basis of the available evidence it is not possible to show whether any of these herbal treatments can improve asthma symptoms'*.

- **A Huntley, E Ernst, Herbal medicines for asthma: a systematic review, 2008, 55(11) *Thorax,* 925-9** [Care's reference 39]: reviewed 17 RCTs and concluded that there was no definitive evidence to support the use of the herbal preparations in the treatment of asthma.

- **S Zeil et al, Tolerance and effect of an add-on treatment with a cough medicine containing ivy leaves dry extract on lung function in children with bronchial asthma, 2014, *Phytomedicine*** [Care's reference 29]: patients used in the study had asthma and were aged 6-11.

- **S Fazio et al, Tolerance, safety and efficacy of Hedera helix extract in inflammatory bronchial diseases under clinical practice conditions: a prospective, open, multicentre post marketing study in 9657 patients, 2009, Phytomedicine 17** [Care's reference 38]: patients received a higher dose of the active ingredient than is used in Care's products.

18. Although this is only a small selection of papers, it demonstrates that the body of evidence in relation to the use of the substance contains evidence that is contrary to Care's claims. This means that even if Care does have evidence to support the claims made for its products, it has not provided justification for how those papers fit in the

context of broader scientific literature, particularly since the papers referred to above contradict Care's claims and were provided by Care in support of them.

19. Accordingly, the Panel finds that the references provided in response to the Arbiter's direction, on which Care relies, do not support the efficacy and safety of Care's Little Coughs products when supplied to children in the 6 months – 2 years age range at the dosages specified by Care, using the relevant ingredient, quantity and extract ratios.

20. The Panel concludes that, in promoting those products for use in children in that age group, Care has engaged in unconscionable commercial practice, in breach of Section 4.1 of the Code.

Classification of breach

21. Having regard to the safety implications for children in the 6 months – 2 years age range, the Panel finds this breach to be a Severe Breach pursuant to Section 10.1.1 of the Code.

Sanctions

22. The Panel notes that the Arbiter determined Care's breach of Section 5.1.4 to be a Severe Breach that has safety implications and directed *inter alia* that, if the claims remain unsubstantiated, as the Panel has now found, a fine of $25,000 should be imposed for Care's breach of that Section.

23. The Panel makes the following findings under Section 10.1.3 of the Code in relation to Care's breach of Section 4.1:

    (i) there is no evidence that publication of the claims has ceased;
    (ii) there is no evidence that steps have been taken to withdraw the material published;
    (iii) there is no evidence that corrective statements have been made;
    (iv) the breach was deliberate in that Care must have known that the evidence on which it relies, as listed in its letter of December 15, 2021, does not support its claims;
    (v) Care has not previously breached the Code;
    (vi) there are safety implications; and
    (vii) the perceptions of consumers have been affected.

24. In the circumstances of this case the Panel considers it appropriate to impose a similar fine of $25,000 for Care's breach of Section 4.1, in addition to the fine imposed by the Arbiter for Care's breach of Section 5.1.4.

25. Accordingly, the Panel directs that, within 10 days of this decision:

    (a) Pursuant to Section 10.2.1 of the Code, Care is to give an undertaking in writing to CHPA:

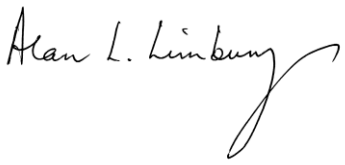
        (i) immediately to discontinue making the claims that its Little Coughs products can be used by children between the age of 6 months to 2 years either in the dosages recommended or at all, or that it is safe to do so; and

(ii) immediately to cease distribution from its premises of Little Coughs products bearing labels representing that they can be used by children between the age of 6 months to 2 years either in the dosages recommended or at all, or that it is safe to do so; and

(b) Care is to pay a total fine of $50,000 to CHPA.

26. The Panel makes no determination to alter the usual operation of section 9.4.2.2 of the Code in relation to the Section 4.1 complaint.

Dated: February 28, 2022.
For the CHPA Complaints Panel



Alan L. Limbury
Panel Chair

Note: although this is called a Final Determination, each party has a right of appeal to the Arbiter. If no appeal is lodged this determination will be published on the CHPA website once the time for lodging an appeal has expired. If there is an appeal, the Arbiter's determination will be published on the CHPA website together with this determination. Until publication on the website, parties and their representatives should maintain the privacy of these proceedings.