MEDSAFE
NEW ZEALAND MEDICINES AND MEDICAL DEVICES SAFETY AUTHORITY
A BUSINESS UNIT OF THE MINISTRY OF HEALTH

Reclassification of choline salicylate from general sale to pharmacy-only medicine

Application to the Medicines Classification Committee

Medsafe
December 2020

Contents

1) Introduction

This application to the Medicines Classification Committee (MCC) from Medsafe requests a change to the classification of choline salicylate, when used for infant teething, from general sale to pharmacy-only medicine.

Choline salicylate is a non-acetyl salicylate medicine [1]. It is regarded as a mild analgesic with an effect similar to lignocaine hydrochloride in that they both may give pain relief [2]. Choline salicylate is a non-irritating compound and is related to aspirin [2].

Choline salicylate is indicated for mild oral and perioral lesions [3]. In New Zealand, it is available as Bonjela Teething & Mouth Ulcer Gel and Bonjela Mouth Ulcer and Teething Gel [4].

At the 179th meeting in September 2019, the Medicines Adverse Reactions Committee (MARC) highlighted a case report (CARM ID #132801) where a child developed respiratory distress, tachypnoea and metabolic acidosis after an overdose of choline salicylate [5]. The MARC recommended that an application be made to the MCC to review the classification of choline salicylate [5].

2) Application to the Medicines Classification Committee

Part A – Administrative Details

1. International Non-proprietary name of the medicine

Choline salicylate.

Choline salicylate is a non-acetyl salicylate medicine [1]. It is regarded as a mild analgesic with an effect similar to lignocaine hydrochloride in that they both may give pain relief [2]. Choline salicylate is a non-irritating compound and is related to aspirin [2].

2. Proprietary name(s)

Table 1 below shows the products containing choline salicylate currently available in New Zealand.

Table 1: Products containing choline salicylate currently available in New Zealand

Product name	TT50-Number	Sponsor
Bonjela Teething & Mouth Ulcer Gel	TT50-0882	Reckitt Benckiser
Bonjela Mouth Ulcer & Teething Gel	TT50-0882/1	Reckitt Benckiser

Source: Medsafe. 2019. *Product/Application Search* 31 May 2019. URL: www.medsafe.govt.nz/regulatory/DbSearch.asp (accessed 1 December 2020).

These products are the same apart from the name and how they are presented:

- Bonjela Teething and Mouth Ulcer Gel comes in a blue pack and has an image of an infant in pink (see Annexe 1).
- Bonjela Mouth Ulcer and Teething Gel comes in a blue pack with an image of an adult in blue (see Annexe 2).

3. Name and contact details of the company/organisation/individual requesting a reclassification

Medsafe, Ministry of Health, 133 Molesworth Street, Thorndon, Wellington, 6011

Email: medsafeadrquery@health.govt.nz

4. Dose form(s) and strength(s) for which a change is sought

All dose forms and strengths.

Table 2 below shows the dose form and strength of products containing choline salicylate (see the current labels for Bonjela, attached as Annexes 1 and 2).

Table 2: Dose form and strength of products containing choline salicylate

Product name	Dose form	Strength
Bonjela Teething & Mouth Ulcer Gel	Oral topical gel	87 mg/g (8.7 %w/w)
Bonjela Mouth Ulcer & Teething Gel	Oral topical gel	87 mg/g (8.7 %w/w)

Both products also contain 33.45 % w/w ethanol [4].

5. Pack size, storage conditions and other qualifications

Table 3 below shows the pack size, storage conditions and other qualifications of products containing choline salicylate (see the current labels for Bonjela, attached as Annexes 1 and 2).

Table 3: Pack size, storage conditions and other qualifications of products containing choline salicylate

Product name	Pack size	Storage conditions	Other qualifications
Bonjela Teething & Mouth Ulcer Gel	15 g	Store below 25°C	Do not use in babies under 4 months
Bonjela Mouth Ulcer & Teething Gel	15 g	Store below 25°C	Do not use in babies under 4 months

6. Indications for which change is sought

When used for infant teething.

Table 4 below shows the indications of products containing choline salicylate (see the current labels for Bonjela, attached as Annexes 1 and 2).

Table 4: Indications of products containing choline salicylate

Product name	Indication(s) described on the current label
Bonjela Teething & Mouth Ulcer Gel	Provides fast-acting, soothing relief from the pain and discomfort associated with infant teething disorders, mouth ulcers and sores and new dentures
Bonjela Mouth Ulcer & Teething Gel	Provides fast-acting, soothing relief from the pain and discomfort associated with infant teething disorders, mouth ulcers and sores and new dentures

7. Present classification of the medicine

Current classification of choline salicylate:

- prescription medicine; **except** in medicines containing 10% or less and in pack sizes of 15 grams or less

- general sale; in medicines containing 10% or less and in packs sizes of 15 grams or less [6].

8. Classification sought

Proposed classification of choline salicylate:

- prescription medicine; **except** when specified elsewhere in this schedule; **except** in medicines containing 10% or less and in pack sizes of 15 grams or less
- pharmacy-only; in medicines containing 10% or less and in packs sizes of 15 grams or less for the treatment of infant teething
- general sale; in medicines containing 10% or less and in pack sizes of 15 grams or less.

Note that infant is not a term currently used in the First Schedule to the Medicines Regulations 1984. It may be more appropriate to define an age in years instead (in children 18 months of age and younger).

9. Classification status in other countries (especially Australia, UK, USA, Canada)

Table 5 below shows the classification of choline salicylate in other countries. It also includes information on any labelling requirements.

Table 5: Classification status and labelling requirements of choline salicylate in other countries

Name of Country	Classification status and labelling requirements of choline salicylate
Australia	**General sale** There are several choline salicylate containing teething gel products registered in Australia targeting use in children and adults, including Bonjela 87 mg/g (15 g tube)[a]. These products are available in both supermarkets and pharmacies with the following Required Advisory Statement for Medicines Labels (RASML): 'Do not exceed the recommended dose. Excessive or prolonged use can be harmful'[b].
Canada	No teething or mouth ulcer products containing choline salicylate.
Singapore	**General sale** There are three products containing choline salicylate for teething and mouth ulcers (Bonjela Gel, Soragel and Ora-Sed Jel) registered in Singapore[c]. These products contain 8.7 to 9% w/w of choline salicylate. There are no mandatory warning statements for products containing choline salicylate for teething and mouth ulcers. There is a warning on the outer carton label for Bonjela Gel to not exceed the stated dose and to seek medical advice in case of an overdose.
Switzerland	**Pharmacy-only** There is a similar medicinal product with choline salicylate in Switzerland (Mundisal, 1 g Gel contains 87.1 mg choline salicylate), but (similar products) are not for sale in supermarkets[d]. There is a warning in the Swiss Product Information for Mundisal stating that children and young people having fever should use Mundisal on medical prescription and as a second choice only, due to possible occurrence of the Reye-Syndrome, a life-threatening encephalopathy.
UK	**General sale – contraindicated for use in children under the age of 16 years** The UK currently has two products for choline salicylate with active marketing authorisation status, Bonjela[e] and Bonjela Cool Mint Gel[f]. Both Bonjela products contain 8.714 % w/w choline salicylate and are contraindicated for use in children under the age of 16 years[e,f]. Both Bonjela products also contain warnings regarding salicylate toxicity in the Summary of Product Characteristics[e,f]: 'Overdose Salicylate toxicity can result if the stated dose is exceeded.

Name of Country	Classification status and labelling requirements of choline salicylate
	Salicylate poisoning is usually associated with plasma concentrations >350 mg/L (2.5 mmol/L). Most adult deaths occur in patients whose concentrations exceed 700 mg/L (5.1 mmol/L). Single doses less than 100 mg/kg are unlikely to cause serious poisoning. Patients should be given supportive therapy or treatment for salicylate poisoning as necessary. This may include treatment like activated charcoal, urinary alkalinisation and in severe cases haemodialysis.'
USA	No teething or mouth ulcer products containing choline salicylate.

Sources:

a. Therapeutic Goods Administration. 2019. *Australian Register of Therapeutic Goods* 29 October 2019. URL: www.tga.gov.au/australian-register-therapeutic-goods (accessed 1 December 2020).
b. Therapeutic Goods Administration. 2019. *Required Advisory Statements for Medicine Labels (RASML)* 1 March 2019. URL: www.tga.gov.au/publication/required-advisory-statements-medicine-labels-rasml (accessed 27 November 2020).
c. Health Sciences Authority Singapore. 2020. *Register of Therapeutic Products* 1 April 2020. URL: www.hsa.gov.sg/e-services/infosearch (accessed 27 November 2020).
d. Swissmedic. 2019. *Medicinal product information* URL: www.swissmedic.ch/swissmedic/en/home/services/medicinal-product-information.html (accessed 27 November 2020).
e. 11. Reckitt Benckiser Healthcare (UK) Ltd. 2020. *Bonjela Summary of Product Characteristics and Patient Leaflet* 20 November 2020. URL: www.medicines.org.uk/emc/product/624/smpc (accessed 1 December 2020).
f. 12. Reckitt Benckiser Healthcare (UK) Ltd. 2020. *Bonjela Cool Mint Gel Summary of Product Characteristics and Patient Leaflet* 6 November 2020. URL: www.medicines.org.uk/emc/product/5614/smpc (accessed 1 December 2020).

New Zealand is harmonised with Australia and Singapore regarding the classification of choline salicylate. In Switzerland, it is classified as a pharmacy-only medicine.

However, in the UK products containing choline salicylate are contraindicated for use in children under the age of 16 years.

In 2009, a Drug Safety Article was published by the Medicines and Healthcare products Regulatory Agency (MHRA) stating that topical oral salicylate gels were no longer indicated for people younger than 16 years for pain associated with infant teething, orthodontic devices, cold sores, or mouth ulcers [7]. This decision aligned with a recommendation by the Commission on Human Medicines (CHM) in Europe following an in-depth review of these products [7]. The review was triggered by the publication of a report of a suspected case of Reye's syndrome associated with the use of an oral gel that contained choline salicylate in a 20-month-old child [7]. An important factor in this decision is stated to be the availability of alternative treatment options to alleviate pain associated with infant teething, orthodontic braces, and mouth ulcers [7].

The Bonjela products indicated for use in children in the UK contain lidocaine hydrochloride [8]. These products are not available in New Zealand

In 2009, Medsafe also reviewed data from the MHRA, the manufacturer of Bonjela, the Centre for Adverse Reactions Monitoring (CARM) and the New Zealand Poisons Centre [9]. Medsafe's review found no evidence linking Reye's syndrome to the use of topical oral choline salicylate containing products [9]. At the time Medsafe advised prescribers, in an article published in *Prescriber Update*, it was satisfied that the safety of these products in children is acceptable when used at recommended doses [9]. However, the review highlighted that the recommended dose of these products is sometimes exceeded [9].

Note that the current labels for Bonjela (see Annexes 1 and 2) state 'unless a doctor has told you, do not use in children under 16 years of age with or recovering from chicken pox, influenza or fever'.

10. Extent of usage in New Zealand and elsewhere (eg, sales volumes) and dates or original consent to distribute

Bonjela Teething and Mouth Ulcer Gel was first approved in New Zealand in 1966 [4]. Due to the date of approval, it is likely an assessment was never conducted as part of the approval process. Bonjela Mouth Ulcer and Teething Gel was subsequently approved in 2004 [4].

See Annexe 3 for Bonjela sales data.

11. Local data or special considerations relating to New Zealand (if applicable)

Medicines Adverse Reactions Committee

At the 179th meeting in September 2019, the Medicines Adverse Reactions Committee (MARC) highlighted a case report (CARM ID #132801) where a child developed respiratory distress, tachypnoea and metabolic acidosis after an overdose of choline salicylate [1].

The MARC:

- discussed whether the current availability of choline salicylate or the current instructions for use are possible issues
- noted that the usage instructions and warning statements are on the package and the availability of choline salicylate as a general sale medicine
- considered that there is likely to be some benefit from choline salicylate being classified as a pharmacy-only medicine to enable some instruction around its use
- recommended that an application be made to the MCC to review the classification of choline salicylate [1].

Media

This case was also reported in the media [10].

12. Labelling or draft labelling for the proposed new presentation(s)

The current labels for Bonjela are attached as Annexes 1 and 2.

13. Proposed warning statements (if applicable)

According to Medsafe's label statements database, there are currently no warning and advisory statements required on the packs of products containing choline salicylate [11].

Proposed warning statements:

a. Do not use in babies under 4 months of age
b. Do not exceed the maximum stated dose
c. Prolonged or excessive use can be harmful
d. Do not use in patients known to be allergic to salicylates.

The above proposed warning statements a, b and c are already included on the current labels for Bonjela (attached as Annexes 1 and 2).

14. Other products containing the same active ingredient(s) and which would be affected by the proposed change

N/A.

Part B – Evidence supporting the classification change proposal including benefit-risk analysis

1. Indications and dose

According to the New Zealand Formulary, choline salicylate is indicated for mild oral and perioral lesions [3].

The dosing regimen for adults is to cover the tip of the index finger with the oral gel and rub well into the affected area not more often than every three hours [3]. For children four months to 18 years old, the dosing regimen is the same [12].

2. Presentation

There are two products containing choline salicylate currently available in New Zealand.

These products are the same formulation but have slightly different names and presentations:

- Bonjela Teething and Mouth Ulcer Gel comes in a blue pack and has an image of an infant in pink (see Annexe 1).
- Bonjela Mouth Ulcer and Teething Gel comes in a blue pack with an image of an adult in blue (see Annexe 2).

3. Consumer benefits

Reclassifying choline salicylate, when used for infant teething, to a pharmacy-only medicine from availability as a general sale medicine will increase the likelihood of a consumer discussing use of the oral gel with a pharmacist.

Discussion will benefit the consumer because the pharmacist can explain how to use the oral gel and recommend alternatives such as giving an infant something cold to suck or chew on [13].

4. Contraindications and precautions

In the absence of a New Zealand data sheet, the following information is from the New Zealand Formulary.

Choline salicylate is contraindicated in children under four months [3, 12].

Frequent application, especially in children, may lead to salicylate poisoning [3, 12].

Patient advice includes:

- avoiding prolonged or excessive use, especially in infants
- for infants under four months consult a doctor
- caution in patients sensitive to salicylates [3, 12].

5. Undesirable effects

Adverse reaction reports from the Centre for Adverse Reactions Monitoring (CARM)

The Centre for Adverse Reactions Monitoring (CARM) has received two reports where choline salicylate was the suspect medicine. Table 6 below summarises these two reports. See Annexe 4 for the full report from CARM.

Table 6: Summary of all cases reported to CARM involving choline salicylate up to June 2020

CARM ID #	Date	Gender	Age	Medicine(s)	Reaction(s)
085258	July 2009	Male	18m	*Bonjela *Paracetamol	Somnolence Irritability Convulsions Thirst Constipation
132801	May 2019	Female	7m	*Bonjela Weleda teething powder Naturopharm teething spray Paracetamol Ibuprofen	Respiratory distress Tachypnoea Acidosis metabolic Overdose effect Medication error

*Indicates the suspect medicine

The Therapeutic Goods Administration (TGA) in Australia has received 14 adverse event reports for choline salicylate containing products since 1983 [14]. Of these, 10 are for infants/small children. Two are coded for overdose. Several other cases are coded for adverse events including gastrointestinal symptoms that could be the result of toxicity/overdose despite not being coded as such.

6. Overdose

Data from the National Poisons Centre in New Zealand

The National Poisons Centre has advised Medsafe that 370 calls relating to the use of products containing choline salicylate were received between 1 January 2017 and 30 June 2020.

368 of these calls related to use in children. Table 7 below shows patient age groups of choline salicylate exposures.

Table 7: Patient age groups of choline salicylate exposures in contacts to the National Poisons Centre across the years 2017-2020 (up to June 2020)

	All callers	
Patient age in years	**Number of Patients**	**% of total**
0	79	21.4
1	145	39.2
2	95	25.7
3-4	43	11.6
5-9	5	1.4
Over 20	2	0.5
Unknown child	1	0.3
Total	370	100%

See Annexe 5 for the full report from the National Poisons Centre.

The National Poisons Centre made a few comments in their report to help place their results in context, as follows:

- while the numbers are small, exposures seem to have increased in 2019 and are on a similar track in 2020
- most exposures suggest child exploratory exposures involving young children of teething age
- a medical referral was advised for 14% of exposures
- there were 18 therapeutic error exposures which could represent situations of high risk as inappropriate administration over time can lead to salicylate toxicity.

Information in the UK Summary of Product Characteristics

Bonjela products in the UK contain warnings regarding salicylate toxicity in the Summary of Product Characteristics [15, 16]:

> 'Overdose
>
> Salicylate toxicity can result if the stated dose is exceeded.
>
> Salicylate poisoning is usually associated with plasma concentrations >350 mg/L (2.5 mmol/L). Most adult deaths occur in patients whose concentrations exceed 700 mg/L (5.1 mmol/L). Single doses less than 100 mg/kg are unlikely to cause serious poisoning. Patients should be given supportive therapy or treatment for salicylate poisoning as necessary. This may include treatment like activated charcoal, urinary alkalinisation and in severe cases haemodialysis.'

In New Zealand there is no requirement for a pharmacy-only or general sale medicine to have a data sheet (ie, summary of product characteristics).

7. Medication errors and abuse/misuse potential

Health Navigator includes the following warning regarding the safe use of Bonjela:

WARNING: Safe use of Bonjela – using too much can harm your baby
If using a teething gel such as Bonjela, follow the directions on the package or ask your pharmacist. In New Zealand, Bonjela teething gel contains a mild pain reliever called choline salicylate – this can be very harmful to your baby if too much is given.
Check the age restriction: this is either on the package or ask your pharmacist, eg, should not be used in children aged less than 4 months old.
Do not exceed the recommended dose: follow the dosing instructions on the packaging or ask your pharmacist about how to use the gel correctly. The dose for Bonjela is to rub a small quantity of gel (a pea-sized amount, or cover the tip of your index finger) to the affected area **no more than every 3 hours** and do not use it more than 6 times in 24 hours. You can overdose your baby by applying too much gel or using it too often.
Keep all medicines out of sight and reach of children
SIGNS OF OVERDOSE include vomiting, unusual sleepiness, fever and rapid breathing. Call Healthline free (within New Zealand) on 0800 611 116 or see your doctor urgently if you are concerned about your child or think accidental overdose may have occurred.

Source: Health Navigator. 2020. *Teething* 25 August 2020. URL: www.healthnavigator.org.nz/healthy-living/t/teething/ (accessed 10 December 2020).

8. Communal harm and/or benefit

Whilst there is little evidence for the effectiveness of oral gels for teething and ulcers, they are still used in New Zealand.

Reclassifying choline salicylate, when used for infant teething, to a pharmacy-only medicine from availability as a general sale medicine will decrease the communal harm and increase the communal benefit.

9. Integrated benefit-risk statement

The expected benefit of this reclassification is an increase in the likelihood of a parent discussing use of the oral gel with a pharmacist. This in turn will reduce the risk of overdose.

There is not much in the literature regarding choline salicylate and very little published in recent years (search conducted using the PubMed database [17]). Most of the literature focuses on teething and use in children.

There are case reports internationally of salicylate intoxication in infants [1]. A 'Lessons from Practice' article in the Medical Journal of Australia in 2011 describes two patients with potential choline salicylate toxicity [1]. The authors conclude:

- chronic salicylate intoxication in infants may be subtle but potentially life-threatening

- significant inadvertent salicylate poisoning from over-the-counter preparations can occur
- all salicylate-containing products should have an appropriate warning label
- warnings are not present on packaging of several salicylate containing teething gels that are marketed for infants in Australia and New Zealand [1].

An article in the British Dental Journal from 2002 describes several topical gels that help with teething, including choline salicylate [2]. The authors describe choline salicylate as an analgesic, anti-inflammatory and antipyretic [2]. However, they do acknowledge that some of the reported relief may be due to the pressure of application.

There is little evidence that teething gels are effective which may be because most of the gel is likely to be quickly removed by the tongue and saliva [13, 18] .

This is supported by article in UpToDate which states that the benefit of topical gels or teething tablets in managing teething pain has not been demonstrated, and they may be harmful [19].

10. Risk mitigating strategies

Reclassifying choline salicylate, when used for infant teething, to a pharmacy-only medicine from availability as a general sale medicine will not require any risk mitigating strategies.

3) Conclusion

Choline salicylate is currently available as a general sale medicine in New Zealand.

This application requests a change in the classification of choline salicylate, when used for infant teething, to pharmacy-only medicine for the following reasons.

- The MARC recommended that an application be made to the MCC to review the classification of choline salicylate following discussion of a report in which a child developed respiratory distress, tachypnoea and metabolic acidosis after an overdose of choline salicylate.
- Frequent application especially in children may lead to salicylate poisoning.
- There have been adverse reaction reports locally and internationally with choline salicylate as the suspect medicine, some of which include overdose in children.
- The National Poisons Centre has received 370 calls regarding exposure to choline salicylate; 368 of these calls were related to children.
- The expected benefit of this reclassification is an increase in the likelihood of a parent discussing use of the oral gel with a pharmacist. This in turn will reduce the risk of overdose.

In the absence of a New Zealand data sheet, it would also be pertinent to update Medsafe's labels statement database with the following proposed warning statements:

a. Do not use in babies under 4 months of age
b. Do not exceed the maximum stated dose
c. Prolonged or excessive use can be harmful
d. Do not use in patients known to be allergic to salicylates.

4) Annexes

1. Reckitt Benckiser. 2019. *Current label for Bonjela Teething & Mouth Ulcer Gel* 5 September 2019 **[CONFIDENTIAL]**.

2. Reckitt Benckiser. 2019. *Current label for Bonjela Mouth Ulcer & Teething Gel* 5 September 2019 **[CONFIDENTIAL]**.
3. Reckitt Benckiser. 2020. *Sales data for Bonjela* 2015 – August 2020 **[CONFIDENTIAL]**.
4. Centre for Adverse Reactions Monitoring. 2020. *Bonjela Review: All cases reported to CARM up to 30 June 2020* August 2020. Dunedin: New Zealand Pharmacovigilance Centre **[CONFIDENTIAL]**.
5. National Poisons Centre. 2020. *Data request for choline salicylate* 23 August 2020. Dunedin: National Poisons Centre. **[CONFIDENTIAL].**

5) References

1. Williams G, Kirk E, Wilson C, et al. 2011. Salicylate intoxication from teething gel in infancy. *The Medical Journal of Australia* 194(3): 146-148. URL: www.mja.com.au/system/files/issues/194_03_070211/wil10690_fm.pdf (accessed 10 December 2020).
2. McIntyre G and McIntyre G. 2002. Teething troubles? *British Dental Journal* 192(251-255. URL: www.nature.com/articles/4801349 (accessed 10 December 2020).
3. New Zealand Formulary. 2020. *New Zealand Formulary v102: Choline salicylate* 1 December 2020. URL: https://nzf.org.nz/nzf_6182 (accessed 10 December 2020).
4. Medsafe. 2019. *Product/Application Search* 31 May 2019. URL: www.medsafe.govt.nz/regulatory/DbSearch.asp (accessed 1 December 2020).
5. Medsafe. 2019. *Minutes of the 179th Medicines Adverse Reactions Committee Meeting held on 12 September 2019* 25 October 2019. URL: www.medsafe.govt.nz/profs/adverse/Minutes179.htm#2.1.2 (accessed 6 November 2020).
6. Medsafe. 2020. Choline salicylate. In: *Medicines Classification Database* 5 November 2020. URL: www.medsafe.govt.nz/profs/class/classintro.asp (accessed 23 November 2020).
7. Medicines and Healthcare products Regulatory Agency. 2009. Oral salicylate gels: not for use in those younger than age 16 years. *Drug Safety Update* 2(11): 4. URL: www.gov.uk/drug-safety-update/oral-salicylate-gels-not-for-use-in-those-younger-than-age-16-years (accessed 1 December 2020).
8. Reckitt Benckiser Healthcare (UK) Ltd. 2019. *Bonjela Junior Gel Summary of Product Characteristics and Patient Leaflet* 3 April 2019. www.medicines.org.uk/emc/product/5176/smpc (accessed 21 December 2020).
9. Medsafe. 2009. Topical oral choline salicylate gels - safety in children. *Prescriber Update* 30(3): 17. URL: www.medsafe.govt.nz/profs/PUArticles/Topical%20oral%20choline%20salicylate%20gels%20-%20safety%20in%20children%20-%20Aug%2009.htm (accessed 8 December 2020).
10. Te M and Moger L. 2019. Baby's Bonjela scare leads mum to call for warnings over mouth gels. In: Stuff 1 May 2019. URL: www.stuff.co.nz/life-style/parenting/112362181/potential-to-kill-mother-calls-for-awareness-over-dangers-of-mouth-gels-for-babies (accessed 15 December 2020).
11. Medsafe. 2020. *Label Statements Database Edition 2.0 (October 2020)* 30 October 2020. URL: www.medsafe.govt.nz/regulatory/labelling.asp (accessed 8 December 2020).
12. New Zealand Formulary for Children. 2020. *New Zealand Formulary for Children v102: Choline salicylate* 1 December 2020. URL: www.nzfchildren.org.nz/nzf_6182 (accessed 10 December 2020).
13. Health Navigator. 2020. *Teething* 25 August 2020. URL: www.healthnavigator.org.nz/healthy-living/t/teething/ (accessed 10 December 2020).

14. Therapeutic Goods Administration. 2020. *Database of Adverse Events Notifications (DAEN) - Medicines* 1 August 2020. URL: www.tga.gov.au/database-adverse-event-notifications-daen (accessed 27 November 2020).
15. Reckitt Benckiser Healthcare (UK) Ltd. 2020. *Bonjela Summary of Product Characteristics and Patient Leaflet* 20 November 2020. URL: www.medicines.org.uk/emc/product/624/smpc (accessed 1 December 2020).
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17. National Library of Medicine. 2020. *PubMed* 2020. URL: https://pubmed.ncbi.nlm.nih.gov/ (accessed 10 December 2020).
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19. Wright J, Griffen A and Torchia M. 2020. Anatomy and development of the teeth. In: UpToDate 22 April 2020. URL: www.uptodate.com/contents/anatomy-and-development-of-the-teeth (accessed 10 December 2020).