1. Application for new medication: Resin-based composite

This submission proposes the inclusion of a new medicine/preparation to Section 30 *Dental Preparations* of the 22nd EML (2021)/8th EMLc (2021). The new medicine is **resin-based composite** as an addition to Section 30 "Dental preparations" that was created in 2021.[1]

Resin-based composites are a group of dental materials with widespread global use for different indications. This document focuses on two main uses/indications:

1) Prevention of dental caries –using resin-based composite for dental sealants. A dental sealant is a coating applied to the biting surface of posterior teeth (molars and premolars), forming a hard shield that keeps food and bacteria from getting into the tiny grooves in the teeth (pits and fissures) and causing caries. Sealants have been used for over 50 years as a tool for dental caries prevention. High-viscosity resin-based composite formulations and high-viscosity glass ionomer cements (GIC) are the materials used as dental sealants. The product group of GIC was already added to the EML/EMLc in 2021.[1]

2) Treatment of dental caries – using resin-based composites as a filling material to treat carious lesions (cavities). Cavities can be filled with resin-based composites after either conventional dental cavity preparation with a drill or the WHO-endorsed Atraumatic Restorative Treatment (ART) approach involving minimal removal of tooth structures with hand instruments.

Resin-based composites is an umbrella term for a wide range of products consisting of a synthetic resin matrix and inorganic fillers (different forms of quartz and glass), held together by a bonding phase (silanes).[2 3]

Risks and adverse effects of resin-based composites are negligible. Cost-effectiveness of resin-based composites for dental sealants and fillings is good, though more studies from different settings are required to provide a more complete assessment in comparison with other materials.

In light of the agreed phase-down of dental amalgam use,mandated for parties to the Minamata Convention on Mercury, [4] resin-based composites are an essential alternative filling material to dental amalgam. The inclusion in the EML/EMLc would enhance availability on different levels of the healthcare system, particularly in primary health care, and further promote use and uptake of the material.

The application is submitted by:

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The application is supported by:

WHO Collaborating Center Quality Improvement & Evidence-based Dentistry (WHO CC USA-429), College of Dentistry, New York University, New York, USA

2. Summary statement (inclusion)

This submission proposes the inclusion of a new medicine to Section 30 *Dental Preparations* of the 22nd EML (2021)/8th EMLc (2021). The new medicine is **resin-based composite** (any preparation) for use as a pit-and-fissure sealant in the context of caries prevention in oral health care services, primary care facilities and community settings (i.e. schools and other education settings); or as mercury-free filing material for anterior and posterior teeth. A large and robust body of evidence indicates that resin-based composites are effective and safe to use in all age groups, as well as people with special needs.

Caries of primary (deciduous) and permanent teeth is among the most common diseases of mankind, affecting 2.5 billion people according to latest available estimations.[5] Caries of primary teeth affects an estimated 514 million children (43% average global prevalence) and caries of permanent teeth affects an estimated 2 billion people (29% average global prevalence). The highest burden of caries is reported from low- and middle-income countries where access to prevention and oral health care is challenging, particularly for disadvantaged population groups. Effective caries prevention and treatment strategies are therefore of high public health importance and the use of resin-based composites is among the most cost-effective and evidence-based interventions available.

The World Health Assembly resolution on oral health (WHA74/A74.R5, 2021)[6] and the WHO Global Strategy on Oral Health (A75/10 Add.1, 2022)[7] emphasize the urgent need to intensify preventive efforts for all oral diseases and especially dental caries. The Global Strategy states that "WHO will develop technical guidance on environmentally sustainable oral health care, including mercury-free products and less invasive procedures." A draft Global Oral Health Action Plan will be proposed at EB152 in January 2023,[8] proposing (among others) a global target related to implementation of the Minamata Converntion on Mercury and the phase-down of dental amalgam.

Application context

This application proposal to include resin-based composites in the EML/EMLc builds on the establishment of Section 30 "Dental preparations" in the EML/EMLc 2021[1 9] Moreover, the wider context of the proposal takes responds to the provisions of the Minamata Convention on Mercury[4] which calls for the elimination of mercury from the environment, including the phase-down of dental amalgam as a commonly used mercury-containing dental filling material.[10–12] The draft Global Oral Health Action Plan (proposed at EB152 in January 2023),[8] will introduce (among others) a target related to the implementation of the Minamata Convention on Mercury and the phase-down of dental amalgam use. It is therefore important that mercury-free alternative filling materials are widely available and affordable.

3. Consultation with WHO technical departments

The submission is made by the WHO Oral Health Programme, Noncommunicable Diseases Department, Division of UHC/Communicable and Noncommunicable Diseases, WHO HQ. The regional focal points for oral health at WHO AFRO (Dr Yuka Makino), WHO EMRO (Dr Huda Abdul Ghaffar), WHO EURO (Ms Carina Ferreira-Borges), WHO PAHO (Dr Carolina Hommes), and WHO SEARO (Dr Nalika Gunawardena) were consulted.

4. Other organization consulted and/or supporting the submission

The WHO Collaborating Center Quality Improvement & Evidence-based Dentistry (WHO CC USA-429), College of Dentistry, New York University, New York, USA, was consulted and supported the development of the application documents (Dr Habib Benzian/Dr Eugenio Beltrán).

5. Key information for the proposed medicine

5.1 International non-proprietary name (INN) of the proposed medicine

N/A

5.2 Anatomical therapeutic chemical (ATC) code of the proposed medicine

Preparations used as filling materials are not listed in the ATC code list, closest available includes:

A01A: Stomatological preparations

A01AA: Caries prophylactic agents (this group comprises all types of fluoride preparations)

5.3 Dosage form(s) and strength(s) of the proposed medicine

Resin-based composite is available in ready-to-use form for either pit-and-fissure sealants (high viscosity) or as filling material (low viscosity). The chemical composition, type and proportion of fillers determine the viscosity. The most common resin used is *Bowen's resin* (bisphenole A-glycidyl methacrylate - Bis-GMA), but other resins are also used such as ethoxylated bisphenol A-glycol dimethacrylate (Bis-EMA), triethylene glycol dimethacrylate (TEGDMA), Hydroxyethyl methacrylate (HEMA), or urethane dimethacrylate (UDMA).[2 3]

Resin-based composite is intended for use by oral health professionals only and is not available to patients.

5.4 Indication(s)

The primary indication is the prevention (dental sealant) and treatment (filling material) of dental caries. A minor indication is the restoration of front teeth after traumatic injury.

ICD-11 Codes: DA08.0 Dental caries

NA0D.0Z Injury of hard dental tissues and pulp

6. Proposal for an individual medicine or representative of a pharmacological class / therapeutic group

This proposal is representative of a therapeutic group: Resin-based composites, which are a group of dental materials with widespread global use for different indications. This proposal focuses on two main uses, the prevention and treatment of dental caries, canvassing the indications and variation in formulation which generally apply.

7. Information supporting the public health relevance

7.1 New medicine

Resin-based composites are a key group of dental filling materials/preparations used to prevent dental caries and restore dental hard tissue that has been lost due to dental caries (or dental trauma). In view of the significant global burden of oral diseases and especially dental caries, the safety, efficacy, cost-effectiveness and its clinical features make resin-based composites a medicine/preparation with very high public health relevance.

Epidemiological information on disease burden

The WHO Global Oral Health Status Report,[5] using the latest available data of the Global Burden of Disease Study 2019, estimates that oral diseases affect close to 3.5 billion people worldwide, the most common disease group of all diseases and conditions studied. Dental caries is the most widespread oral disease with more than 2.5 billion cases of untreated disease. This includes more than 2 billion estimated cases of caries in permanent teeth (global average prevalence of 29%) and 514 million estimated cases of caries in primary (deciduous) teeth (global average prevalence of 43%). Among the 194 Member States, 134 have prevalence figures greater than 40% for caries in primary teeth. More than three-quarters of cases of untreated caries teeth are found in middle-income countries. Over the last 30 years there has been an increase of cases that is surpassing the demographic population growth during the same period.[5]

Target population(s)

The target population is in principle everyone with untreated dental caries – about 2.5 billion people. The caries burden is hugely unequal across populations, within and between countries, with a clear socio-economic gradient showing higher disease burden in deprived and disadvantaged populations who at the same time have less access to prevention and oral care services.[5 13] Dental caries is a disease affecting people across the entire life course. All age groups are affected with different trajectories of burden - an onset in early childhood, generally significant prevalence increases in adolescent age groups and continued increase in adulthood.[14]

Untreated dental caries causes pain, infection, and may lead to systemic infections requiring hospitalization and complex treatment. Also, a high prevalence and severity of untreated dental caries is a co-factor for low BMI and stunting in children;[15 16] it also leads to significant absenteeism in school and workplaces.[17 18] Good oral health is also vital for healthy ageing, playing a crucial role with regard to nutrition.[19 20]

Alternative medicines currently listed on the EML for the proposed indication

There is currently no medicine/preparation listed on the EML/EMLc with a usage profile similar to resin-based composite. Glass ionomer cement (GIC), a preparation added in 2021, shares the role as a dental sealant and filling material used in the prevention and treatment of dental caries. The characteristics of resin-based composite are, however, rather different from GIC. In particular, the aspect of adhesive application and the esthetic properties of composites make them especially suitable for fillings in anterior teeth. Other comparative aspects are detailed in Section 9.

Moreover, in the context of the phase down of dental amalgam use as a filling material for posterior teeth (as outlined by Minamata Convention on Mercury), it is crucial that a mercury-free alternative filling material is available. Resin-based composite fillings offer better durability compared to GIC in this regard.

8. Treatment details

8.1 Dosage regimen and duration of treatment

Resin-based composites are available in a range of dosage and application forms, depending on the indication and intended usage.

Pit and fissure sealant[3]

Resin-based sealants (RBS) have been used since the mid-1960s and have evolved as a product class since then. RBS generally have low viscosity (reduced or no filler content) so that the material can flow into the pits and fissures to seal them off and reduce the risk of caries development. RBS almost liquid when applied to the tooth surface and hardened either by activation of chemical catalysts (auto-polymerization) or through light-sensitive activators using specific wave lengths in the blue spectrum emitted from an appropriate light curing device (light polymerization).

Pit and fissure sealants are placed on posterior teeth as soon as they erupt. Typical age recommendations range from 6-12 years (eruption of the first molar at 6 years/second molar at 12 years), but application at a later stage is also possible.[21 22] Applying RBS to primary teeth is possible and even recommended by professional organizations,[21 22] though a recent Cochrane review found only low-level evidence due to paucity of quality trials.[23–25]

Low viscosity resin-based composites suited for dental sealants are available in single-use packaging, generally enough for 4-6 tooth surfaces (0.25ml) including a brush applicator. Multi-patient syringe systems are also available (containing 1.2ml or more). The standard procedures for placing an RBS are described in detail by Naaman et al. (2017) and many other publications.[26]

Filling material for anterior teeth

Resin-based composites are the filling material of choice for restoration of carious lesions (or to restore tooth fractures caused by dental trauma) in anterior teeth where both function and esthetics are important.[27] Extensive reviews of chemical composition and clinical properties are

available, [28–30] including detailed descriptions of the clinical process of placing a composite filling in anterior teeth.[31]

Resin-based composites are generally placed in an adhesive manner following superficial etching of enamel, application of a low-viscosity primer resin and followed by the composite. Manufacturers generally offer a complete filling system with appropriate combinations of products for placing an adhesive filling. Resin-based composites are available in multi-use syringe systems with disposable tips for direct application or indirect application with a spatula into the cavity. Single-use applicator systems are also available

Filling material for posterior teeth

Resin-based composites are also used to restore carious defects in posterior teeth, ranging from small occlusal cavities to large multi-surface cavities in a direct or indirect procedure.[32] The application technique influences the amount of shrinkage during polymerization of the material.[29 33]

Resin-based composites for use in posterior teeth have a generally higher filler component to increase abrasive resistance of the material on the biting surfaces, but a universal material that can be used for both anterior and posterior teeth is also available. Packaging and dosage aspects are similar to the ones described for fillings in anterior teeth.

Other uses of resin-based composites such as luting of orthodontic or prosthetic devices are not part of the application proposal and hence not further discussed here.

8.2 Requirements to ensure appropriate use of the medicine

Resin-based composites are a widely-used and rather well-researched material in oral healthcare. Standard procedures for placing composite fillings are part of every clinical curriculum worldwide, although adaptations are required to address the increasing use for posterior fillings.[34] Every oral health professional is well familiar with the procedures and requirements to place a sealant or filling successfully.

There are no specific requirements or recommendations for patients to observe after a resin-based sealant or filling has been placed.

If any of the medical contraindications exist (see Section 10.1.) resin-based composite should not be used.

8.3 Recommendations in existing WHO guidelines

A WHO technical report from 2009 summarizes and comprehensively reviews the role of different filling materials. The document synthesizes history, uses and limitations of different filling materials, as well as risks and side-effects, and many other aspects.[35] While the conclusions and recommendations of the report remain valid, material sciences have advanced the composition of resin-based composites significantly. Some of the limitations regarding composites mentioned in the report are no longer relevant in the light of these developments. The report already emphasizes the need and urgency to replace dental amalgam as a common filling material with more sustainable mercury-free alternatives.

A recent WHO briefing note on *Prevention and treatment of dental caries with mercury-free products and minimal intervention* in the context of the Minamata Convention on Mercury[36] provides updated guidance on resin-based composites. The list below from the publication summarizes comprehensively the public health relevance of resin-based composites and related aspects:

- Effectiveness against caries: Composite resin fillings are estimated to have good durability in small to moderate restorations, lasting for approximately eight years. Composite resin is a more durable option for large, multisurface, load-bearing restorations than the main mercury-free, tooth-coloured alternative, glass ionomer cement.
- Minimally invasive and preserves more of the tooth: Minimal intervention restoration with composite resin protects more of the natural tooth structure than conventional methods do. Composite resin relies on chemical etching and bonding to tooth dentine and/or enamel for retention, not mechanical retention within a cavity, which may require removal of healthy tooth tissue for placement of dental amalgam.[37] [38]
- Improved health and quality of life: In protecting teeth and preventing caries, composite resin restorations reduce infection, pain, tooth damage and the need to fill future cavities. This decreases financial burdens on individuals as well as health systems. Other potential positive impacts include reduced absence from school and work and improved quality of life.
- Aesthetics: Unlike dental amalgam, composite resin can match the colour and translucency of natural teeth, so restorations are not easily visible in the mouth. Indeed, for aesthetic reasons, composite resin is often a first choice for restorative veneers of teeth that are easily visible in the mouth.
- Environmental protection and public health: Composite restorations are an important mercury-free alternative to conventional dental amalgam fillings. Use of dental amalgam is being phased down globally to protect human health and the environment from the adverse effects of mercury, in accordance with the Minamata Convention on Mercury.[39]
- Safety and cost-effectiveness: Use of composite resin is cost-effective and potentially widely available, and it has low risks or adverse effects, based on intensive study over 60 years of use around the world. However, composite resin contains monomers, can cause allergic reactions and hypersensitivity, and may affect long-term pulp vitality.
- Suitable for use in primary care: Treatment with composite resin fillings can be provided through primary care facilities by trained dentists, improving the availability, accessibility and acceptability of essential restorative dental care.[40] However, in rural and remote settings, health facilities' sustainable provision of supplies may be a challenge, as well as continued availability of electricity and water, which are necessary for the proper use of resin-based composites.

8.4 Recommendations in other current clinical guidelines

Numerous other clinical guidelines from public health and professional organizations are recommending the use of resin-based composites for the indications mentioned. Selected examples include, but are not limited to:

- American Dental Association: Evidence-based clinical practice guideline on nonrestorative treatments for carious lesions (2018)[41] – available at: https://www.ncbi.nlm.nih.gov/pubmed/30261951
- Public Health England: Delivering better oral health. An evidence-based toolkit for prevention (2021)[42] – available at: https://www.gov.uk/government/publications/delivering-better-oral-health-an-evidence-based-toolkit-for-prevention/chapter-9-fluoride
- Chinese Stomatological Association[43] – available at: https://pubmed.ncbi.nlm.nih.gov/26629554/

Moreover, a comprehensive overview of international guidelines related to pit-and-fissure sealants, including resin-based composite sealants is available in the Annex.[44]

9. Review of benefits: summary of evidence of comparative effectiveness

9.1 New medicine(s) / indication(s)

A large number of authoritative reviews from the last ten years regarding the clinical evidence of effectiveness and comparative effectiveness of resin-based composites as dental sealants and filling materials are available, including several Cochrane reviews.

9.2 Systematic literature search

Information used in application relies on available systematic literature reviews, meta-analyses, and other quality studies. No additional systematic reviews were undertaken.

Literature used was searched on Medline and Scopus using the following search syntax:

(((((caries) OR (dental cavity)) OR (tooth decay)) AND (composite* OR resin filling* OR resin sealant*) AND ((comparative AND (effective* OR analysis)) OR ((effective*) OR (efficacy))))

Filter: review/systematic review/meta analysis – sort by: most recent

9.3 Summary of available evidence for comparative effectiveness

General aspects of resin-based composites

Several reviews report about historical, chemical, material, clinical and safety aspects of composites, including Cochrane reviews.[28 45–48]

The summary findings of these studies indicate that:

- Resin-based composites have been used for more than 50 years worldwide in diverse settings and populations.
- Resin-based composites are a viable mercury-free alternative to dental amalgam and allow for less invasive treatment of dental caries.
- There is currently no alternative material for fillings in anterior teeth with both high functional and aesthetic requirements.
- New materials able to release fluoride or with additional anti-bacterial properties have been developed that show promising results, but require more robust evidence.

Resin-based composites as sealants

A Cochrane review (2017, update from initial review in 2004)[49 50] evaluated dental sealants for dental caries prevention in children and adolescents, while two more specific Cochrane reviews examined comparative aspects with other fluorides and fluoride varnish in particular.[51 52] Another Cochrane review looked at the use of dental sealants in primary teeth.[23]

In addition, several systematic and summary reviews focused on or included resin-based composite and reported comparative aspects with other sealants and/or topical fluoride interventions.[53–60]

The summary findings of these studies indicate that:

- Sealant vs. no sealant: Dental sealants are highly effective in preventing dental caries at rates reaching 80%
- Resin-based sealant vs. glass ionomer sealant: Resin-based sealants have a higher retention rate
- Resin-based sealant vs. fluoride varnish: Both interventions have similar effectiveness with low-level evidence of marginal superiority for resin-based sealant.

It should be noted that when considering and choosing interventions in real-life more factors than comparative effectiveness need to be taken into account such as cost, available resources, capacities and population profile.

Resin-based composites as filling material

Several reviews, including Cochrane reviews, report and summarize evidence for using resin-based composites as a filling material (both in anterior and posterior teeth), as well as comparative aspects with using dental amalgam as a filling material in posterior teeth.[28 30 32 60–63]

The summary findings of these studies indicate that:

- Fillings have a high effectiveness of around 80%
- Resin-based composite is highly suitable for fillings in anterior and posterior teeth (and is far superior than any other material for fillings in anterior teeth)
- Available evidence for use of resin-based composites in posterior teeth vs. dental amalgam fillings shows some shortcomings of the material (higher failure rate, higher risk of secondary caries development, clinical differences in procedures and requirements, higher cost).

However, the most recent Cochrane review recognizes “that composite resin materials have undergone important improvements in the years since the trials informing the primary analyses for this review were conducted. The global phase-down of dental amalgam use via the Minamata Convention on Mercury is an important consideration when deciding between amalgam and composite resin dental materials.“ [62]

9.4 Assessment of applicability of the available evidence across diverse populations and settings

Resin-based composites are being used almost universally around the world, for diverse populations and in a broad range of clinical and community settings (see also Section 8.3 and WHO Briefing Note 2022).[36]

10. Review of harms and toxicity: summary of evidence of comparative safety

10.1 New medicine

Seyed et al. (2015)[64] review allergic reactions to dental materials comprehensively, taking both patients and providers into account. For resin-based composites the main potential allergen is the metacrylate compound, but reports of allergic reactions to resin-based composite fillings or dental sealants are rare. If symptoms occur, they are generally local (such as erythema of the surrounding gum) and subside after removal of the material. Recent studies confirm that the materials are safe with no ill health effects.[62] There is also no indication of any association between placing resin-based composites and adverse pregnancy outcomes.[65]

However, resin-based composites should not be used when a clear medical contraindication such as an allergy against one or several of the product ingredients is known.

11. Summary of available data on comparative cost and cost-effectiveness

11.1 New medicine

Cost and cost-effectiveness depend on a broad range of contextual factors, including the setting, equipment used, workforce cost, treatment duration, and many more. Cost and cost-effectiveness of using resin-based composites are not well researched.

A study from Chile modelled cost-effectiveness of different caries preventive programmes and found sealants to be the least cost-effective intervention at a cost of $11.56 USD per averted diseased tooth.[66] Schwendicke et al (2021)[67] found that sealants are generally cost-effective with a slight disadvantage for resin-based composites compared to GIC sealants.

For using resin-based composite as a filling material for posterior teeth, a study involving 9 EU member states showed that a dental amalgam filling was considerably less expensive (€2.03 EUR for amalgam vs. €4.75 EUR for resin-based composite).[68] Differences resulted from less intervention time required for dental amalgam.

There is no summarized information on international market prices of resin-based composites.

The direct patient costs for a resin-based composite filling or dental sealant generally include the costs of the professional service and any material required. Privately insured patients are often billed separately for material cost. Some health systems using fee-for-service payments have dedicated dental billing codes for fillings (depending on the size of the restoration) and dental sealants, though reimbursements depend on coverage rules, inclusion of age groups and

several other factors. Other health systems use a capitation approach to cover caries preventive interventions such as sealants which then also include the required medicine/preparation.

For public services, procurement of supplies such as resin-based composite is generally undertaken by the service administration (i.e. Ministry of Health or related agency). For such situations bulk purchasing agreements may be negotiated in the context of public tender processes, but information is not publicly available.

12. Regulatory status, market availability and pharmacopoeia standards

12.1 New medicine

Resin-based composites are available via medical/dental retailers for professional use.

12.2 Regulatory status of the proposed medicine

European Union: Resin-based composites fall under medical devices:[69] – Class IIa Rule 8 (invasive devices – intended to be placed in teeth) or Rule 14 for preparations containing nanoparticles

Australia: dental filling materials and sealants must be listed by the Australian Therapeutic Goods Administration (https://www.tga.gov.au)

United States: Class II medical device; Department of Health and Human Services, Food and Drug Administration (FDA). Dental devices; general provision and classifications of 110 devices (21 CFR Part 872)[70]

A number of ISO Standards relate to aspects of resin-based composites in dentistry:

- ISO 4049:2019 Dentistry – Polymer-based restorative materials

Specifies requirements for dental polymer-based restorative materials supplied in a form suitable for mechanical mixing, hand mixing or energy activation, and intended for use primarily for the direct or indirect restoration of teeth and for luting. Available at: https://www.iso.org/standard/67596.html

- ISO 17304:2013 Dentistry – Polymerization shrinkage

Specifies a test method for the measurement of the polymerization shrinkage of external energy-activated polymer-based restorative materials such as composites and core materials. Available at: https://www.iso.org/standard/59772.html

- ISO 29022:2013 Dentistry – Adhesion – Notched-edge shear bond strength test

Specifies a shear test method used to determine the adhesive bond strength between adhesive direct dental restorative materials and tooth structures. Available at: https://www.iso.org/standard/45285.html

- ISO 6873:2015 Dentistry – Polymer-based pit and fissure sealants

Specifies requirements and test methods for polymer-based materials intended for sealing pits and fissures of teeth. Available at: https://www.iso.org/standard/67595.html

- ISO/DIS 3990 Dentistry – Evaluation of antibacterial activity of dental restorative materials, luting cements, fissure sealants and orthodontic or luting materials (under development)
  The standard aims to to define a scheme for testing which requires decisions to be made in a series of steps rather than to specify a single test. This should lead to the selection of the most appropriate test for a respective dental restorative material to be evaluated. Available at: https://www.iso.org/standard/79697.html

12.3 Market availability of the proposed medicine

Comprehensive or authoritative Information on market availability of resin-based composites is not readily available. Private market research companies provide costly analysis reports for corporate use.

A tentative estimate of the global market in 2021 amounts to $4.7 billion USD with high projected growth rates (source: https://dataintelo.com/report/global-dental-composites-sales-market/)

Considering that resin-based composite is a standard product for any dental retailer/distributor it can be assumed that general availability for private oral health professionals is good. In contrast, availability of such supplies and medicines is oftentimes limited in public oral health services.[71]

12.4 Pharmacopoieal standards

N/A

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14. Annex

Annex 1: International guidelines related to sealants, including resin-based sealants[44]

Title	Organization	Year	Country	Exclusion criteria
Pit and fissure sealants. Evidence-based guidance on the use of sealants for the prevention and management of pit and fissure (40)	Irish Oral Health Services	2012	Ireland	
Oral Health Assessment: Best practice guidance for providing an oral health assessment program for school-aged children in Ireland (41)	Irish Oral Health Services	2012	Ireland	Fissure sealants are not the main topic
Guideline on xylitol use in caries prevention (42)	The American Academy of Pediatric Dentistry (AAPD)	2011	USA	Fissure sealants are not the main topic
Guideline for the use of fissure sealants including management of the stained fissure in first permanent molars (43)	British Society of Paediatric Dentistry	2010	UK	No full text available
Prevention and management of dental caries in children (44)	NHS Scotland Scottish Dental Clinical Effectiveness Programme	2010	Scotland	Fissure sealants are not the main topic
Leitlinie Fissurenversiegelung (Pit and fissure sealing) (45)	Zahnarztliche Zentralstelle Qualitatssicherung (ZZQ)	2010	Germany	No English version. Fissure sealants are not the main topic
Karieksen hallinta (Management of dental caries) (46)	Finnish Medical Society Duodecim & Finnish Dental Society Appollonia Association	2009	Finland	No English version
Preventing dental caries through school-based sealant programs: updated recommendations and reviews of evidence (5)	Centers for Disease Control and Prevention (CDC)	2009	USA	Not European
Guideline on management of dental patients with special health care needs (47)	American Academy of Pediatric Dentistry	2009	USA	Not European Fissure sealants are not the main topic
Guidelines for the use of fluorides (48)	New Zealand Guidelines Group (NZGG)	2009	New Zealand	Not European Fissure sealants are not the main topic
Guideline on pediatric restorative dentistry (49)	American Academy of Pediatric Dentistry	2009	USA	Not European Fissure sealants are not the main topic
Strategies to prevent dental caries in children and adolescents (50)	Irish Oral Health Services	2009	Ireland	Fissure sealants are not the main topic
Evidence-based clinical recommendations for the use of pit-and-fissure sealants: a report of the American Dental Association Council on Scientific Affairs (51)	American Dental Association: Council on Scientific Affairs.	2008	USA	Not European
Pit and fissure sealants: Use of in Oral Health Services NSW (52)	Department of Health, NSW	2008	Australia	Not European
Health Partners Dental Group and Clinics caries guideline (53)	Minneapolis (MN): Health Partners Dental Group	2008	USA	Not European Fissure sealants are not the main topic
Topical Fluorides: Guidance on the use of topical fluorides for caries prevention in children and adolescents in Ireland (54)	Irish Oral Health Services	2008	Ireland	Fissure sealants are not the main topic
Adolescent oral health care (55)	American Academy of Pediatric Dentistry	2005	USA	Not European Fissure sealants are not the main topic
Assessment of caries risk and indications for pit and fissure sealants (first and second permanent molars) (56)	HAS (FR)-French National Authority for Health (ANAES).	2005	France	
European Academy of Paediatric Dentistry – EAPD guidelines for the use of fissure sealants (39)	European Academy of Paediatric Dentistry	2004	Europe	