

<b>Glass Ionomer Cement</b>
<b>1. Summary statement of the proposal for inclusion, change or deletion.</b>
<p>The listing for glass ionomer cement (GIC) on both the core EMLc and core EML is being sought. The entry should be part of the new category “30. Dental medicines” and a subgroup “30.1. Medicines for dental caries”.</p> <p>The rationale for the modification and addition of a new category for dental medicines is grounded in the significant burden of oral diseases, particularly untreated dental caries. Oral diseases are major public health problems in all countries worldwide. Caries is the most common disease of mankind, affecting about 530 million children (deciduous teeth) and 2.3 billion adolescents and adults (permanent teeth).<sup>11</sup> This makes nearly a third of the world’s population the target group of caries-related interventions using GIC.</p> <p>GIC is a dental material with widespread global use for different indications. This document focuses on two main uses:</p> <p>1) Prevention of caries – by using GIC for dental sealants. A dental sealant is a coating applied to the biting (occlusal) surface of the back teeth (molars and premolars), forming a hard shield that keeps food and bacteria from getting into the tiny grooves in the teeth (fissures) and causing caries. Sealants have been used for over 50 years. GICs and high-viscosity glass ionomer cements (HV-GICs) are used as dental sealing material (besides resin-based products).</p> <p>2) Treatment of caries – by using GIC as a filling material to treat initial non-cavitated and cavitated carious lesions. The latter can be filled with GIC after either conventional dental cavity preparations or the WHO-endorsed Atraumatic Restorative Treatment (ART) approach involving minimal removal of tooth structures with hand instruments.</p> <p>GIC has caries-preventive properties due to continued capture and release of fluoride ions that remineralise carious tooth structures and have a bacteriostatic effect. GIC results in lower rates of recurring caries compared to composite resin or amalgam fillings; and reduces incidence of new cavities on other teeth. The simplicity of application makes GIC suitable for primary health care and field settings, including for people with special needs.</p> <p>Risks and adverse effects of GIC are negligible.</p> <p>Cost-effectiveness of the GIC 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.</p> <p>In the light of the agreed phase-down of dental amalgam as stated in the UN Minamata Convention on Mercury,<sup>26</sup> GIC provides a cost-effective alternative. Its inclusion on the EML 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 unique caries-preventive properties of the material make it superior to any other material available.</p>
<b>2. Relevant WHO technical department and focal point (if applicable).</b>
Dr Benoit Varenne, Dental Officer, Oral Health Programme, Noncommunicable Diseases Department, Division of UHC/Communicable and Noncommunicable Diseases
<b>3. Name of organization(s) consulted and/or supporting the application.</b>
<p>University of Washington, Department of Dental Sciences, Seattle, USA</p> <p>WHO Collaborating Center Quality Improvement &amp; Evidence-based Dentistry (WHO CC USA-429), College of Dentistry, New York University, New York, USA</p> <p>University of the Pacific, Arthur Dugoni School of Dentistry, San Francisco, USA</p> <p>Department of Dentistry, Radboud University Medical Centre, Nijmegen, The Netherlands</p>
<b>4. International Nonproprietary Name (INN) and Anatomical Therapeutic Chemical (ATC) code of the medicine.</b>
<p>ATC Code: To be confirmed</p> <p>A01A: Stomatological preparations – To be confirmed</p> <p>A01AA: Caries prophylactic agents – To be confirmed</p>
<b>5. Dose forms(s) and strength(s) proposed for inclusion; including adult and age-appropriate paediatric dose forms/strengths (if appropriate).</b>

Glass ionomer cement (GIC) used for caries preventive (dental sealants) and caries treatment (fillings) comes in two primary dose forms with similar composition but different conveniences. GIC can be used as single-use capsules, containing 0.4 g powder and 0.09 ml liquid. Capsules offer a consistent and fast mix due to precise liquid-powder ratio and isolation during mix, but require a spring-loaded or an electric triturator (mixer). The other dose form are multi-use bottles, which may contain 15 g powder and 6.4 ml liquid and can be used anywhere; the final product can be affected by mix precision and humidity.

There are no differences in composition when used in children or adults. Typical doses for dental sealants are approximately 0.1 ml per tooth, or 0.4 ml for four molars placed simultaneously. Actual applied dose scales by indication. Primary teeth are smaller, dose is smaller.

Powder (fluoro-alumino-silicate glass) contains: 25-50% silicate, 20-40% aluminium oxide, 1-20% fluoride, 15-40% metal oxide, 0-15% phosphate, remainder are polyacrylic acid powder and metals in minimal quantities. Liquid (aqueous) contains: 7-25% polybasic carboxylic acid, 45-60% polyacrylic acid.

Aspects of GIC are standardized by ISO 9917-1:2007, such as testing methodology, minimum requirements, labeling and other matters.<sup>14</sup>

Example patents provide further composition details: <https://patents.google.com/patent/US3814717A/en>, <https://patents.google.com/patent/US4775592A/en>, <https://patents.google.com/patent/US10646408B2/en>, <https://patents.google.com/patent/US4342677A/en>

Suggested new entry: Glass Ionomer Cement

Glass Ionomer Cement in any formulation for preventive dental sealants and fillings

## 6. Whether listing is requested as an individual medicine or as representative of a pharmacological class.

Individual medicine

## 7. Treatment details (requirements for diagnosis, treatment and monitoring).

The GIC can be clinically applied without complex equipment, nor is specialised equipment needed for the diagnosis of visible caries. For using GIC as dental sealant no diagnosis is required as it can be performed as a preventive intervention without any caries present.

Treatment procedure/therapeutic regimen:

1. *Preventing caries with dental sealant:* Early after eruption of both primary and permanent molars - clean the tooth with a toothbrush, consider use of 10-20% polyacrylic acid conditioner, dab dry with cotton, mix and place ~0.1 mL of HV-GIC, contour and remove excess, cover with thin layer of hydrophobic material such as petroleum jelly or cocoa butter. Treatment is performed once per erupting molar tooth, for example four permanent first molars around 6 years of age and sealing of four permanent second molars around 12 years of age.

This procedure can be performed in a dental clinic or in a community setting such as in a school. Diagnosis is not necessary. The therapeutic effect does not require long term retention of the bulk material, so monitoring is not essential. Minimal training for a dental assistant, dental therapist, dental nurse, dental hygienist, or dentist is required, but non-dental healthcare workers have also been successfully trained to apply dental sealants.

2. *Treating carious lesions with a filling:* Excavate the bulk of decayed lesions and clean the cavity margins with dental hand instruments. Consider use of 10-20% polyacrylic acid conditioner, dab dry with cotton, mix and place a sufficient amount of HV-GIC to fill the cavity, contour and remove excess, cover with thin layer of hydrophobic material such as petroleum jelly or cocoa butter.

The procedure described above is called Atraumatic Restorative Treatment (ART) and is part of WHO-endorsed concepts for caries management across the lifecourse (see also WHO PAHO website at <https://bit.ly/33wqkIQ>).<sup>7, 8, 29</sup> Monitoring is not essential and may be performed during regular dental check-up visits.

## 8. Information supporting the public health relevance.

Epidemiological information on disease burden / public health need:

The Global Burden of Disease Study 2017 estimated that oral diseases affect close to 3.5 billion people worldwide, with caries of permanent teeth being the most common condition. Globally, it is estimated that

2.3 billion people suffer from caries of permanent teeth and more than 530 million children suffer from caries of primary teeth.<sup>11</sup> The majority of caries remains untreated. 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 that at the same time have less access to care, including prevention.<sup>23</sup> Caries is a disease of all age groups with an onset in early childhood and continued increase over the life-course. Most significant increases in incidence are observed in adolescent age groups. A high prevalence and severity of untreated dental caries is a co-factor for low BMI and stunting; it also leads to significant absenteeism in school and workplaces. Good oral health is also vital for healthy ageing, playing a crucial role with regard to nutrition.

#### Assessment of current use of GIC

There is no publicly available data on use, sales or market share of GIC, besides commercial databases and market surveys. Clinical claims and documentation data generally does not report on types of materials used. However, it is safe to assume that GIC is widely available and widely used for various indications. The predominance of dental amalgam as the standard filling material will be reduced in the coming years, following a trend observed in many countries and in reaction to the provisions of the Minamata Convention. For dental sealants the simplicity of application and superior preventive properties of GIC will lead to an increased share of HV-GIC as compared to resin-based sealant materials.

#### Population impact of using GIC

Globally, prevalence and incidence of untreated caries have remained almost unchanged between 1990 and 2017<sup>11</sup>, while the total number of individuals affected has significantly increased due to population demographics, particularly in LMIC. With the majority of tooth decay remaining untreated, all forms of prevention, particularly fluoride toothpaste and other forms of fluoride delivery as well as prevention through dental sealants are essential. After the onset of carious process and cavitation, availability of simple, cost-effective options for dental fillings are required to improve access and affordability of restorative dental care, and to avoid tooth extraction as the only other treatment option.

The Minamata Convention on Mercury requests a phase-down of the current predominantly used dental filling material, dental amalgam, due to its mercury content.<sup>6; 26</sup> In view of the burden of untreated caries and the need to expand coverage of basic dental services in the context of Universal Health Coverage, availability of GIC as an alternative dental filling material will have crucial importance.<sup>5; 6</sup> Moreover, GIC is also part of the public health tools to provide appropriate levels of fluoride for dental health and to address early childhood caries (ECC).<sup>24; 28; 30</sup>

The expected health-related positive impacts of GIC sealants and fillings include the reduced impact on quality of life through reduction of pain and infection from caries, reduced absence in school and at work, as well as significant health system cost savings. Since the application of GIC sealants and fillings on teeth does not require extensive dental training, it is an alternative to provide access to dental care for caries in rural, remote and otherwise disadvantaged populations through the primary healthcare system.<sup>23</sup>

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

Dental sealants using HV-GIC prevent carious lesions in approximately 71% of treated surfaces regardless of initial lesion presence<sup>1; 13; 18; 31</sup>, with immediate outcomes for treated surfaces similar for conventional resin or HV-GIC, but better longer term results for HVGIC.<sup>21</sup> In addition, HV-GIC reduces new caries incidence by 335 on untreated teeth adjacent to teeth with HV-GIC sealant, no other material shows similar effects.<sup>2</sup> HV-GIC fillings placed with the ART technique have a success rate of 87% after 3 years for single surface carious lesions and 77% after 5 years for multiple surface carious lesions.<sup>4</sup>

HV-GIC fillings have the same success rates as amalgam in preventing recurrent signs of caries (enlarged carious lesion) when used with conventional techniques<sup>3; 9; 17; 19; 20</sup>. Even though HV-GIC fillings tend to fall out more<sup>27</sup>, the caries-preventive effects are better than all other materials.

#### **10. Review of harms and toxicity: summary of evidence of safety.**

Since their introduction in the market more than 30 years ago, the biocompatibility aspects of GIC has been intensively studied. In general, cytotoxicity was shown to be minimal to negligible. A recent Cochrane review concluded that included studies analysing HV-GIC used for dental sealants did not report any adverse effects

of the material.<sup>15</sup> Various in-vitro and in-vivo studies did not find any significant negative effects on pulp, dentine or gingival tissues and cells.<sup>16; 17</sup>

#### **11. Summary of available data on comparative cost and cost-effectiveness of the medicine.**

The average costs for dental sealant, ART or conventional filling using GIC are between \$2 and \$3 per application on multiple teeth.<sup>1; 10; 22</sup> Average conventional fillings using other materials were found to cost between €8 and 156€, though comparability of data is limited and depends on the size and location of the filling and additional supplies or procedures included in the costing.<sup>25</sup> A cost-benefit study conducted in China showed that the incremental cost of four different GIC sealant types in preventing one cavity in permanent molars of school children. Cost ranged between \$52 and \$105 USD per 1000 sealants.<sup>12</sup> The authors conclude that “ease of application, minimal technical and infrastructure requirements, and cost-effectiveness make glass-ionomers a practicable option for governments making decisions under economic constraints.”

#### **12. Summary of regulatory status and market availability of the medicine.**

It is safe to assume that GIC is available in every country worldwide and regulated as a medicinal product. Aspects of GIC are standardized by ISO 9917-1:2007, such as testing methodology, minimum requirements, labeling and other matters.<sup>14</sup>

European Union: GIC must conform with EU Council Directive 93/42/EEC concerning medical devices and falls under Class IIa.

#### **13. Availability of pharmacopoeial standards (British Pharmacopoeia, International Pharmacopoeia, United States Pharmacopoeia, European Pharmacopoeia).**

To be confirmed

#### **14. Comprehensive reference list and in-text citations.**

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