Silver diamine fluoride

Essential medicine status ✓

Section: 30. Dental medicines and preparations

EMLc | ATC codes: Pending

Indication	Dental caries ICD11 code: DA08.0
Medicine type	Chemical agent
List type	Core (EML) (EMLc)
Formulations	Local > Dental > Solution: 38% w/v
EML status history	First added in 2021 (TRS 1035)
Sex	All
Age	Also recommended for children
Therapeutic alternatives	The recommendation is for this specific medicine
Patent information	Patents have expired in most jurisdictions Read more about patents.
Wikipedia	Silver diamine fluoride

Expert Committee recommendation

The Expert Committee noted that dental caries of permanent teeth affects 2.3 billion people worldwide and more than 530 million children suffer from caries of primary teeth. Inequalities throughout the life course and across populations in low-, middle- and high-income countries were also noted, with the highest burden in countries with limited resources for prevention and control. The Expert Committee also noted that primary oral health care in low-resource settings is often limited by a lack of essential supplies such as filling materials or caries preventive agents, a situation which leads to an unnecessary focus of treatment on tooth extraction. The application of silver diamine fluoride is minimally invasive, pain free and particularly suitable for people unable to tolerate conventional invasive dental treatment, such as young children, elderly people, and patients with mental health conditions who may have difficulty cooperating. The Expert Committee considered the evidence included in the application that showed silver diamine fluoride was effective in arresting dental caries in over 80% of cases, being more effective than other management options or placebo. In addition, with a 2-year follow-up, the application of silver diamine fluoride significantly reduced the development of new dentinal carious lesions compared with placebo, no treatment or fluoride varnish. The Committee noted that silver diamine fluoride also has antibacterial effects (from the silver) and remineralizing effects (from the fluoride). Evidence on the benefits of silver diamine fluoride in the prevention of dental caries came from a meta-analysis of two small trials that showed positive effects of silver diamine fluoride compared with placebo or no treatment. However, the included trials had important limitations in study design and implementation, reducing the Committee's confidence in the estimates of the benefit of silver diamine fluoride in caries prevention. The Committee took into account that topical silver diamine fluoride is considered a cost-effective method to prevent and manage dental caries. Moreover, since its application is possible by community health workers or other trained non-dentist personnel, the additional implementation costs of programmes using silver diamine fluoride are much lower than dentist-led fluoride applications. The Expert Committee, therefore, recommended the listing of silver diamine fluoride on the core list of the EML and EMLc in the new section for dental preparations for the treatment of dental caries on the basis of its relevant benefits in arresting dental caries. The Committee considered that inclusion of silver diamine fluoride on the Model List, in alignment with WHO technical guidance on oral health, will support countries to deliver an expanded range of interventions that will benefit the oral health of their populations. The Committee did not recommend the listing of silver diamine fluoride for use in prevention due to uncertainty in the estimates of benefit. The Committee would welcome new evidence supporting its use in prevention of dental

caries for consideration in the future.

Background

Silver diamine fluoride solution has not previously been considered for inclusion on the Model Lists.

Public health relevance

The 2017 Global Burden of Disease Study estimated that oral diseases affect close to 3.5 billion people worldwide, with caries of permanent teeth being the most common condition. Globally, 2.3 billion people are estimated to suffer from caries of permanent teeth and more than 530 million children suffer from caries of primary teeth (1). Most caries are untreated. The caries burden is very unequal across populations within and between countries, with a clear socioeconomic gradient showing higher disease burden in deprived and disadvantaged populations who at the same time have less access to care, including preventive care (2). 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. Silver diamine fluoride application can arrest the progression of existing dental caries and prevent the incidence of new dental caries by about 80% (3). The procedure is painless and arrested carious lesions do not cause further pain and infection (4,5). Silver diamine fluoride treatment is a minimally invasive alternative for treatment for dental caries and is also indicated for people unable to tolerate conventional treatment due to their specific condition (6,7). The expected health-related positive effects of silver diamine fluoride treatment include: improved quality of life through reduction of pain and infection from caries, reduced absence from school and work, and substantial cost savings for health systems. Since the application of silver diamine fluoride on teeth does not require extensive dental training, it can be used to provide people living in rural and remote areas and otherwise disadvantaged populations with access to dental care for caries through the primary health care system (8–10).

Benefits

A 2019 umbrella review, summarizing 11 systematic reviews, evaluated the evidence on silver diamine fluoride for arresting and preventing root and coronal caries (4). Silver diamine fluoride was found to have a positive effect on prevention and arrest of coronal and root caries, consistently outperforming comparators (fluoride varnish, atraumatic restorative treatment and placebo). For root caries prevention, the prevented fraction was 25–71% higher for silver diamine fluoride than placebo. Compared with placebo, silver diamine fluoride was associated with higher prevented fraction for root caries arrest (100–725%), coronal caries prevention (70–78%) and coronal caries arrest (55–96%). Reported caries arrest rates for silver diamine fluoride in primary dentition ranged from 65% to 91%. In comparison, arrest rates for fluoride varnish were 38–44%, for glass ionomer cement were 39–82% and for placebo was 34%. A 2020 review of systematic reviews found that topical application of silver diamine fluoride was effective in arresting dentinal caries in preschool children, with success rates from 79% to 90% reported in the trials (3). A systematic review and meta-analysis of silver diamine fluoride for controlling caries progression in primary teeth found that application of silver diamine fluoride was more effective than other management options or placebo (11). At 12 months, arrest of caries with silver diamine fluoride was 66% higher (95% CI 41 to 91%; $P < 0.00001$) than with other active materials, and 154% higher (95% CI 67 to 85%; $P < 0.00001$) than with placebo. A systematic review and meta-analysis evaluated the effect of silver diamine fluoride in preventing caries in the primary dentition (12). After 2 years of follow-up, application of silver diamine fluoride led to a statistically significant reduction in the development of new dentinal carious lesions compared with placebo or no treatment (weighted mean difference 1.15, prevented fraction 77.5%), and fluoride varnish (weighted mean difference –0.43, prevented fraction 54.0%). In older adults, silver diamine fluoride has also been found to be effective in arresting and preventing root caries (13,14). Silver diamine fluoride was found to arrest root caries by 90% after 30 months of follow-up in a randomized trial of annual silver diamine fluoride application in elderly people living in the community (15).

Harms

No severe harm and adverse health outcomes due to the application of silver diamine fluoride have been reported. Silver diamine fluoride application results in a black stain on the arrested dentine caries lesions, which may cause aesthetic concerns (12,16–18). Tooth pain or gingival irritation, e.g. white lesions on mucosa, gum swelling and gum bleaching, rarely occurred after the application of silver diamine fluoride and subsided rapidly (16,17). Gingival and mucosa reactions are generally related to insufficient compliance with application protocols, such as incidents of spill-over from the dental cavity. As pharmacokinetic studies are

difficult to conduct in children to test the silver disposition after topical silver diamine fluoride application, a pharmacokinetic model was developed to predict silver disposition in children. The findings showed that the topical application of silver diamine fluoride to prevent or arrest dental caries in children resulted in plasma and tissue silver concentrations lower than the toxic concentration (19).

Cost / cost effectiveness

Topical application of silver diamine fluoride is considered a cost-effective method to prevent and manage dental caries. A study in the United States of America found that silver diamine fluoride treatment as a caries management strategy reduced dental care expenditures within the Medicaid programme by avoiding expensive caries treatment options and preventing complex restorative procedures (20). A German study found that silver diamine fluoride application was more cost-effective than chlorhexidine varnish and fluoride rinse. Silver diamine fluoride was considered the most effective and least costly option in populations with a high risk of caries (21). To achieve a high preventive effect (80% prevented fraction), application twice a year is recommended at a total material cost of about US$ 0.20 (22,23). Since application can be done by community health workers or other trained personnel (non-dentists), the additional implementation costs of programmes using silver diamine fluoride are much lower than other dentist-led forms of fluoride applications. The retail price of silver diamine fluoride varies by manufacturer and market. Different brands and can be ordered online through different retailers, depending on the country and location.

WHO guidelines

The WHO implementation manual on ending childhood dental caries (10) states the following in relation to silver diamine fluoride. "Carious lesions that have progressed to cavitation should be stabilized in order to preserve tooth structure and to prevent negative health consequences such as pain and infection. Annual or semi-annual application of 38% silver diamine fluoride (silver diamine fluoride) solution is effective in arresting the progression of cavitated carious lesions in primary teeth and in hardening these lesions. The effectiveness of silver diamine fluoride is greater with semi-annual application. This can minimize discomfort and potential pulp damage, and help to keep the caries-affected primary teeth symptomless and functional until their natural exfoliation. This is a painless, simple and low-cost treatment that can be widely promoted as an alternative to conventional invasive caries management techniques, especially in populations and areas with low accessibility to dental care services."

Availability

Silver diamine fluoride is approved as a class II medical device by the United States Food and Drug Administration. Silver diamine fluoride is available in several countries around the world, including Argentina, Australia, India, Japan, Thailand and United States of America, and can be ordered online from global distributors. In some countries, national licensing is limited to silver diamine fluoride use for root caries and desensitization.

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