

Fluoride Varnish and Silver Diamine Fluoride: Fluoride Release Analysis and Clinical Guidance

Introduction

Fluoride varnishes were created to extend the delivery time of fluoride and increase its uptake by the enamel. However, fluoride uptake might not be the principal mechanism of action of existing fluoride products, and the focus shifted to the formation of calcium fluoride-like compounds (CaF_2). The CaF_2 crystals will precipitate onto the tooth surface blocking the dentin tubules, decreasing the dentin sensitivity. In parallel, the CaF_2 crystals formed in the enamel and within plaque, will act as reservoirs for slow fluoride delivery for weeks, preventing demineralization and enhancing remineralization. The benefit of fluoride varnishes is based on the gel-adherent consistency, associated to a concentration of 5% NaF (22,600 ppm of fluoride), favoring the overall formation of CaF_2 overtime.

Recently, a new topical fluoride product was introduced into the U.S. market. Silver diamine fluoride (SDF) is approved for the treatment of dentin sensitivity, and has been used to arrest caries progression in cavitated caries lesions. The chemical formulation indicates a high concentration of 5-6% of fluoride, combined with 24-27% of silver (Ag) and 7.5-11 % of ammonia (NH_3). The Ag will create a protective layer blocking the dentin tubules, decreasing the discomfort associated to dentin sensitivity. In addition, Ag is a well known antimicrobial agent that, when combined with the remineralization properties of fluoride, will create a solid surface once applied to a cavitated caries lesion that is able to withstand the oral environment without the need for restorative procedures.

The mechanism of action of topical fluoride products is directly related to fluoride release rates, modulated by the unique formulations available. The working group on fluoride varnishes of the American Dental Association Standards Committee on Dental Products (ADA SCPD) is evaluating different methodologies that could support the development

of an International Standard. This Professional Product Review contains a laboratory report evaluating the continued fluoride release of fluoride varnishes from 10 to 240 minute time points. The analysis was done at the University of Michigan, in parallel with the American Dental Association (ADA) laboratories. The agreement between the results from the two laboratories was evaluated to verify the reliability of the methodology selected. Due to the fluid nature of the SDF, a different process was used to evaluate the release of fluoride from 10 to 240 minute time points.

ACE Panel Survey and Clinical Guidance

To better understand how ADA members are using and selecting topical fluoride products, a study was conducted with the American Dental Association Clinical Evaluators (ACE) panel. Over 350 ACE panel members completed a survey, providing a unique opportunity to hear directly from practicing dentists about their preferences. The findings of this survey can be found on page 4 of this issue. To consolidate the information from the laboratory and ACE panel reports, a group of researchers from different universities in the U.S. were invited to share important recommendations on the use of fluoride varnishes and SDF. The goal is to provide ADA members cutting-edge scientific results gathered by world-wide renowned clinician scientists that will ultimately benefit the patient.

Products tested for fluoride release

Product	Manufacturer	Fluoride Source	Carrier (% by wt.)	Solvent (% by wt.)	Ca-P	Component	Other Ingredients
Duraphat	Colgate	5% NaF	Colophonium	30 - 60	Ethanol		
Vanish White Varnish	3M ESPE	5% NaF	Pentaerythritol glycerol ester of colophony resin	30 - 75	Ethanol	TCP* (< 5%)	n-Hexane (10-15%), flavor enhancer (1-5%), thickener (1-5%)
MI Varnish	GC America	5% NaF	Hydrogenated rosin	10 - 30	Ethanol	CPP-ACP*	Polyvinyl acetate (30-50%), silicon dioxide (1-5%), flavoring
Prevident	Colgate	5% NaF	Methyl hydrogenated rosin		Ethanol		Xylitol (sweetener)
NuPro White Varnish	Dentsply	5% NaF	Urethane dimethacrylate resin* and hydrogenated rosin	30 - 40	Isopropyl alcohol		Titanium dioxide; natural and artificial flavors
Duraflor Halo	Medicom	5% NaF	Synthetic resin	50 - 70	Ethanol		Xylitol (sweetener)
SDF	Elevate	38% SDF	DI Water	≤ 62.5			

*TCP = tri-calcium phosphate; CPP-ACP = Casein phosphopeptide-amorphous calcium phosphate.

▲ **Table 1.** List of materials included in the experiment, along with their components (as compiled from publicly-available sources, including published studies, informational product package inserts, and product safety data sheets).

Approach

The fluoride products included in the present experiment are listed in Table (1). Six of the most common 5% NaF varnishes, in addition to SDF, were tested and compared for rate of release of fluoride. Custom holders were made from an acrylic rod with a #6 nylon washer creating a well. Scintillation vials of 7 mL capacity were used for incubation of artificial saliva (6.5 mM NaCl, 1.5 mM CaCl₂·2H₂O, 5.4 mM KH₂PO₄, 15.0 mM KCl, 0.22% w/v mucin powder; pH 7.0). A sufficient amount of varnish for all samples of one type (three single-unit doses for individually packed, or the comparable amount from a multi-dose tube) was mixed thoroughly, and aliquots of approximately 20 mg were added to the wells of tared sample holders.

Fluoride varnish samples (n=10) were incubated at 36–37°C in 3 ml of stirring artificial saliva representing clinically relevant conditions. At time zero, samples were placed into the appropriate liquid medium (pre-equilibrated to temperature) stirring at 120 RPM. At each time point (10, 20, 30, 45, 60, 120, 240 minutes), holders carrying varnish samples were transferred with the vial caps to fresh liquid media for continued incubation; after incubation, liquids were stored at -20°C until the time of fluoride analysis.

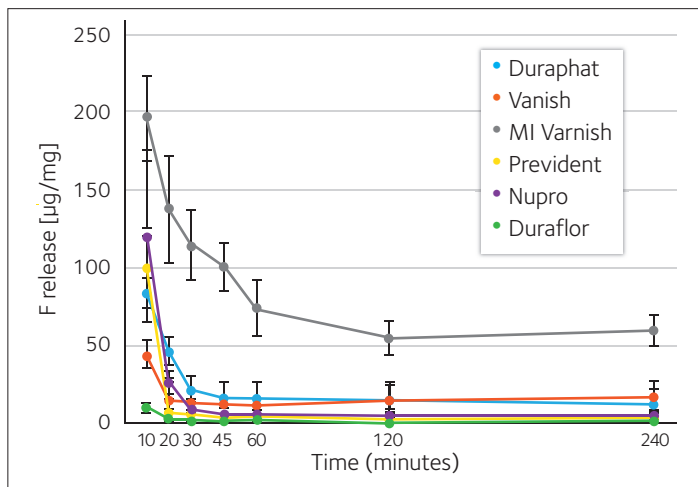
For determination of fluoride ion concentration, liquid media samples were brought to room temperature. Each sample was mixed by vortexing, and a 1 ml aliquot was combined with an equal volume of total ionic strength adjustment buffer (TISAB II, Ricca Chemical Co.). Electrode potential (mV) of each solution was determined with a meter and fluoride ion

specific electrodes (Orion Ionplus Fluoride Electrode, Model 9609BNWP) at the University of Michigan and at ADA laboratories. Verifications of electrode operation (slope) and drift (< 2%) was performed according to the manufacturer's specifications during each set of readings. Fluoride ion concentration was calculated by comparison to standard curves generated from a series of dilutions which were mixed with equal volumes of TISAB II.

Due to the fluid nature of SDF, the holders developed for the fluoride varnish evaluation were not used, and a different process was employed. Approximately 20 mg was dispensed directly into 3 ml of pre-warmed artificial saliva and allowed to elute for the duration of the designated time period. Ten samples (n=10) were tested for each time point selected (10, 30, 60, 240 minutes). Samples were analyzed immediately after being removed from the environmental chamber (36–37°C) at ADA. The fluoride ion concentration analysis followed the protocol used for fluoride varnish samples (described in the previous paragraph).

Data analysis: The level of agreement between testing of the four varnishes conducted in parallel at University of Michigan and ADA was evaluated using intraclass correlation coefficients (ICC) from a two-way random effects model. ICC can be classified as: poor reliability (≤ 0.5); moderate reliability (0.5 < x ≤ 0.75), good reliability (0.75 < x ≤ 0.9), and excellent reliability (> 0.9). One-way analysis of variance (ANOVA) with post hoc Tukey-Kramer tests were used to compare mean fluoride release of each brand at each time point for varnishes,

Fluoride Release from Fluoride Varnishes up to 240 minutes



▲ **Figure 1.** Fluoride Release ($\mu\text{g F/mg}$ varnish) at (minutes) 0-10, 10-20, 20-30, 30-45, 45-60, 60-120, and 120-240 intervals. Mean \pm SD. The values reflect microgram of fluoride per milligram of fluoride varnish. Values reported at 45 minutes, 1h, 2h and 4h were adjusted to reflect the release equivalent to a 10 minutes interval. Fluoride varnishes were tested at the University of Michigan and ADA laboratories.

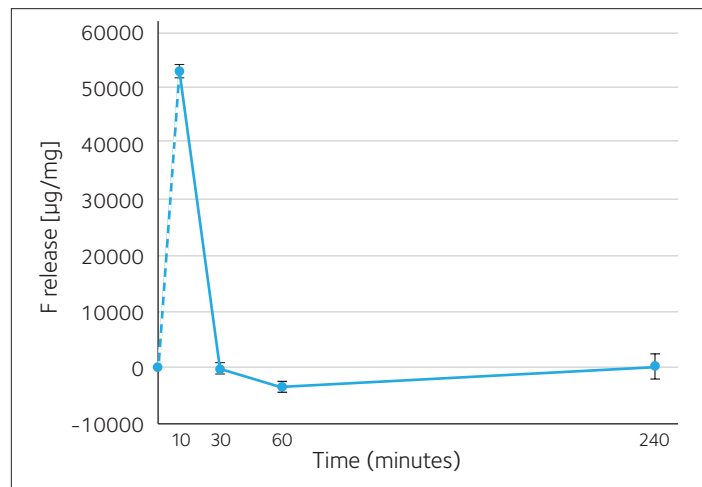
and compare fluoride release at each time point for SDF. Alpha was set at 0.05, and with the Bonferroni correction for multiple comparisons in the varnish experiment, significance was set at p-value: 0.00039.

Our findings

The consistency of agreement between the results from the University of Michigan and the ADA laboratories was excellent (ICC(2,1) = 0.987, F-test p-value < 0.0001), so results from both laboratories were pooled for the statistical analysis. The fluoride release at each interval varies among the fluoride varnishes evaluated (Figure 1). At each tested time point, there were statistically significant differences between varnish brands' mean fluoride release (F-test p-value < 0.0001). Tukey-Kramer tests identified which varnish brands differed up to 240 minutes.

At 10 minutes, higher release of fluoride ($\mu\text{g F/mg}$ varnish) was observed from MI varnish (196.1) compared to Nupro (120.2), Prevident (99.9), and Duraphat (83.5), followed by Vanish (43.5) and Duraflor (10.9). At 20 minutes, higher release for MI varnish (137.1) was detected compared to Duraphat (44.3), and Nupro (26.4), followed by Vanish (13.9), Prevident (6.2) and Duraflor (1.8). A relevant finding is the steep decrease of fluoride values from 10 to 20 minutes observed for Prevident (85.8%), Duraflor (83.3%), Vanish (83.4%), Nupro (73.5%), and Duraphat (63.2%), whereas MI varnish values decrease was

Rapid Initial Availability of Fluoride from SDF



▲ **Figure 2.** Fluoride availability from silver diamine fluoride at (minutes) 10, 30, 60 and 240 minute intervals. Mean \pm SD. Similar fluoride release was calculated up to 4h at different intervals, indicating that the fluoride available in SDF is released within the first 10 minutes. SDF was tested at the ADA laboratories. Interval from 0-10 minutes (dashed line) calculated from a theoretical data point.

limited to 30.1%. For the time points ranging from 30 to 240 minutes, a steady decrease in the fluoride values was observed for all varnishes, ranging from 10 to 20 $\mu\text{g/mg}$ for Duraphat and Vanish, and below 10 $\mu\text{g/mg}$ for Prevident, Nupro and Duraflor, except for MI varnish that showed a decrease from 114.8 (30 minutes) to 60.9 (240 minutes).

In contrast to the data from the fluoride varnishes, fluoride availability ($\mu\text{g F/mg}$) from SDF at 10 minutes (53,567.5) was similar to 30 minutes (53,463.9) and 240 minutes (53,087.9), indicating that all fluoride contained in the solution was available within the first 10 minutes (t-test p-values > 0.9) (Figure 2). A decrease of 6.6% of the fluoride concentration was detected at 60 minutes (50,026.0) compared to the remaining time points evaluated (t-test p-values < 0.02), likely related to the handling and loading of the SDF samples into the vials.

The results from the present experiment done at the University of Michigan, in collaboration with the ADA laboratories, tested two topical fluoride categories available in the U.S. market. The results demonstrated two different patterns of fluoride availability in artificial saliva. Fluoride release from varnishes was observed over an extended period at lower levels, whereas the SDF produced an initial rapid spike with a concentration of fluoride 250x higher than the observed to the varnishes at 10 minutes. ■

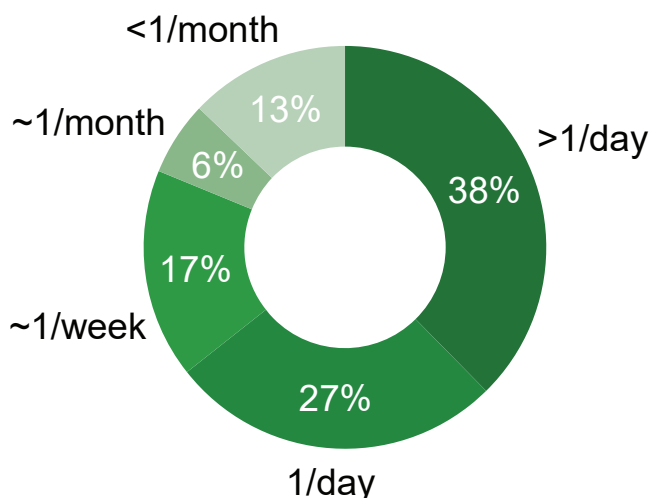
ACE Panel Report

Professional-Use Fluoride Products

Results reflect the opinion of 350 practicing dentists in the United States who participate in the ADA Clinical Evaluators Panel. The ADA does not endorse off-label use of any professional product.

*Note that some questions allowed for multiple answers to be registered.

Frequency of fluoride varnish use



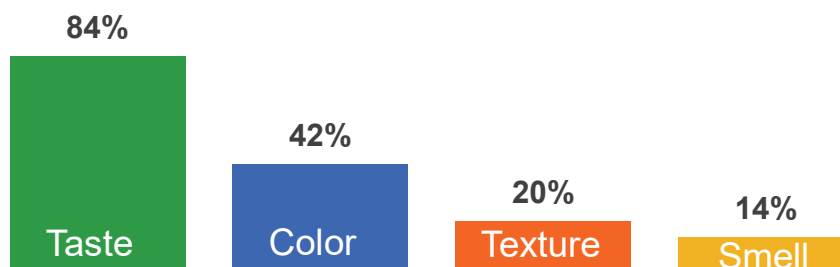
Purpose of fluoride varnish use*



- 77%** report use for caries prevention in high risk patients
- 33%** for hypersensitivity
- 22%** for caries prevention in low risk patients

Observed attributes of fluoride varnish

- ADA Clinical Evaluators prefer the **ease of application** (74%) and **fluoride release** (46%) of a particular product.*
- **84%** of them report using their preferred fluoride varnish for less than 5 years.
- Patient-reported attributes that influence fluoride varnish selection include:*



78%

ADA Clinical Evaluators reported **never** having used **silver diamine fluoride** for dental treatments. About 16% use it on a monthly basis.

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New treatment options for dental caries provide dentists and patients with more tools than ever to manage this disease. But because caries development involves a broad spectrum of factors, choosing the right treatment at the right time is crucial to any successful plan. This section will break down the differences between two product categories in use on the anti-caries effort: fluoride varnish and silver diamine fluoride (SDF), including clinical indications, tips, and special considerations.

Clinical Indications

Fluoride varnish and SDF are both non-invasive and painless treatment options for caries management. While fluoride varnish and SDF are primarily indicated for tooth hypersensitivity, both are also commonly used off-label to manage carious lesions at different stages in their development process. Fluoride varnish is recommended for the prevention of new carious lesions when used on sound tooth surfaces (in both coronal and root surfaces), and for the management of existing non-cavitated lesions (also called white-spot or initial, or incipient lesions). If left untreated, and if the disease process continues, these non-cavitated lesions may advance into cavitated lesions. At this stage, the use of SDF is more appropriate to arrest caries progression on coronal and root surfaces, in the absence of signs and symptoms of irreversible pulpitis. SDF may also be used on exposed root surfaces for prevention of caries lesions (similarly to fluoride varnish).

Key Points:

- ▶ Fluoride varnish and SDF are safe, effective, non-invasive caries management treatment options that provide a comfortable experience for patients of all ages.
- ▶ Fluoride varnish is recommended for patients at risk of caries, both for the prevention of new carious lesions, as well as for the management of non-cavitated initial lesions, in both coronal and root surfaces
- ▶ SDF is recommended for arresting the progression of cavitated carious lesions on the crown and root surfaces.
- ▶ Both products should be utilized as part of a comprehensive treatment plan for the prevention and management of caries.

Potential Treatment Selection Factors

While the extent of a carious lesion (non-cavitated or cavitated) determines when the use of each product is most appropriate for lesion arrest, patients and external factors such as a patient's age, mobility, or clinical setting, may also be considered when developing a treatment plan.

Patient Groups: For very young children or individuals with special health care needs whose fear, reluctance or low tolerance for time-intensive procedures may limit conventional restorative treatment, SDF may be a useful tool for arresting the progression of cavitated carious lesions. The non-invasive nature of the SDF application will provide the required therapeutic effect without exposing a young patient

to needle and burs. Similarly, SDF may provide an attractive (albeit temporary) alternative to more intensive caries treatment options in patients with complex needs, as well as those with geographic or income-related treatment access issues. For senior patients whose limited mobility may restrict the number of office visits, SDF can be an attractive option for root carious lesion management.

Clinical Setting: Both products can be used in a wide range of clinical or non-clinical settings (including traditional, medical, or school settings) and by a wide range of health-care providers. However, because SDF requires a more precise application, its use may be best limited to providers with an ability to identify cavitated lesions in a targeted manner.

Clinical Tips

In addition to differing in their primary indications, fluoride varnish and SDF have very different physical properties and application techniques that may impact how and when these products are used.

Fluoride Varnish: With varnishes, the biggest difference between brands is the product's consistency. In general, the product will be easiest to work with if the tooth is clean (gross plaque removed) and dry (using air or gauze). Once the tooth (including coronal and root surfaces) has been cleaned and dried, varnish should be painted on the sound surface areas of higher risk (e.g., near the cervical area/gumline, interproximally, and pits/fissures) and

surface areas presenting active non-cavitated lesions. While only a thin coat is necessary, varnish does not need to be precisely applied, as it is essentially colorless or yellow and will cause no harm to healthy teeth, more advanced lesions (e.g., cavitated lesions) or the surrounding tissue. Varnish should be left on the tooth for the amount of time recommended by the manufacturer (longer is better). As such, eating, drinking and brushing should be delayed following treatment. Any stickiness or the presence of residual product will likely diminish within 24-hours. Reapplication of fluoride varnish should be dictated by an individual's caries risk and management needs, but the American Dental Association's recommendation is every 6-12 months.

SDF: Unlike fluoride varnish, SDF will turn the affected carious dentin black after application. As such, targeted application is incredibly important. SDF should only be used after cavitated lesions have been identified, and treatment options have been considered and adequately discussed with the patient. Because based on currently published literature the product's exposure to dentin is crucial to its success, the targeted lesions should be isolated, cleaned (e.g. from food debris, gross plaque deposits) and dried (air or gauze) prior to application. SDF is applied onto the lesion site and should be given the amount of time recommended by the manufacturer to react directly with the affected carious dentin. While SDF can be applied using a brush or sponge, the most appropriate tool will depend on the size of the cavity access, as the treatment's effectiveness is dependent on access to the lesion. Petroleum jelly can be applied to lips or gingival tissue to reduce staining, though care should

be taken to avoid coating the desired target lesion with the jelly. The reaction of the product with the dentin will cause the application site to turn black, but this process is not immediate. If desired, the reaction can be accelerated with a curing light to ensure proper application and placement, but there is a lack of evidence as to whether light-curing improves efficacy, and some concerns that it could actually diminish it. Once the product has had time to set, blotting excess product, or rinsing the mouth with a saliva ejector can minimize the amount of product swallowed or loose in the patient's mouth. As with varnish, patients should delay eating, drinking or brushing following treatment per the manufacturer's recommendations. While there is no general consensus on the timing of reapplication, annual or biannual reapplication may be needed, and the treatment's success can be determined by assessing the hardness of the treatment site at the next office visit (i.e., if the cavitated lesion is soft, regardless of color, it is likely still active). While SDF can be used to successfully arrest carious lesions, it is not a final restoration, nor does it replace other strategies needed to decrease a patient's caries risk. Limited evidence suggests SDF can also be used to prevent dental caries on exposed root surfaces, similarly to fluoride varnish, with the caveat that SDF results in dentin discoloration, as explained previously.

Benefits and Success Rates

The success of any treatment is strongly based on effective and appropriate usage. When applied appropriately, fluoride varnish is a safe and reasonably effective (30-40%) treatment for preventing the development of carious lesions and the progression of non-

cavitated lesions on both coronal and root surfaces. There is no evidence to indicate that fluoride varnish is an effective treatment for cavitated lesions.

While fluoride varnish is effective on non-cavitated lesions, SDF is an effective tool against cavitated lesions, with a general success rate of 60-80% after one application. However, because SDF requires a targeted application, that success rate can be largely impacted by proper use and access. While there is limited evidence to suggest a difference in success rates between anterior vs. posterior or buccal vs. proximal surfaces, the existing evidence suggests that SDF requires a direct reaction to the affected carious dentin. As such, treatment of lesions that are more difficult to access may prove less successful, or may require more reapplications for lesion arrest.

SDF: Common Misconceptions, Questions, or Concerns

If used appropriately, SDF is generally safe for use with all patient groups. While the concentration of fluoride in SDF is higher than over-the-counter fluoride products, the actual dosage is limited because of the relatively small amount of product that is used, and is far below the safety threshold established by the U.S. Environmental Protection Agency. For young children, extra precautions should be taken to minimize ingestion, as excessive fluoride can cause stomach discomfort.

Tooth Staining: The staining caused by the reaction between SDF and carious dentin is a common and legitimate concern. While the stain itself does not harm either the dental or surrounding soft tissues, patients, parents or other caregivers should be made aware of the aesthetic implications of this treatment

option. (An effective informed consent tool may include graphic representations of SDF application results.) Because the product will result in a black appearance on treated caries lesions, targeted application is crucial, and care should be taken to avoid the surrounding mucosa or tissue. SDF will also stain clothing, hands, and other surfaces, so care must be taken in the handling of the product. While it is possible to cover the dark stained dentin with a restoration, doing so immediately after SDF application may turn a glass ionomer gray. Similarly, while the application of potassium iodine on top of the SDF may temporarily mask the staining, the treated area will ultimately turn grayish over time.

Contra-Indications: SDF can potentially cause minor gingival irritation where the product is applied close to the gum line, but this reaction is temporary. SDF is contraindicated for patients with heavy metal allergies (particularly silver), as well as for teeth with signs and symptoms of irreversible pulpitis.

CDT Codes and Insurance Coverage

While both of these products are primarily indicated for hypersensitivity, newer CDT codes have been approved to reflect their use in caries prevention and arrest. Fluoride varnish is a covered benefit for most children and some adults, but the number of yearly reimbursements may vary based on caries risk, age, and insurance type. Due to its newer emergence in the U.S. market, SDF insurance approval and reimbursement may vary based on caries risk, age, state, and insurance type. While a range of codes may result in ultimate approval, it is best to consult the ADA's most recent CDT resources and bill based on a product's specific usage. The ADA publishes its Code on Dental Procedures and Nomenclature (CDT Code) annually, available at: ADA.org/CDT. The current version (effective through December 31, 2017) provides the following CDT codes for the use of fluoride varnishes and SDF in the office setting:

D1206: Topical application of fluoride varnish. [Fluoride varnish] Prescription strength fluoride product designed solely for use in the dental office, delivered to the dentition under the direct supervision of a dental professional. The fluoride varnish must be applied separately from prophylaxis paste, during the same appointment.

D1354: Interim caries arresting medicament application. [SDF] Conservative treatment of an active, non-symptomatic carious lesion by topical application of a caries arresting or inhibiting medicament and without mechanical removal of sound tooth structure.

D9910: Application of desensitizing medicament. [Fluoride varnish or SDF] Fluoride varnishes and SDF are recommended for the treatment of root sensitivity. Typically reported on a "per-visit" basis for application of topical fluoride. ■

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Shape what you see in future ADA publications by becoming a member of the ADA Clinical Evaluator (ACE) Panel. Through brief monthly surveys, the ACE Panel gives practicing ADA member dentists a direct line to the ADA Science Institute. Participants will provide valuable clinical input about day-to-day experiences with products in their practice, and will learn more about products that can help them to improve their practice and provide the best care for their patients.

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