

PRODUCT MONOGRAPH
INCLUDING PATIENT MEDICATION INFORMATION

PrSOFRACORT®

Framycetin sulphate, Dexamethasone and Gramicidin Ophthalmic/Otic Solution
Solution, 5 mg Framycetin sulphate, 0.5 mg Dexamethasone, and 0.05 mg Gramicidin
Ophthalmic/Otic

Antibiotic - Corticosteroid

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RECENT MAJOR LABEL CHANGES

Contraindications Nov. 2020

Warnings and Precautions Nov. 2020

Adverse Reactions, Post-Market Adverse Reactions Nov. 2020

Drug Interactions Nov. 2020

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PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

Eye: Blepharitis and infected eczema of the eyelid; allergic, infective and rosacea conjunctivitis; rosacea keratitis; scleritis and episcleritis; iridocyclitis, and other inflammatory conditions of the anterior segment of the eye.

Ear: Otitis externa (acute and chronic) and other inflammatory and seborrheic conditions of the external ear.

SOFRACORT contains antibacterial ingredients, framycetin and gramicidin. To reduce the development of drug-resistant bacteria and maintain the effectiveness of framycetin and gramicidin, SOFRACORT should only be used for the authorized indication.

2 CONTRAINDICATIONS

Eye:

- Herpes simplex and other viral diseases of the cornea and conjunctiva; tuberculosis and fungal diseases of the eye; trachoma.
- Acute purulent, untreated infections of the eye, which, like other diseases caused by micro-organisms, may be masked or enhanced by the presence of the steroid.
- Known hypersensitivity to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see Dosage Forms, Strengths, Composition and Packaging.
- Glaucoma.

Ear:

- Viral and fungal infections.
- Acute purulent, untreated infections.
- Perforation of the eardrum because of the risk of ototoxicity.
- Known hypersensitivity to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see Dosage Forms, Strengths, Composition and Packaging.

3 DOSAGE AND ADMINISTRATION

3.1 Recommended Dose and Dosage Adjustment

Ear: Instill 2 or 3 drops in the ear canal 3 or 4 times daily by tilting head to one side. Squeeze the dropper carefully. To avoid possibility of reinfection later, do not touch ear with dropper. Alternatively, a saturated gauze wick may be inserted by the physician into the external auditory meatus.

Eye: In acute conditions, 1 or 2 drops every 1 to 2 hours may be instilled (generally for 2 or 3 days). Subsequently, 1 or 2 drops 3 or 4 times daily. To avoid possibility of reinfection later, do not touch eye with dropper.

3.2 Missed Dose

If a dose is missed, it should be administered as soon as possible, and the regular dosage schedule should be resumed. If it is almost time for the next dose, the missed dose should be skipped, and the regular dosing schedule should be resumed. A double dose should not be administered.

4 OVERDOSAGE

Long-term intensive topical use may lead to systemic effects.

For management of a suspected drug overdose, contact your regional poison control centre.

5 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table – Dosage Forms, Strengths, Composition and Packaging.

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Ophthalmic/Otic	Solution, 5 mg Framycetin sulphate, 0.5 mg Dexamethasone, and 0.05 mg Gramicidin	Citric acid monohydrate, hydrochloric acid, industrial methylated spirit (IMS 66OP), lithium chloride, polysorbate 80, sodium citrate, sodium hydroxide, 2-phenyl ethanol, water for injections

Each milliliter of solution contains: 5 mg framycetin sulphate, 0.5 mg dexamethasone as dexamethasone sodium metasulfobenzoate), and 0.05 mg gramicidin.

SOFACORT is available in an amber glass bottle with rubber dropper bulb, containing 8 mL of solution.

6 WARNINGS AND PRECAUTIONS

General

Aminoglycosides antibiotics may cause irreversible, partial or total deafness when applied topically to open wounds or damaged skin. This effect is aggravated by renal or hepatic impairment and by prolonged duration of treatment. The treatment should not be continued after resolution of symptoms.

Susceptibility/Resistance

Treatment with corticosteroid/antibiotic combinations should not be continued in the absence of clinical improvement, since prolonged use may lead to occult extension of infections due to the masking effect of the steroid. Prolonged use may also lead to skin sensitization and the emergence of resistant organisms.

Development of Drug Resistant Bacteria:

Prescribing SOFRACORT in the absence of the authorized indications is unlikely to provide benefit to the patient and risks the development of drug-resistant bacteria.

Potential for Microbial Overgrowth:

The use of SOFRACORT may promote the selection of non-susceptible organisms. Should superinfection occur during therapy, appropriate measures should be taken.

Driving and Operating Machinery

SOFRACORT may cause transient blurring of vision on instillation. Warn patients not to drive or operate hazardous machinery unless vision is clear.

Endocrine and Metabolism

During therapy with SOFRACORT, a possibly increased need for insulin or antidiabetics should be considered in patients with diabetes.

Immune

SOFRACORT should be discontinued if there are signs of sensitivity to any of its ingredients. Patients are advised to inform the physicians of the prior use of corticosteroids.

In patients known to be allergic to other aminoglycoside antibiotics (neomycin, kanamycin), cross-sensitization to framycetin may occur, but not invariably so.

Neurologic

Pheochromocytoma crisis, which can be fatal, has been reported after administration of corticosteroids. Corticosteroids should only be administered to patients with suspected or identified pheochromocytoma after an appropriate risk/benefit evaluation.

Ophthalmologic

Visual disturbance may be associated with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR). Treatment with corticosteroid preparations should not be repeated or prolonged without regular review to exclude raised intraocular pressure, cataract formation or unsuspected infections. In conditions

causing thinning of the cornea, topical steroids may cause perforation. Cataract has occurred after prolonged treatment with topical steroids.

Topical corticosteroids should never be given for an undiagnosed red eye as inappropriate use is potentially blinding.

6.1 Special Populations

6.1.1 Pregnant Women

There are no available data on SOFRACORT use in pregnant women. The safety of prolonged use of topical steroids during pregnancy has not been substantiated. No conclusions can be drawn regarding whether or not SOFRACORT is safe for use during pregnancy. SOFRACORT should be used during pregnancy only if the potential benefits to the mother outweigh the potential risks, including those to the fetus.

6.1.2 Breast-feeding

There are no available data on the presence of SOFRACORT in human milk, milk production, or the effects on the breast-fed infant. No conclusions can be drawn regarding whether or not SOFRACORT is safe for use during breast-feeding. SOFRACORT should be used during breast-feeding only if the potential benefits to the mother outweigh the potential risks, including those to the breast-fed child.

6.1.3 Pediatrics

Although it is unlikely that infants will be treated with SOFRACORT for prolonged periods, there is a risk of adrenal suppression, even without occlusive dressings, after prolonged treatment of these patients with topical steroids.

7 ADVERSE REACTIONS

7.1 Clinical Trial Adverse Reactions

Because clinical trials are conducted under very specific conditions, the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

Eye disorders

Increased intra-ocular pressure; perforation of the cornea; hypersensitivity; burning or stinging of the eye.

7.2 Post-Market Adverse Reactions

Endocrine disorders

Iatrogenic Cushing's Syndrome; adrenal atrophy.

Eye disorders

Blurred vision; chorioretinopathy; increased intra-ocular pressure leading to optic nerve damage, reduced visual acuity and visual field defects; glaucoma; cataracts.

Immune disorders

Hypersensitivity reactions, usually of the delayed type, may occur, leading to irritation, burning, stinging, itching and dermatitis.

Metabolism and nutrition disorders

Diabetes mellitus; decreased glucose tolerance.

8 DRUG INTERACTIONS**8.1 Drug-Drug Interactions**

The drugs listed in this table are based on either drug interaction case reports or studies, or potential interactions due to the expected magnitude and seriousness of the interaction (i.e., those identified as contraindicated).

Table 1 - Established or Potential Drug-Drug Interactions

Proper/Common name	Source of Evidence	Effect	Clinical comment
CYP3A inhibitors	T	Increased risk of side effects	Co-treatment with CYP3A inhibitors, including cobicistat-containing products, is expected to increase the risk of systemic side-effects. The combination should be avoided unless the benefit outweighs the increased risk of such side-effects, in which case patients should be monitored.

Legend: C = Case Study; CT = Clinical Trial; T = Theoretical

9 STORAGE, STABILITY AND DISPOSAL

Store between 15-25° C. Do not refrigerate.

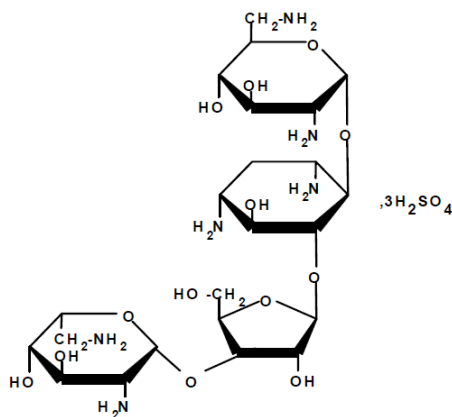
Use within four weeks of opening.

PART II: SCIENTIFIC INFORMATION

10 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name:	Framycetin sulphate or Neomycin B sulphate
Chemical name:	Sulphate of 2-deoxy-4-O-(2,6-diamino-2,6-dideoxy- α -D-glucopyranosyl)-5-O-[3-O-(2,6-diamino-2,6-dideoxy- β -L-idopyranosyl)- β -D-ribofuranosyl]-D-streptomine
Molecular formula:	$C_{23}H_{46}N_6O_{13}, 3H_2SO_4$
Molecular mass:	Mr 908.9 (Framycetin sulphate); Mr 614.6 (Framycetin)
Structural formula:	

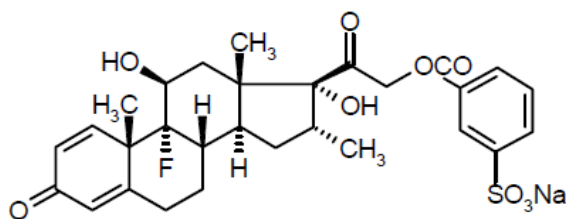


Physicochemical properties: Hygroscopic, white to slightly yellowish powder, not granular to the touch. Framycetin sulphate is highly soluble in water, very slightly soluble in alcohol and practically insoluble in acetone, chloroform and ether. Not more than 80 mcg can be dissolved in 1 mL of cyclohexane.

Drug Substance

Proper name:	dexamethasone sodium metasulfobenzoate or Dexamethasone 21 (sodium metasulfobenzoate)
Chemical name:	(11 β ,16 α 9-Fluoro-11, 17-dihydroxy-16-methyl-21-[(3-sulfobenzoyl)oxy]-pregna-1, 4-diene-3, 20-dione Monosodium salt (9 α -Fluoro-11 β , 17 α -dihydroxy-16 α -methyl-3, 20-dioxopregna-1, 4-dien-21-yl), m-sulfobenzoate, sodium salt
Molecular formula:	C ₂₉ H ₃₂ FNaO ₉ S
Molecular mass:	Mr = 598.6 (Dexamethasone sodium metasulfobenzoate); Mr = 392.5 (Dexamethasone)

Structural formula:



Physicochemical properties: White to practically white microcrystalline powder. The polymorphism analyses show the crystalline form I. In addition to an amorphous form, 10 crystalline forms (solvate, hydrate and anhydrous forms) were identified during the polymorph screening. The water content, the TGA and DSC results show that form I is a monohydrate form.

Solvent	Descriptive term	Solubility (g/L)
Water	Soluble	between 30 and 100
Acetone	Sparingly soluble	between 10 and 30
Ether	Sparingly soluble	between 10 and 30

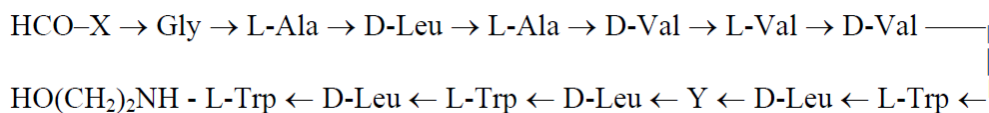
Drug Substance

Proper name:	Gramicidin
Chemical name:	Gramicidin A1 (Val-Gram A) Gramicidin A2 (Ile-Gram A) Gramicidin B1(Val-Gram B) Gramicidin C1 (Val-Gram C) Gramicidin C2 (Ile-Gram C)
Molecular formula:	Gramicidin A1: C ₉₉ H ₁₄₀ N ₂₀ O ₁₇ Gramicidin A2: C ₁₀₀ H ₁₄₂ N ₂₀ O ₁₇ Gramicidin B1: C ₉₇ H ₁₃₉ N ₁₉ O ₁₇ Gramicidin C1: C ₉₇ H ₁₃₉ N ₁₉ O ₁₈ Gramicidin C2: C ₉₈ H ₁₄₁ N ₁₉ O ₁₈
Molecular mass:	Gramicidin A1: 1882 g/mol Gramicidin A2: 1896 g/mol Gramicidin B1: 1843 g/mol Gramicidin C1: 1859 g/mol Gramicidin C2: 1873 g/mol

Structural formula:

The gramicidins constitute a family of end-substituted linear pentadecapeptides where the N-terminal amino group is formylated and the C-terminal carboxylic group is amidated with ethanolamine. Change of the two amino acids elements (first and eleventh) of the polypeptide chain gives the components of the gramicidin family: A1, A2, B1, C1 and C2.

The general structure of the gramicidins is:



The peptide bond is indicated by \rightarrow .

The amino acid at X and that at Y for each component of the gramicidin family is indicated in the table below:

Gramicidin A1	X = L-Val	Y = L-Trp
Gramicidin A2	X = L-Ile	Y = L-Trp

Gramicidin B1	X = L-Val	Y = L-Phe
Gramicidin C1	X = L-Val	Y = L-Tyr
Gramicidin C2	X = L-Ile	Y = L-Tyr

Physicochemical properties: Gramicidin is a white or almost white, crystalline powder. It is slightly hygroscopic. It is very stable both in the dry form and in solution, also at elevated temperatures. Gramicidin is practically insoluble in water, sparingly soluble in alcohol, and soluble in methanol.

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE
PATIENT MEDICATION INFORMATION

PrSOFRACORT®

5 mg Framycetin sulphate, 0.5 mg Dexamethasone, 0.05 mg Gramicidin
Ophthalmic/Otic solution

Read this carefully before you start taking **SOFRACORT** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **SOFRACORT**.

What is SOFRACORT used for?

It is used in the eye(s) to treat:

- inflammation due to infection (redness, itching, swelling, burning) in the front parts of the eye:
 - white of the eye (scleritis)
 - clear layer on top of the white part of the eye (episcleritis)
 - coloured part of the eye (iridocyclitis)
 - muscles and tissue involved in focusing the eye
- inflammation due to infection (redness, swelling, burning) of the eyelid (blepharitis)
- infected itchy, red rash of the eyelid
- allergic and contagious eye infections
- face skin reddening leading to red and yellow bumps (rosacea keratitis)

It is used in the ear(s) for:

- redness and swelling of the ear canal (otitis externa)
- red, scaly, greasy, itchy and inflamed skin of the outer ear.

SOFRACORT contains antibacterial ingredients called framycetin and gramicidin, and it should be used exactly as directed by your healthcare professional.

How does SOFRACORT work?

SOFRACORT is a combination product that contains:

- 2 antibiotics (framycetin and gramicidin) that kill the bacteria that are causing the infection.
- 1 steroid (dexamethasone) that lowers inflammation.

What are the ingredients in SOFRACORT?

Medicinal ingredients: framycetin sulphate, dexamethasone sodium metasulfobenzoate, gramicidin

Non-medicinal ingredients: Citric acid monohydrate, hydrochloric acid, industrial methylated spirit (IMS 66OP), lithium chloride, polysorbate 80, sodium citrate, sodium hydroxide, 2-phenyl ethanol, water for injections

SOFRACORT comes in the following dosage forms:

Each milliliter of solution contains: 5 mg framycetin sulphate, 0.5 mg dexamethasone (as dexamethasone sodium metasulfobenzoate), and 0.05 mg gramicidin.

SOFRACORT is available in an amber glass bottle with rubber dropper bulb, containing 8 mL of solution.

Do not use SOFRACORT if:**Eye:**

- You are allergic to any of the ingredients in SOFRACORT or to a component of the container;
- You have herpetic eye disease or other viral diseases of the cornea and conjunctiva;
- You have tuberculosis and fungal diseases of the eye;
- You have trachoma;
- You have untreated eye infections with thick discharges.
- You have glaucoma.

Ear:

- You are allergic to any of the ingredients in SOFRACORT or to a component of the container;
- You have viral or fungal infections;
- You have untreated ear infections of the ear discharges;
- Your eardrum is punctured.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take SOFRACORT. Talk about any health conditions or problems you may have, including if you:

- Used corticosteroids before.
- Have open wounds or damaged skin since deafness might happen if SOFRACORT is used directly on them.
- Are diabetic. Your healthcare professional may need to increase your dose of insulin or medication.
- Have tumors of the adrenal gland called pheochromocytoma.

Experience Allergies

- New itching, rash, redness or irritation that happens after using SOFRACORT.

Experience Eye Problems

- blurred vision or other changes in vision (cataracts).
- increased eye pressure.
- perforation of the cornea due to thinning of the cornea.

Get Pregnant

- If you become pregnant or plan to breast-feed while taking SOFRACORT, talk to your healthcare professional right away.
- SOFRACORT should not be used for a long period of time during pregnancy or breast-feeding unless the benefits outweigh the risks.

Other warnings you should know about:

SOFRACORT may cause blurred vision. Do not drive or operate dangerous machinery unless your vision is clear.

You should not take SOFRACORT for a long period of time unless your healthcare professional tells you to. If you do, your healthcare professional will check your eyes for cataracts or infections regularly. They will also check your eye pressure regularly.

You should not take SOFRACORT for red eye that has not been diagnosed by your healthcare professional. Using SOFRACORT inappropriately could cause blindness.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with SOFRACORT:

- Medicines called CYP3A inhibitors. These medicines use a system called CYP3A in the body. If you are not sure whether a drug you take is a CYP3A inhibitor, talk to your healthcare professional. A few examples of these medicines are:
 - o clarithromycin, erythromycin (used to treat bacterial infections)
 - o itraconazole, ketoconazole (used to treat fungal infections)
 - o diltiazem, verapamil (used to treat chest pain)
 - o ritonavir (used to treat HIV/AIDS)

How to take SOFRACORT:

Use in the Eye(s):

- Wash your hands.
- Remove the cap on the bottle.
- Tilt your head back. Pull down the lower lid of your eye.
- Squeeze 1 drop at a time into the pocket made by the lower lid.
- To avoid possibility of reinfection later, do not touch eye with dropper.
- Close your eye.
- Wipe away any excess drops with a clean tissue.

- Always put the cap back on the bottle as soon as you have used it.

Use in the Ear(s):

- Wash your hands.
- Remove the cap on the bottle.

- Tilt your head on one side.
- Squeeze 2 or 3 drops into your ear. Squeeze the dropper carefully.
- Lie your head with your affected ear facing upwards for a few minutes.
- To avoid possibility of reinfection later, do not touch ear with dropper. Alternatively, a saturated gauze wick may be inserted by the physician into the external ear canal.
- Wipe away any excess drops with a clean tissue.
- Always put the cap back on the bottle as soon as you have used it.

Misuse or overuse of SOFRACORT could lead to the growth of bacteria that will not be killed by framycetin or gramicidin. This means that SOFRACORT or other medicines that contain framycetin or gramicidin may not work for you in the future.

Do not share your medicine.

Usual dose:

In the eye(s)

- 1 or 2 drops every 1 to 2 hours (generally for 2 or 3 days).
- Afterwards, 1 or 2 drops 3 or 4 times daily.

In the ear(s)

- 2 or 3 drops in the ear canal 3 or 4 times daily.

Overdose:

If you think you have taken too much SOFRACORT, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

It is important to take this medication exactly as prescribed by your doctor. If you miss a dose, administer it as soon as possible and continue with your regular schedule. If it is almost time for your next dose, skip the missed dose and continue with your regular dosing schedule. Do not administer a double dose to make up for a missed one. If you are not sure what to do after missing a dose, contact your doctor or pharmacist for advice.

What are possible side effects from using SOFRACORT?

These are not all the possible side effects you may feel when taking SOFRACORT. If you experience any side effects not listed here, contact your healthcare professional.

Eye disorders

- increased eye pressure (glaucoma);

- perforation of the cornea (the transparent layer forming the front of the eye);
- eye allergies;
- burning or stinging of the eye;
- cloudy vision;
- blurred or distorted vision (chorioretinopathy).

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
UNKNOWN Allergic reaction: <ul style="list-style-type: none"> • rash; hives; itching; red, swollen, blistered, or peeling skin with or without fever; • wheezing; tightness in the chest or throat; trouble breathing, swallowing, or talking; unusual hoarseness; • swelling of the mouth, face, lips, tongue, or throat. 			√
Decreased vision			√
Eye infection		√	
Eye pain			√
Gradual blurring or loss of vision			√
Glaucoma (an eye disease that can cause loss of vision): decreased vision, loss of vision			√
Cataracts (a condition where the lens of your eye gets cloudy): gradual blurring, loss of vision			√
Dizziness/feeling of spinning			√
Hearing loss			√
ringing in the ears		√	
Unsteadiness/loss of balance			√

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Iatrogenic Cushing's Syndrome (a disorder caused by high levels of cortisol): abnormal obesity with thin arms and legs, acne, high blood pressure, rounded face			√
Adrenal atrophy (a condition where the adrenal gland does not produce enough cortisol): dehydration, disorientation, low blood sugar, weight loss			√
Diabetes mellitus (a condition where blood sugar is high): frequent urination, increased thirst and hunger, weight loss			√

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

<p>Reporting Side Effects</p> <p>You can report any suspected side effects associated with the use of health products to Health Canada by:</p> <ul style="list-style-type: none"> • Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or • Calling toll-free at 1-866-234-2345. <p><i>NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.</i></p>
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Storage:

Store between 15-25° C. Do not refrigerate.

Use within 4 weeks of opening.

Keep out of reach and sight of children.

If you want more information about SOFRACORT:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (<https://health-products.canada.ca/dpd-bdpp/index-eng.jsp>); the manufacturer's website www.sanofi.ca, or by calling 1-800-265-7927.

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