

Mupirocin

A topical-only isoleucyl-tRNA synthetase inhibitor for impetigo and nasal MRSA decolonization, with a unique target that shares no cross-resistance with other antibiotic classes.

Online guide: <https://www.medguideglobal.com/pharmacology/antibiotics/mupirocin>

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Quick revision

One Liner: Mupirocin (pseudomonic acid A) mimics isoleucine to inhibit bacterial isoleucyl-tRNA synthetase - a target no other antibiotic class touches - making it the topical agent for impetigo and nasal MRSA decolonization, until the mupA plasmid supplies a bypass enzyme.

1. Mechanism: inhibits bacterial isoleucyl-tRNA synthetase by mimicking the enzyme's isoleucine binding site, halting protein and RNA synthesis. [1]
2. Bacteriostatic at low concentrations, bactericidal at the higher concentrations achieved topically. [1]
3. Clinical focus is gram-positive skin flora: Staphylococcus aureus including MRSA, and Streptococcus pyogenes. [1]
4. The unique target means no cross-resistance with any other antibiotic class. [1]
5. Uses: impetigo, secondarily infected skin lesions, and intranasal decolonization of S. aureus/MRSA carriers before surgery. [1][2]
6. Topical only - any absorbed drug is rapidly de-esterified to inactive monic acid, so systemic therapy is impossible. [1]
7. High-level resistance is plasmid-mediated via mupA, which encodes a bypass isoleucyl-tRNA synthetase - the classic cause of decolonization failure. [1]
8. The polyethylene glycol ointment vehicle can be absorbed from large open wounds and warrants caution in renal impairment. [1]

Overview

1. Mupirocin, also called pseudomonic acid A, is a topical antibiotic originally derived from Pseudomonas fluorescens. It occupies a niche no other agent fills: a drug active against Staphylococcus aureus, including methicillin-resistant strains, through a molecular target that no systemic antibiotic class uses. [1]
2. Its two defining clinical roles are treating superficial gram-positive skin infection - impetigo and secondarily infected lesions - and eradicating nasal carriage of S. aureus and MRSA before surgery. Decolonization of nasal carriers roughly halves the odds of S. aureus surgical site infection, which has made nasal mupirocin a fixture of pre-surgical prevention bundles. [1][2]
3. Two facts frame everything else about the drug. First, it is topical only: absorbed mupirocin is rapidly de-esterified to monic acid, which has no antibacterial activity. Second, widespread use has driven resistance - most importantly plasmid-mediated high-level resistance via mupA, which supplies a bypass version of the target enzyme and explains why decolonization sometimes fails. [1]

Classification and drug examples

Intro: Mupirocin is a single-drug class pharmacologically, but it is prescribed as two distinct products whose roles should not be confused: a dermal preparation for skin infection and a nasal preparation for carrier decolonization.

1. Name: Dermal (skin) preparations

1. Note: Ointment in a polyethylene glycol base and a cream formulation, used on infected skin lesions.

Name: Mupirocin

1. Bactroban
2. Pseudomonic acid A

Route: Topical (skin)

Note: For impetigo and secondarily infected traumatic skin lesions; the polyethylene glycol ointment vehicle is the source of the large-open-wound caution. [1] [1]

2. Name: Nasal preparation

2. Note: A separate intranasal ointment formulation used for decolonization, not for treating skin lesions.

Name: Mupirocin nasal ointment

Bactroban Nasal

Route: Intranasal

Note: Eradicates nasal carriage of *S. aureus* including MRSA; used in pre-surgical decolonization bundles, often paired with chlorhexidine body wash. [1][2] [1]

Mechanism of action

Summary: Mupirocin structurally mimics isoleucine and binds bacterial isoleucyl-tRNA synthetase, preventing the enzyme from charging tRNA with isoleucine. Protein synthesis stalls for want of charged tRNA, and RNA synthesis fails with it - bacteriostatic at low concentrations, bactericidal at the high concentrations achieved topically.

Target: Bacterial isoleucyl-tRNA synthetase (isoleucine binding site)

Cidal Static: concentration-dependent: bacteriostatic at low, bactericidal at high concentrations

Kill Kinetics: concentration-dependent

1. Step: 1

1. Title: The drug mimics isoleucine

1. Detail: Part of the mupirocin molecule resembles isoleucine closely enough to occupy the isoleucine binding site of bacterial isoleucyl-tRNA synthetase. [1]

2. Step: 2

2. Title: Isoleucyl-tRNA synthetase is inhibited

2. Detail: With the enzyme blocked, tRNA cannot be charged with isoleucine, and the pool of charged isoleucyl-tRNA is depleted. [1]

3. Step: 3

3. Title: Protein and RNA synthesis halt

3. Detail: Translation stalls at every isoleucine codon, and bacterial protein and RNA synthesis are obstructed. [1]

4. Step: 4

4. Title: Effect scales with concentration

4. Detail: At low concentrations the organism is merely inhibited; at the high concentrations reached on skin and nasal mucosa the effect is bactericidal. [1]

5. Step: 5

5. Title: The target is unique, so cross-resistance is absent

5. Detail: No other antibiotic class inhibits isoleucyl-tRNA synthetase, so resistance mechanisms against beta-lactams, macrolides, aminoglycosides or glycopeptides leave mupirocin's activity untouched. [1]

Spectrum of activity

Intro: A deliberately narrow, gram-positive skin-pathogen spectrum, with the clinically decisive feature being retained activity against MRSA.

Subclass Id: class-wide

1. *Staphylococcus aureus*, including MRSA

2. *Streptococcus pyogenes*

3. Other streptococci of skin and soft tissue

Limited activity against certain gram-negative organisms; not a clinical target

1. Normal resident skin flora such as *Propionibacterium* (largely spared)

2. Enterococci and anaerobes
3. Any organism at a site requiring systemic therapy [1]

Major clinical uses

1. Drug: Mupirocin (dermal)
1. Organism: *S. aureus* and *S. pyogenes*
1. Indication: Impetigo
1. Line: first-line
1. Note: For localized impetigo, topical mupirocin is among the treatments of choice; widespread disease needs systemic therapy instead. [1][3]
2. Drug: Mupirocin (dermal)
2. Organism: *S. aureus* and *S. pyogenes*
2. Indication: Secondarily infected traumatic skin lesions
2. Line: first-line
2. Note: Small, superficial secondarily infected lesions such as minor cuts and abrasions. [1]
3. Drug: Mupirocin (nasal)
3. Organism: Nasal carriage of *S. aureus*, including MRSA
3. Indication: Pre-surgical decolonization of identified nasal carriers
3. Line: prophylaxis
3. Note: With or without chlorhexidine body wash, decolonization roughly halves the odds of *S. aureus* surgical site infection in carriers. [2]
4. Drug: Mupirocin (nasal)
4. Organism: MRSA
4. Indication: Decolonization of carriers during institutional outbreak control
4. Line: prophylaxis
4. Note: Screen-and-decolonize strategies target transmission; mupA-mediated resistance is the recognised cause of failure. [1]

Pharmacokinetics

Drug: Mupirocin

Route: Topical (skin) / intranasal

Absorption: Minimal through intact skin; absorption increases through broken or damaged skin

Csf Penetration: Not applicable - no systemic therapeutic exposure

Metabolism: Any absorbed drug is rapidly de-esterified to monic acid, which has no antibacterial activity

Elimination: Absorbed drug and monic acid are renally excreted; topically applied drug is largely shed with desquamating skin

Half Life: Very short systemically (of the order of minutes), which is irrelevant to its topical action

Dose Adjust: None for topical use; avoid the polyethylene glycol ointment on large open wounds in renal impairment [1]

1. The pharmacokinetics are the pharmacology here: rapid systemic inactivation to monic acid is precisely why mupirocin exists only as a topical drug, and why systemic *S. aureus* infection is never a mupirocin indication. [1]
2. The ointment's polyethylene glycol vehicle can be absorbed through large open wounds and damaged skin; because polyethylene glycol is renally cleared and potentially nephrotoxic, extensive application in renal impairment is cautioned against. [1]
3. This page gives no dose regimens by design. Application schedules and treatment durations depend on the product, formulation and indication, and belong in a prescribing reference used by the treating clinician.

Adverse effects

Effect: Local irritation

Detail: Burning, stinging, itching and mild contact dermatitis at the application site are the most frequent problems; nasal use can cause local irritation, rhinorrhoea and taste disturbance. [1]

1. Effect: Hypersensitivity reactions

1. Detail: Rare systemic allergic reactions, including angioedema and anaphylaxis, have been reported.

1. Action: Stop the drug and manage as for any drug hypersensitivity. [1]

2. Effect: Polyethylene glycol absorption from large open wounds

2. Detail: The ointment vehicle can be absorbed through extensive open or damaged skin and is potentially nephrotoxic, particularly when renal function is already impaired.

2. Action: Avoid the polyethylene glycol ointment on large open wounds and use caution in renal impairment. [1]

Drug: Mupirocin (any formulation)

Effect: As with other topical antibacterials, prolonged use can permit overgrowth of non-susceptible organisms, including fungi. [1]

Contraindications, precautions and interactions

Known hypersensitivity to mupirocin or to any component of the formulation. [1]

1. Large open wounds or extensively damaged skin, especially with renal impairment, because of polyethylene glycol absorption from the ointment vehicle. [1]

2. Not for ophthalmic use, and the dermal and nasal products are not interchangeable - each formulation is designed for its own site. [1]

With: Systemic drugs

Effect: Clinically significant systemic drug interactions are not expected, because meaningful systemic exposure does not occur with topical use. [1]

Resistance mechanisms

1. Mechanism: High-level resistance: plasmid-mediated mupA

1. Detail: The mupA gene, carried on transferable plasmids, encodes an alternative isoleucyl-tRNA synthetase that mupirocin cannot inhibit - a complete bypass of the target. This is the mechanism behind decolonization failure and can spread between staphylococci.

MRSA decolonization failure in nasal carriers

1. Countermeasure: Restrict mupirocin to genuine indications, screen for resistance where decolonization fails, and use alternative decolonization strategies when high-level resistance is present. [1]

2. Mechanism: Low-level resistance: chromosomal target mutation

2. Detail: Point mutations in the native chromosomal isoleucyl-tRNA synthetase gene reduce mupirocin binding, raising the minimum inhibitory concentration modestly. Topical concentrations may still exceed it, so the clinical impact is smaller than with mupA.

S. aureus with reduced mupirocin susceptibility after repeated exposure

2. Countermeasure: Avoid prolonged or repeated courses that select stepwise mutants. [1]

Stewardship Note: Mupirocin's value rests entirely on a single unique target, so resistance is an all-or-nothing threat: once mupA spreads through local staphylococci, both impetigo therapy and the MRSA decolonization bundle lose their key agent. Reserving mupirocin for its proper indications, rather than using it as a general wound salve, is what preserves it.

Comparison tables

Title: Low-level versus high-level mupirocin resistance

Caption: The distinction that decides whether topical concentrations still work and whether decolonization can succeed. Local susceptibility data and a prescribing reference govern actual therapy.

1. Key: feature

1. Label: Feature

1. Is Row Header: true

2. Key: low_level

2. Label: Low-level resistance

3. Key: high_level

3. Label: High-level resistance

1. Feature: Genetic basis

1. Low Level: Chromosomal point mutation in the native isoleucyl-tRNA synthetase gene

1. High Level: Plasmid-borne mupA encoding a bypass isoleucyl-tRNA synthetase [1]

2. Feature: Transferability

2. Low Level: Not transferable between organisms

2. High Level: Plasmid-mediated, so it can spread between staphylococci [1]

3. Feature: Effect of topical concentrations

3. Low Level: Often still exceeded by the high concentrations applied topically

3. High Level: Not overcome - the drug cannot inhibit the bypass enzyme [1]

4. Feature: Clinical significance

4. Low Level: Modest; a warning sign of selection pressure

4. High Level: Decolonization failure and loss of mupirocin as a therapeutic option [1]

High-yield exam pearls

1. Pearl: Mupirocin's target is one of a kind.

1. Why: It is the only antibiotic in clinical use that inhibits bacterial isoleucyl-tRNA synthetase, so resistance to beta-lactams, macrolides or any other class does not confer resistance to mupirocin - the reason it still works on MRSA. [1]

2. Pearl: Static or cidal depends on concentration, and topical use delivers cidal.

2. Why: At low concentrations mupirocin is bacteriostatic, but the concentrations achieved on skin and nasal mucosa are far higher and bactericidal - an exam favourite on concentration-dependent classification. [1]

3. Pearl: Nasal mupirocin is a surgical infection-prevention tool, not just a skin treatment.

3. Why: Decolonizing *S. aureus* nasal carriers with mupirocin, with or without chlorhexidine body wash, roughly halves the odds of *S. aureus* surgical site infection, which is why it appears in pre-surgical bundles. [2]

4. Pearl: Monic acid is why mupirocin is topical-only.

4. Why: Absorbed mupirocin is rapidly de-esterified to monic acid, which has no antibacterial activity, so the drug cannot be given systemically no matter how attractive its spectrum looks. [1]

5. Pearl: mupA equals decolonization failure.

5. Why: The plasmid-borne mupA gene encodes an alternative isoleucyl-tRNA synthetase the drug cannot inhibit, producing high-level resistance and failed MRSA clearance - the mechanism to name when a carrier remains positive after treatment. [1]

6. Pearl: It spares normal skin flora.

6. Why: Mupirocin is largely inactive against *Propionibacterium* and other resident skin organisms, so it treats the pathogen without stripping the skin's ecology. [1]

Common exam traps

1. Trap: "Mupirocin can be given orally or IV for serious MRSA infection."
1. Correction: It is topical only. Systemically absorbed drug is rapidly de-esterified to inactive monic acid, so there is no systemic formulation and invasive MRSA infection needs a systemic agent such as a glycopeptide. [1]
2. Trap: "MRSA is resistant to most antibiotics, so it must be resistant to mupirocin too."
2. Correction: Methicillin resistance involves altered penicillin-binding proteins and is irrelevant to mupirocin's target. Mupirocin retains activity against MRSA unless the organism separately carries mupirocin resistance such as mupA. [1]
3. Trap: "Mupirocin is simply bactericidal."
3. Correction: It is bacteriostatic at low concentrations and bactericidal at the higher concentrations achieved with topical application - the classification depends on concentration. [1]
4. Trap: "A topical antibiotic in an ointment base is harmless on any wound."
4. Correction: The polyethylene glycol vehicle can be absorbed through large open wounds or damaged skin and is potentially nephrotoxic, so the ointment is used cautiously on extensive open areas and in renal impairment. [1]

Self-test questions

1. Question: Mupirocin acts by inhibiting which bacterial target?
 1. The 50S ribosomal subunit
 2. Bacterial isoleucyl-tRNA synthetase
 3. DNA-dependent RNA polymerase
 4. Dihydrofolate reductase
1. Explanation: Part of the molecule imitates isoleucine well enough to occupy the amino-acid binding site of the enzyme that charges the matching transfer RNA. With that pool depleted, translation stalls wherever an isoleucine codon appears, and bacterial RNA synthesis is obstructed alongside protein production. [1]
2. Question: Why does mupirocin exist only as a topical preparation?
 1. It is destroyed by gastric acid but remains stable when injected
 2. Its molecular size prevents it leaving the vascular compartment
 3. Drug reaching the circulation is rapidly de-esterified to monic acid, which has no antibacterial activity
 4. It is too irritant to be tolerated by any other route
2. Explanation: Systemic exposure converts the compound almost immediately into an inactive breakdown product, so useful concentrations exist only at the surface where it is applied. Invasive staphylococcal disease therefore has to be treated with an agent from a different class, however attractive this drug's activity against resistant staphylococci looks on paper. [1]
3. Question: A student reasons that because MRSA resists so many antibiotics it must resist mupirocin too. What is the flaw?
 1. Methicillin resistance rests on altered penicillin-binding proteins, which are irrelevant to an isoleucyl-tRNA synthetase inhibitor
 2. MRSA does not express isoleucyl-tRNA synthetase at all
 3. Concentrations achieved on skin are too low for any resistance mechanism to matter
 4. MRSA is always eradicated by chlorhexidine before mupirocin is applied
3. Explanation: Resistance is target-specific, and the machinery altered in methicillin-resistant strains is not the machinery this drug attacks. No other antibiotic in clinical use inhibits the same enzyme, so nothing acquired against beta-lactams, macrolides, aminoglycosides or glycopeptides carries over; an isolate only fails to respond if it has separately picked up a mupirocin-specific mechanism. [1]
4. Question: How is mupirocin best classified on the bacteriostatic-versus-bactericidal axis?
 1. Bacteriostatic regardless of concentration

2. Bactericidal regardless of concentration
3. Bactericidal only when combined with chlorhexidine
4. Bacteriostatic at low concentrations and bactericidal at the higher ones achieved by topical application
4. Explanation: The label is not fixed but follows exposure. Small amounts merely hold growth in check, whereas the far greater concentrations reached on skin and nasal mucosa actually kill the organism, which is exactly why the distinction is worth asking about for a drug applied directly to the site. [1]
5. Question: High-level mupirocin resistance is explained by which mechanism?
 1. A chromosomal point mutation that raises the minimum inhibitory concentration only modestly
 2. Overexpression of an efflux pump shared with the macrolides
 3. Enzymatic acetylation of the drug molecule
 4. A plasmid-borne mupA gene supplying an alternative isoleucyl-tRNA synthetase that the drug cannot inhibit
5. Explanation: This is a complete bypass rather than weakened binding: the organism simply provides a second version of the enzyme over which the drug has no hold, so piling on more concentration achieves nothing. Because the gene travels on transferable plasmids it can move between staphylococci, and it is the recognised explanation for a carrier who remains positive after decolonization. The chromosomal mutation route, by contrast, lifts the inhibitory concentration only slightly and topical levels often still exceed it. [1]
6. Question: What benefit is documented for nasal mupirocin in surgical patients identified as Staphylococcus aureus carriers?
 1. It removes any need for perioperative systemic prophylaxis
 2. It roughly halves the odds of S. aureus surgical site infection
 3. It shortens operating time by reducing wound preparation
 4. It prevents colonization of the operating team
6. Explanation: Clearing carriage from the nose before an operation, with or without a chlorhexidine body wash, cuts the odds of a staphylococcal infection at the surgical site by around half. That measured effect is why the practice belongs to pre-surgical prevention bundles rather than being regarded as an optional skin remedy. [2]
7. Question: Why is the polyethylene glycol ointment formulation used cautiously over extensive open wounds?
 1. Wound exudate inactivates mupirocin on contact with the vehicle
 2. The vehicle can be absorbed through damaged skin and is potentially nephrotoxic
 3. The vehicle accelerates selection of mupA-carrying strains
 4. The vehicle drives systemic mupirocin concentrations to toxic levels
7. Explanation: The concern belongs to the base, not to the antibiotic dissolved in it. Spread across large areas of broken skin the glycol carrier can be taken up, and since it is cleared renally and carries nephrotoxic potential, extensive application is cautioned against where kidney function is already impaired. [1]

Frequently asked questions

1. Question: Why does mupirocin work against MRSA when so many antibiotics fail?
 1. Answer: Methicillin resistance works through altered penicillin-binding proteins, which has nothing to do with mupirocin's target. Because mupirocin is the only clinical antibiotic that inhibits isoleucyl-tRNA synthetase, resistance to other classes does not touch it - MRSA is only mupirocin-resistant if it separately acquires a mupirocin resistance mechanism such as mupA. [1]
2. Question: Why can't mupirocin be given by mouth or injection for serious infection?
 2. Answer: Any mupirocin that reaches the circulation is rapidly de-esterified to monic acid, which has no antibacterial activity. Effective concentrations can only be achieved by applying the drug directly where the infection is - skin or nasal mucosa. [1]
3. Question: What is nasal mupirocin actually for?
 3. Answer: Eradicating nasal carriage of S. aureus, including MRSA. In surgical patients identified as nasal carriers, decolonization with mupirocin - with or without chlorhexidine body wash - roughly halves the odds of S. aureus surgical

site infection, which is why it features in pre-surgical prevention bundles. [2]

4. Question: Why does MRSA decolonization sometimes fail despite correct use?

4. Answer: The leading pharmacological explanation is high-level mupirocin resistance from the plasmid-borne mupA gene, which supplies an alternative isoleucyl-tRNA synthetase the drug cannot inhibit. Topical concentrations, however high, cannot overcome a bypassed target. [1]

5. Question: Is mupirocin ointment safe on any wound?

5. Answer: Not on large open wounds, particularly in renal impairment. The polyethylene glycol vehicle can be absorbed through extensive broken skin and is potentially nephrotoxic, so extensive application in those settings is cautioned against. [1]

References

[1] Mupirocin (StatPearls). StatPearls Publishing / NCBI Bookshelf 2024. <https://www.ncbi.nlm.nih.gov/books/NBK599499/>

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[3] Impetigo (StatPearls). StatPearls Publishing / NCBI Bookshelf 2023. <https://www.ncbi.nlm.nih.gov/books/NBK430974/>

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