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Emergency Medicine Pharmacotherapy with Resuscitation (EMPoweRx) Conference

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Skin and Soft Tissue Infection Treatment Utilizing Long Acting Antibiotics

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Disclosure

- I have no actual or potential conflicts of interest

Objectives

- Discuss the key differences in using lipoglycopeptides compared to traditional therapies for acute bacterial skin and skin structure infections (ABSSSI).
- Determine the clinical and financial impacts of using a lipoglycopeptide protocol in the Emergency Department.

University of Kentucky HealthCare

- 927 bed, tertiary care center
  - 124 adult ICU beds
- Level 1 trauma center
- Comprehensive stroke center
- Case mix index (CMI) 2.21
- Accepts the most transfers, nationally
  - 5,114 transfers from January – May 2021

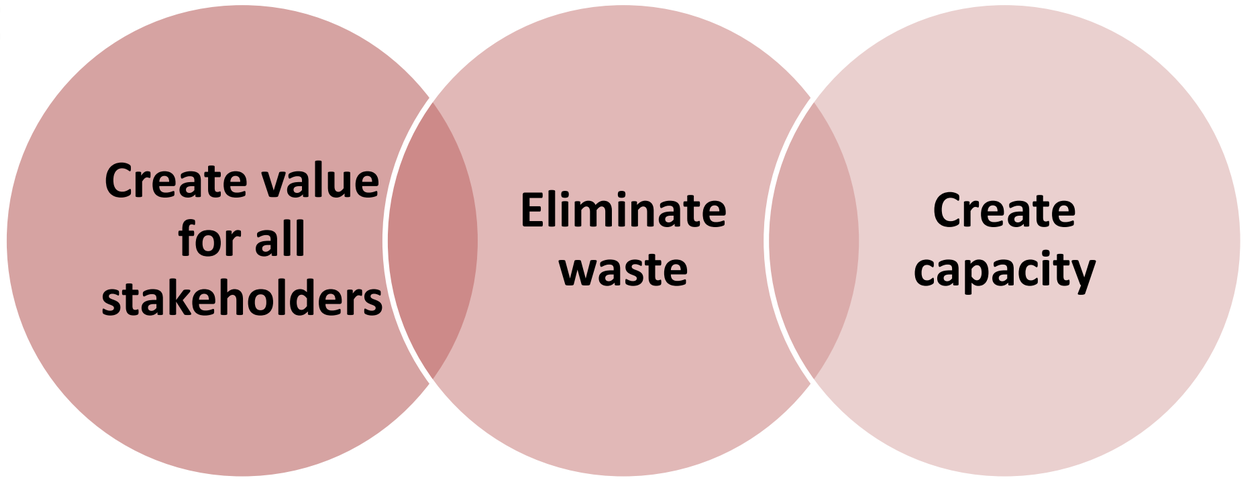
Image source: UK HealthCare

The Emergency Department - The Front Door to the Healthcare System

- > 375,000 boarding hours annually
- Time from ED Arrival to Admit: 287 min_{AVG}
- Time from ED Admit to Departure: 1038 min_{AVG}
- Boarding time per patient: 17.3 h
- Turn down > 2400 transfers, annually

Shifting in Historical Models of Care Delivery

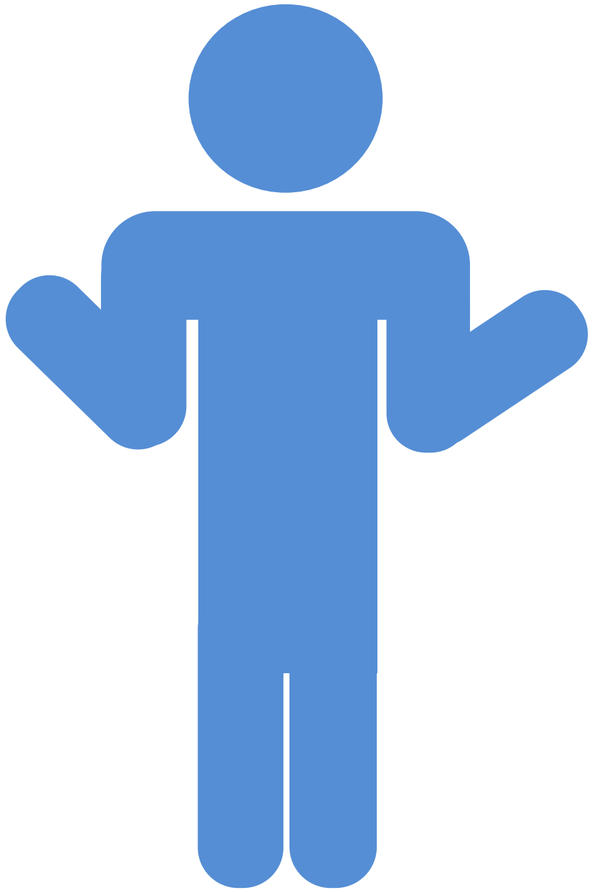
- From volume to value and outcomes
- Focus on the right care at the right time
- Avoiding unnecessary admissions
- Connections to care in the outpatient realm
- Avoiding readmissions



Healthcare Delivery Through Time

1960s

- Staffing resources
- Care primarily inpatient
- Admissions elective
- Average LOS 12 days
- System-wide inefficiencies

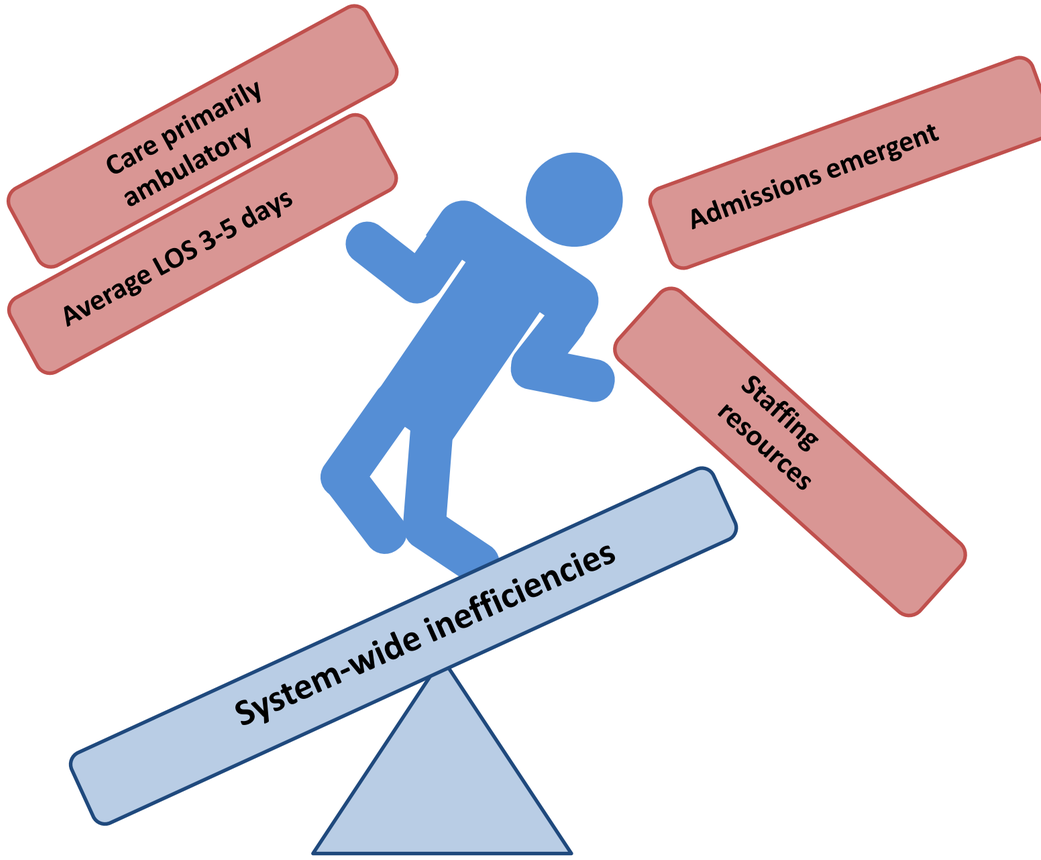


2022

- Staffing resources
- Care primarily ambulatory
- Admissions emergent
- Average LOS 3-5 days
- System-wide inefficiencies

Emergency Department as America's Safety Net

- Safety net providers
  - Overburdened other providers cannot meet the needs of the community
- Hospital closures
- Lack of access
- Erosion of emergency care systems
- Limited capacity for system-wide inefficiencies



Acute Bacterial Skin and Skin Structure Infections (ABSSSIs)

- Incidence increased > 50% since 1997
- Most common infection encountered in the healthcare setting
  - Nearly 900,000 hospitalizations
- Account for over 2 million ED visits annually

Increased Patient Cost

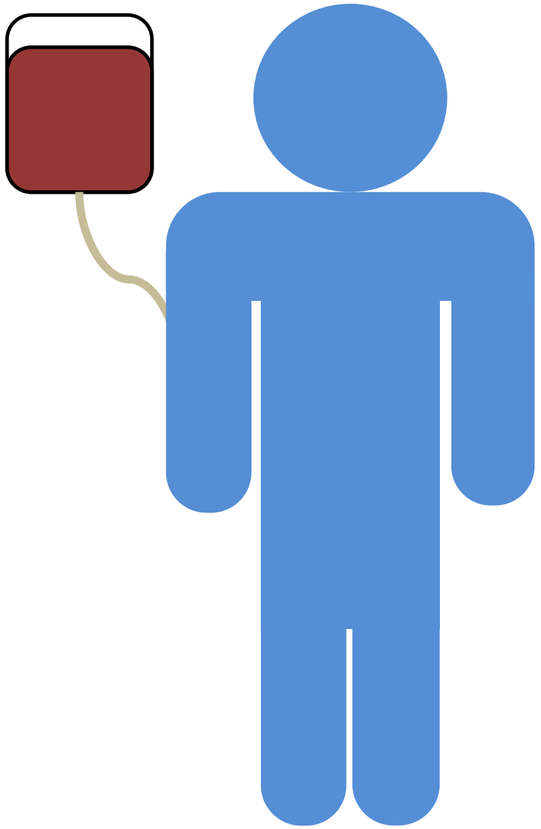
Diminished Bed Capacity

Transitions of Care Barriers

JAMA Dermatol. 2017;153:141-146
Ann Pharmacother 2019 Nov;53(11):1093-1101

Shifting the Paradigm in the Treatment of ABSSSI

- Need for additional agents active against MRSA
- Shortcomings of vancomycin
  - Complex dosing
  - Therapeutic monitoring
  - MIC creep
  - Renal dysfunction
  - Barriers to outpatient parenteral antimicrobial from the Emergency Department



Roberts et al Pharmacotherapy 2015;35(10):935–948)

Lipoglycopeptides for Treatment of ABSSSI

Dalbavancin

- Two-Dose Regimen:
  - 1000mg on D1
  - 500mg on D8
- Single-Dose Regimen:
  - 1500mg on D1
- Recommended renal dose adjustments exist
- Prepared in 250mL of 5% dextrose
- 1-hour infusion

Oritavancin

1200mg on D1

No renal dose adjustments

Oritavancin (Kimyrsa®)

250mL of 5% dextrose

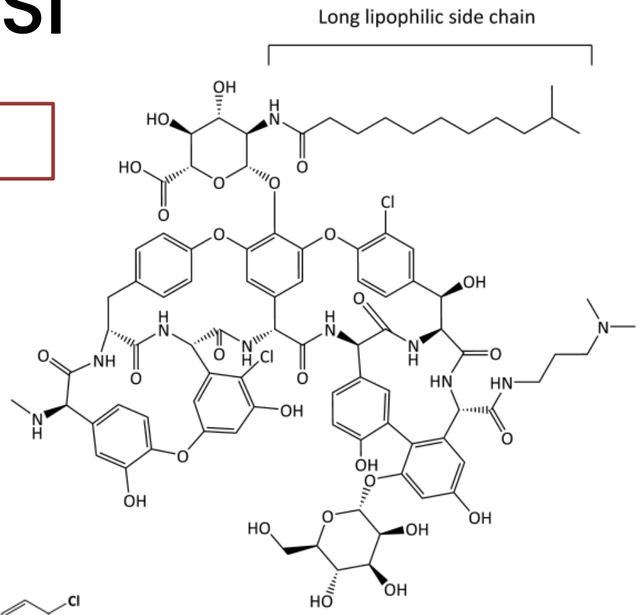
1-hour infusion

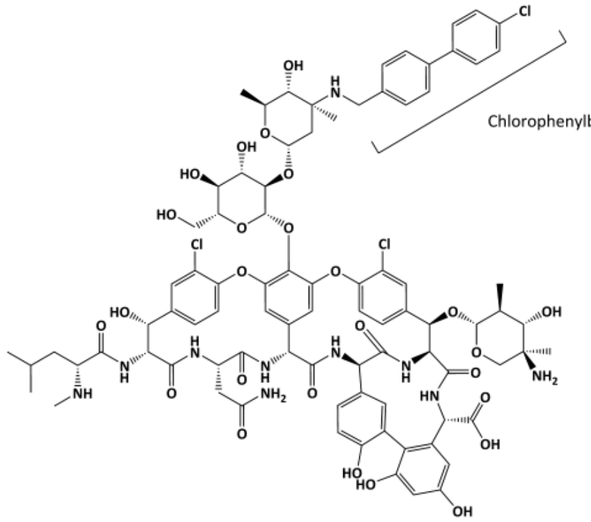
Oritavancin (Orbactiv®)

3-hour infusion

1000mL of 5% dextrose

Dalbavancin





Oritavancin

Roberts et al Pharmacotherapy 2015;35(10):935–948)
Kimyrsa. Package insert. Melinta Therapeutics; 2021
ORBACTIV® [package insert]: Melinta Therapeutics, Inc.; 2019

Long-Acting Lipoglycopeptides: Spectrum of Activity

- Prolonged terminal half-life
  - Long lipophilic side chain creates enhanced potency and extending its half-life, allowing for once-weekly dosing
- Dalbavancin & Oritavancin
  - Terminal half-life of 2 weeks
  - Highly protein bound
- Oritavancin
  - In vitro activity against resistant isolates (VRSA, VISA, and VRE) but approved only for use in vancomycin-susceptible isolates of Enterococcus

Staphylococcus aureus	***Streptococcus pyogenes,***
Streptococcus agalactiae	***Streptococcus anginosus***
Enterococcus faecalis*	**Enterococcus faecium***

* Dalbavancin shows only in vitro activity against Enterococcus species

Dalbavancin for Infections of the Skin Compared to Vancomycin at an Early Response: DISCOVER 1 & DISCOVER 2

- Phase III noninferiority trials
- Compare dalbavancin versus vancomycin followed by oral linezolid
  - Dalbavancin: 1000 mg on day 1 followed by 500 mg on day 8
  - Vancomycin 1 g or 15 mg/kg IV every 12 hours for a minimum of 3 days
  - Option to switch to oral linezolid 600 mg every 12 hours to complete 10–14 days

Primary end point

- Early clinical response at 48–72h
- Reduction in lesion size of 20% or more

Secondary end point

- Clinical status

DISCOVER 1	DISCOVER 2
• Early clinical response seen in 83.3% • Lesion size reduction in 88.6% • Clinical status indicating success in 90.7% • Noninferior	• Early clinical response seen in 76.8% • Lesion size reduction in 80.3% • Clinical status indicating success in 93.5% • Noninferior

Roberts et al Pharmacotherapy 2015;35(10):935–948)
Boucher et al; N Engl J Med 2014;370:2169-79

Single-Dose Oritavancin in the Treatment of Acute Bacterial Skin Infections: SOLO I

- Double-blind, noninferiority study
- Compare Oritavancin 1200mg versus vancomycin twice daily for 7-10 days

Primary end point (composite)

- Cessation of spreading or reduction in lesion size, absence of fever, and no need for administration of a rescue antibiotic 48 - 72h after therapy

Secondary end point

- Clinical cure 7 to 14 days after the end of treatment
- Reduction in lesion size of 20% or more 48 to 72 hours after administration

SOLO I

- Early clinical response seen in $82.3\%_{ORI}$ vs $78.9\%_{VAN}$
- Clinical cure $79.6\%_{ORI}$ vs $80\%_{VAN}$
- Reduction in lesion size $86.9\%_{ORI}$ vs $82.9\%_{VAN}$
- Noninferior

Corey et al. NEJM 2014;370:2180-90

Single-Dose Oritavancin v 7–10 Days of Vancomycin in the Treatment of Gram-Positive Acute Bacterial Skin and Skin Structure Infections: SOLO II

- Double-blind, noninferiority study
- Compare Oritavancin 1200mg versus vancomycin twice daily for 7-10 days

Primary end point (composite)

- Cessation of spreading or reduction in lesion size, absence of fever, and no need for administration of a rescue antibiotic 48 - 72h after therapy

Secondary end point

- Clinical cure 7 to 14 days after the end of treatment
- Reduction in lesion size of 20% or more 48 to 72 hours after administration

SOLO II

- Early clinical response seen in $80.1\%_{ORI}$ vs $82.9\%_{VAN}$
- Clinical cure $82.7\%_{ORI}$ vs $80.5\%_{VAN}$
- Reduction in lesion size $85.9\%_{ORI}$ vs $85.3\%_{VAN}$
- Adverse event rate similar
- Noninferior

Corey et al. Clinical Infectious Diseases 2015;60(2):254–62

Lipoglycopeptides in the Emergency Department

- Retrospective cohort
- Compare recurrences between patients who received dalbavancin as part of standard of care versus patients who received dalbavancin as part of a telehealth program

Methods

- 1500mg in the ED
- APRN follows up in 24 and 72 h following discharge

Outcomes

- Primary: ABSSSI recurrence within 1 month
- Secondary: Hospital admission as a result of ABSSSI, ED LOS (hrs), Adverse effects

Patel et al 2019

- Recurrence 14% $(6/42)_{TEL}$ and 22% $(5/23)_{SOC}$ ($P = 0.5$)
- ED LOS $5h_{TEL}$ vs $25h_{SOC}$
- Adverse event rate similar
- Safe option for ED telehealth program

Patel et al; Parmacother. 2019 Nov;53(11):1093-1101.

Dalbavancin for Treatment of ABSSSI at UK HealthCare

Identification	**Admission for intravenous antibiotics**
Candidacy	**Lesion ≥ 75 cm^2** **Evaluate risk of gram negative infections**
Pharmacist Assessment	**Contraindications** **Financial barriers** **Patient counseling** **Transitions of care**

Follow Up Process

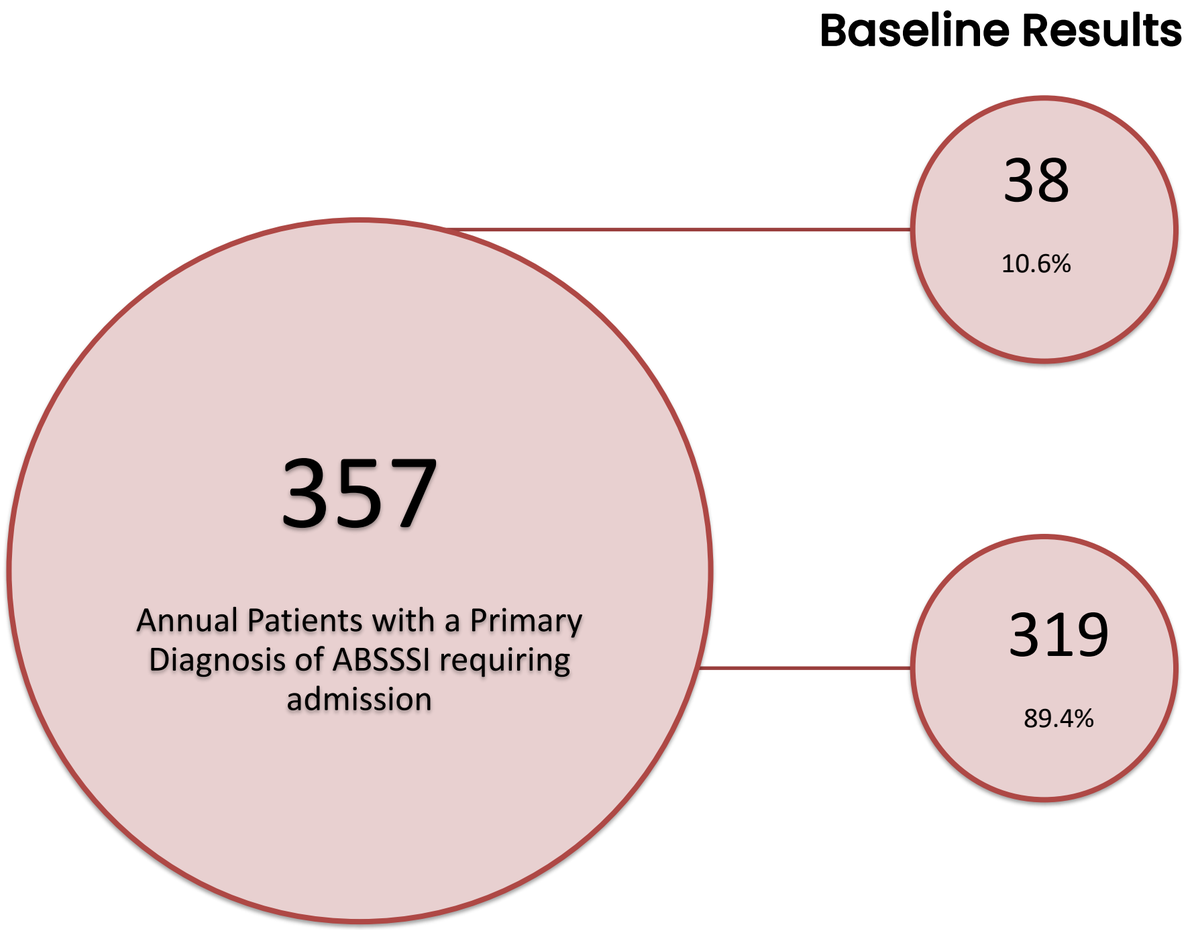
- Performed by pharmacists
- 72 hours post administration
- Assessment
  - Improvement in clinical symptoms
  - Improvement in lesion
  - Additional counseling on clinical course
- Barriers to implementation
  - Drug cost
  - Patient financial barriers
  - Discharge workflows
  - Bandwidth for evaluating patients

Telehealth

Infectious Disease Follow Up

Discharge Clinic Referral

Lipoglycopeptides in the ED at UK HealthCare



Treated with Dalbavancin in the ED resulting in an avoided Inpatient admission

ABSSSI Inpatient Admissions

- 4.24 ALOS
- 1,351 Inpatient Days
- .9053 CMI
- 4.68 CMI Adjusted LOS

Capacity Creation

Backfill Criteria:

≥ 18 year of age

Transferred from an outside facility

91.3% Success rate for patients treated with Dalbavancin

Baseline Results:

38

Transfer Capacity Created:

Patients	23
Patient Days	161
ALOS	6.98
CMI	2.1802
CMI Adj LOS	3.2

Target:

357

Maximal Transfer Capacity:

Patients	174
Patient Days	1,214
ALOS	6.98
CMI	2.1802
CMI Adj LOS	3.2

Admission Rate (8.7%):

Patients	31
Patient Days	131

Cost-Consequence Analysis of Dalbavancin

- Retrospective cohort
- Standard of care could be oral antibiotics
- Important when defining value
  - Net cost
  - ACER & ICER
- Payer mix and financial outcomes
- Stewardship implications

Primary end point

- Average net cost to the healthcare system per patient
  - Calculated as the difference between reimbursement payments and the total cost to provide care to the patient

Secondary end point

- Proportion of cases successfully treated, defined as no ABSSSI-related readmission within 30 days after the initiation of treatment

Gonzalez et al 2021

- Average total cost per patient
  - Dalbavancin$4770
  - SoC $2709 (P < 0.0001)
- Average reimbursement per patient
  - Dalbavancin $3084
  - SoC $2633 (P = 0.527)
- Net cost
  - Dalbavancin $1685
  - SoC $75 (P = 0.013)
- Treatment success rate
  - Dalbavancin 74%
  - SoC 85% with (P = .004)

Gonzalez et al; Clin Infect Dis. 2021 Oct 5;73(7):e1436-e1442
Bookstaver et al; Clinical Infectious Diseases® 2021;73(7):e1443–4

Takeaways

- Evaluate the use of long-acting lipoglycopeptides for formulary addition
- Consider unique models including telehealth options as well as discharge clinics or infusion center pathways
- Collaborate with pharmacists in infectious diseases/antimicrobial stewardship
- Consider implementation of a pharmacist-led discharge follow up process

Self-Assessment Questions

Question 1

Advantages of using long-acting lipoglycopeptides for the treatment of acute bacterial skin and skin structure infections (ABSSSIs) in the Emergency Department include which of the following (select all that apply):

a. Avoiding an inpatient admission

b. Reducing Emergency Department length of stay

c. Positive financial benefits for payors and the healthcare enterprise

d. Improved clinical outcomes in the treatment of ABSSSI

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Question 2

Which of the following medications has the potential to Emergency Department reduce length of stay when provided to patients for the treatment of ABSSSI in the ED?

a. Dalbavancin

b. Vancomycin

c. Linezolid

d. Nafcillin

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Question 3

Barriers to implementing a protocol for a long-acting lipoglycopeptide include which of the following:

a. Financial barriers including drug cost

b. Transitions of care barriers

c. Safety barriers including adverse events with need for prolonged observation period

d. All the above

Question 3

Barriers to implementing a protocol for a long-acting lipoglycopeptide include which of the following:

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Skin and Soft Tissue Infection Treatment Utilizing Long Acting Antibiotics

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