Guidance on management of uncomplicated bloodstream infections from Gram-negative organisms

Candidates for Short Course & Oral Therapy:

Patients with Gram-negative bloodstream infection (GN-BSI) that meet all of the following criteria may be candidates for both treatment with 7 days of total antimicrobial therapy and early switch from IV to oral antibiotics:

- Infection from an organism other than *Salmonella* spp., *Acinetobacter* spp., or *Stenotrophomonas* spp.
  - Recommend ID consultation for noted exceptions.
- No evidence of endovascular infection, unresected osteomyelitis, central nervous system infection or retained prosthetic material at the site of infection.
  - Recommend ID consultation for noted exceptions.
- Patient is clinically improving on current antibiotics; hemodynamically stable without vasopressor use
- Causative organism is known to be susceptible to at least one recommended oral agent
- Patient is able to tolerate oral (PO) medications without concern for poor gastrointestinal absorption
- Adequate source control has been achieved, if needed. Examples include:
  - **UTI**: exchange or removal of urinary catheter, nephrostomy tubes or urinary stents present when infection developed, resolution of any known obstruction
  - **Intra-abdominal infection**: drainage of abscesses/infected fluid collections, debridement of infected tissues
  - **Skin and soft tissue infection**: Drainage of abscesses or fluid collections, debridement or amputation of necrotic tissues
  - **Line associated bacteremia**: Removal or exchange of catheter if failure to improve or if persistently positive blood cultures (see below for repeat blood culture guidance).
    - If line is retained, patient can be a candidate for oral antibiotic therapy, however a longer duration may be required.
  - If uncertain about source control, consult ID

Repeat blood cultures

Repeat blood cultures are not routinely recommended. If required, obtain at least 48 hours after starting appropriate antibiotic therapy

Consider in patients with:

- Persistent fevers
- Concern for endovascular infection
- Retained intravascular catheters or prosthetic devices
- No clinical improvement on appropriate therapy

**Oral therapy antibiotic choice and doses recommended for IV-PO switch**

Treatment selection should be guided by antibiotic susceptibility data. It is important that bioavailable oral agents are used at doses that will achieve adequate concentrations to treat systemic infection.

**Preferred** oral therapies for uncomplicated GN-BSI:

- **Levofloxacin** 750mg PO daily
- **Trimethoprim/sulfamethoxazole (TMP/SMX)** 7-10 mg/kg TMP based on Adjusted Body Weight (AdjBW) rounded to nearest double strength (DS, 160mg) tablet size:
  - 40-49kg AdjBW: 1 DS tablet BID PO
  - 50-69kg AdjBW: 1 DS tablet TID PO
  - 70-95kg AdjBW: 2 DS tablet BID PO
  - >95kg AdjBW: call antimicrobial stewardship pharmacist
- AdjBW is equal to ideal body weight (IBW) plus 40% of the difference between total and IBW

**Alternative** therapies, in order of preference (utilize if patient has a medication contraindication or non-susceptible organism to preferred agents, and organism is susceptible)

- **Amoxicillin** 1g TID PO*
- **Cephalexin** 1g TID PO or **Cefadroxil** 1g BID PO**
- **Amoxicillin/clavulanate** 875/125mg TID PO

* Ampicillin susceptibility can be utilized to determine susceptibility to oral amoxicillin.
** Cefazolin susceptibility can be utilized to determine susceptibility to oral cephalosporins (cephalexin and cefadroxil). **Ceftriaxone should not be utilized as a surrogate for susceptibility of oral cephalosporins.**

Agents generally not recommended as oral therapy for GN-BSI:

- Penicillin VK
- Cefuroxime
- Cefdinir
- Cefpodoxime
- Doxycycline
- Fosfomycin
- Nitrofurantoin

**Duration of therapy**

Several studies have demonstrated that treatment durations of 7 days result in outcomes equivalent to 14 days in uncomplicated GN-BSI (both oral and intravenous antibiotics). Bacteremia secondary to pyelonephritis may require a longer duration of 10-14 days if utilizing trimethoprim-sulfamethoxazole or a beta-lactam agent for definitive therapy.
Figure 1: Treatment decision algorithm

Bone, central nervous system or endovascular infection?

Yes
Continue parenteral antibiotic, obtain source control, and recommend ID consult. May require longer duration of antibiotics

No
Source controlled?
(see below for definitions)

No
Clinically improving?
(Fever curve improving, hemodynamically stable)

Yes
Continue parenteral antibiotics

Yes
Preferred:
Levofoxacin 750mg daily PO
OR
Trimethoprim/sulfamethoxazole
40-49kg AJBW: 1 DS tablet BID PO
50-69kg AJBW: 1 DS tablet TID PO
70-95kg AJBW: 2 DS tablet BID PO
>95kg AJBW: call antimicrobial stewardship pharmacist

Alternative:
Amoxicillin 1g TID PO
Cephalexin 1g TID PO
Augmentin 875/125mg TID PO
Cefadroxil 1g BID PO

Duration:
7 days total antibiotic therapy

Source control
UTI: exchange or removal of urinary catheter/nephrostomy tubes, resolution of any known obstruction
Intra-abdominal infection: drainage of abscesses or infected fluid collections, debridement of infected tissues
Skin and soft tissue infection: Drainage of abscesses or fluid collections, debridement or amputation of necrotic tissues
Line associated bacteremia: Removal or exchange of catheter if not clinically improving or persistent bacteremia

Note: Antibiotic selection should be guided by antibiotic susceptibility