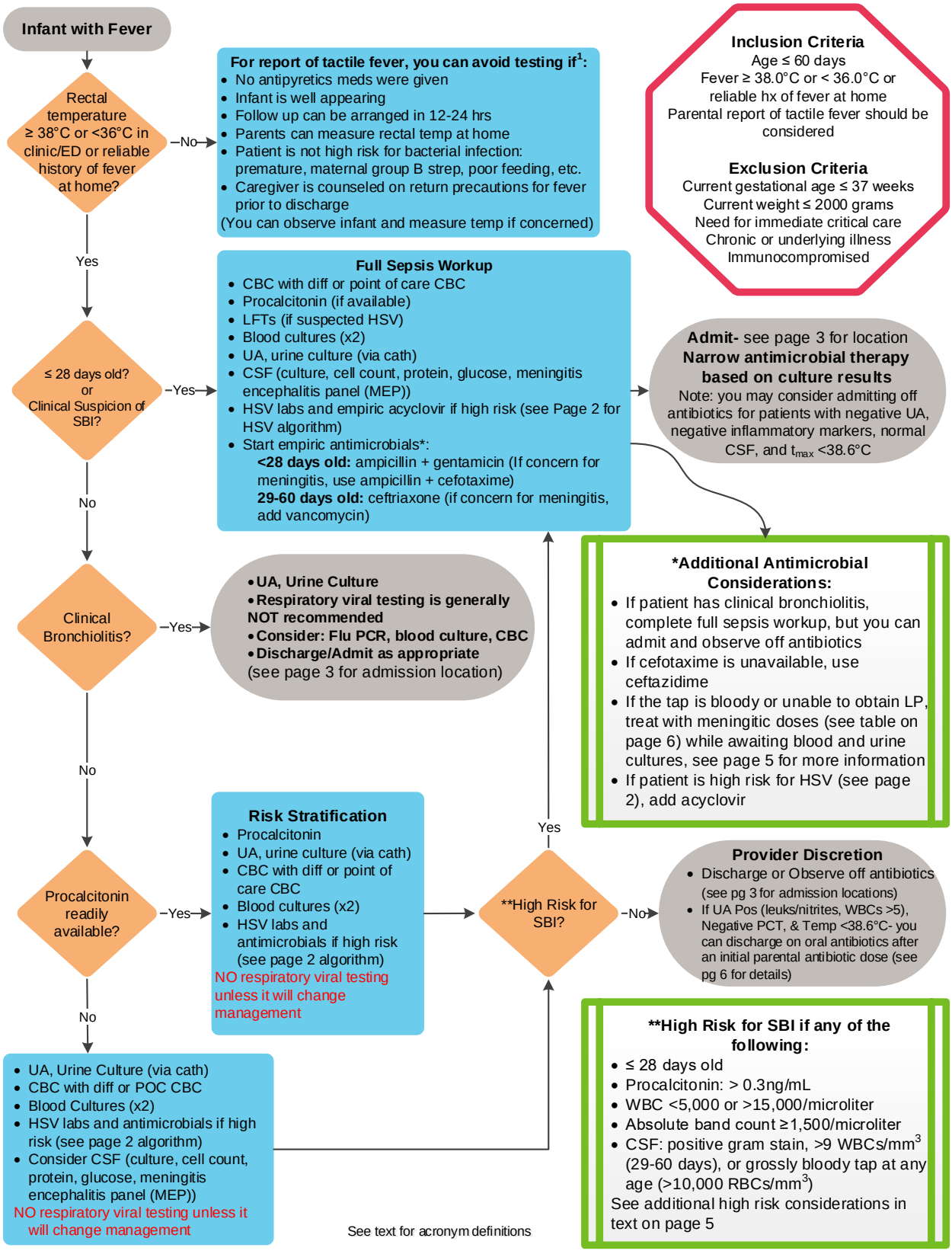
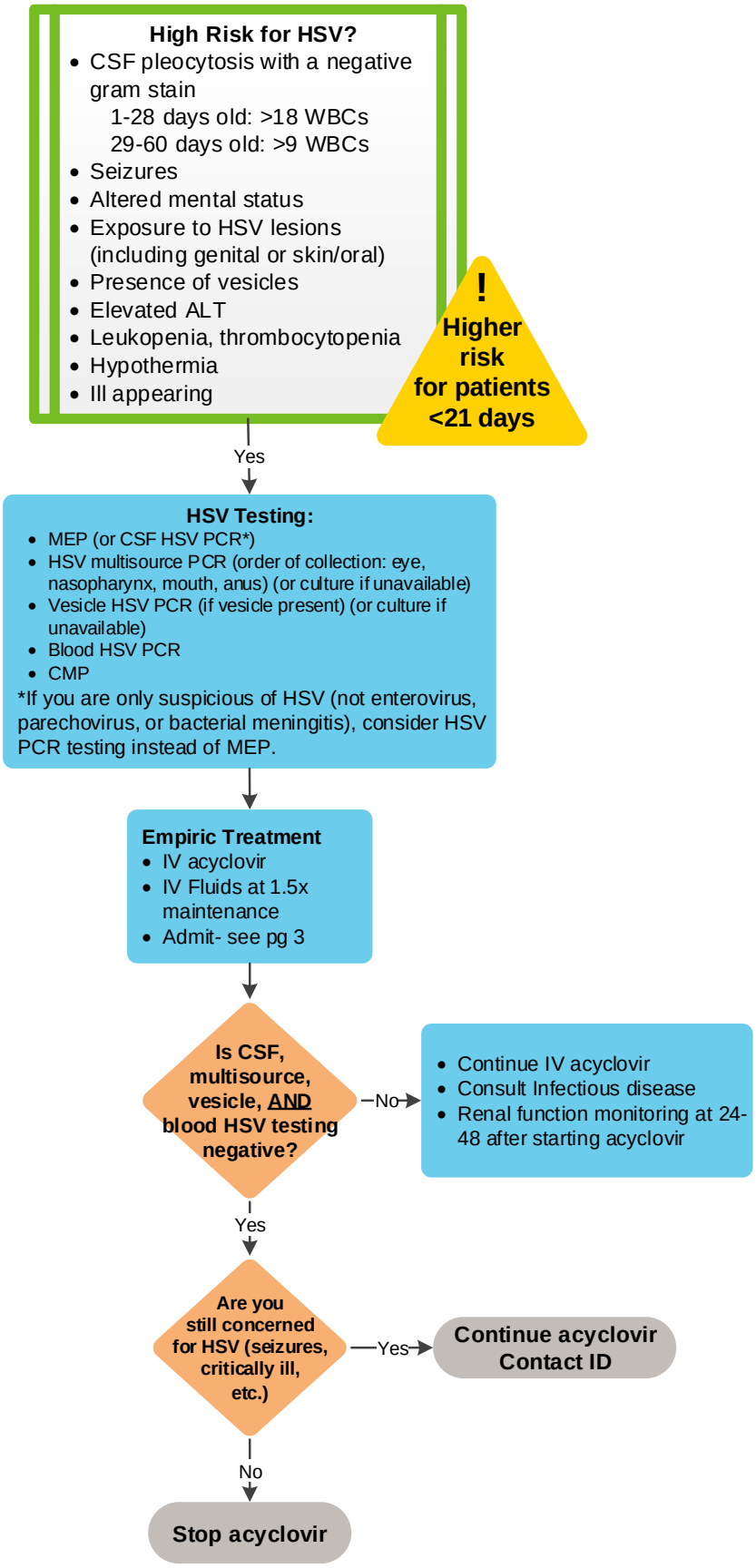
FEVER IN INFANTS LESS THAN 60 DAYS

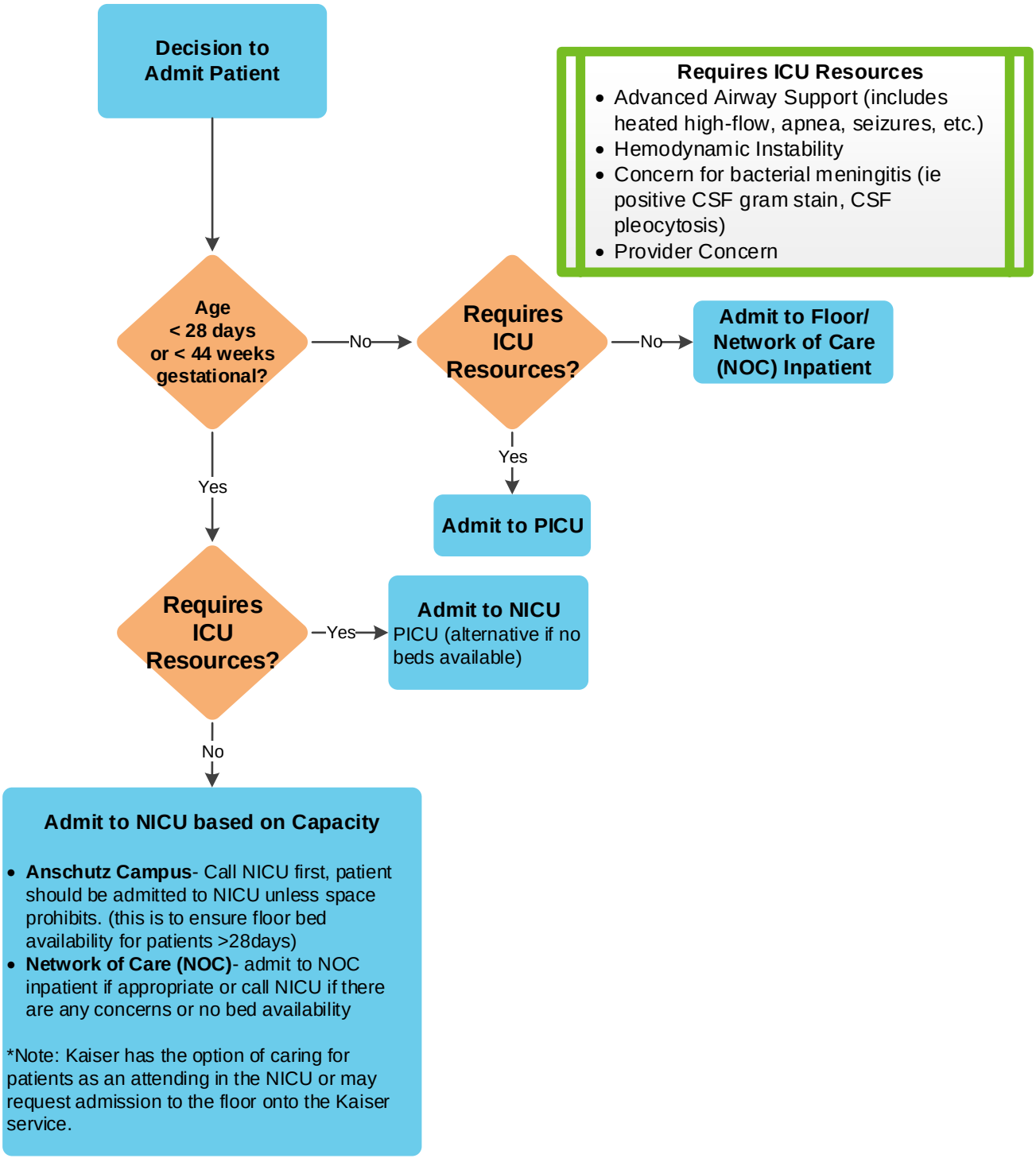
ALGORITHM



ALGORITHM- HSV Testing



ALGORITHM- Admission



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TARGET POPULATION

Inclusion Criteria

- Age less than or equal to (≤) 60 days
- Fever (greater than or equal to (≥) 38.0°C (100.4° F)) or less than (<) 36.0°C (96.8° F)
- Parental report of tactile fever should be considered
- Gestational age greater than (>) 37 weeks AND weight greater than (>)2000 grams

Exclusion Criteria

- Need for immediate critical care
- Chronic or underlying illness
- Immunocompromised

BACKGROUND | DEFINITIONS

- Serious Bacterial Illness (SBI):
  - Includes bacteremia/sepsis, meningitis, and urinary tract infections (UTIs)
  - Febrile infants less than 28 days are at higher risk of SBIs
  - For febrile infants, no universal risk stratification currently exists to identify SBI either by clinical examination, routine laboratory tests, biomarkers or selection criteria.[2,3]
- Rectal temperature correlates most closely with core body temperature[5]
- Infants with otitis media are at the same risk of bacteremia as patients without an otitis media
- Infants with enterovirus identified in cerebrospinal fluid (CSF) are lower risk for SBI, have decreased length of stay, exposure to antibiotics, and hospital costs.[6,7,8,9]

Table 1: Incidence of SBI in infants[4]

	Incidence of infection in febrile infants 7-90 days
Urinary Tract Infection (UTI)	17%**
Bacteremia	2%
Meningitis	0.9%

**10% of patient with UTI will have bacteremia

INITIAL EVALUATION

Thorough history and physical examination including these high-risk considerations:

- Maternal history of intra-partum fever, antibiotic treatment, group B strep infection
- Infant history of prior antibiotic treatment, hospitalization longer than mother, previous hospitalization, unexplained hyperbilirubinemia, prematurity (less than 37 weeks), temp greater than 38.5°C[10]

LABORATORY STUDIES | IMAGING

Procalcitonin[11,12,13]

- For well-appearing infants 29-60 days, a normal procalcitonin lowers the risk of serious bacterial infection. (Can consider discharge home without antibiotics after blood and urine cultures are obtained.)
- An elevated procalcitonin warrants further investigation for serious bacterial infection and antibiotic initiation while awaiting blood, urine, and CSF cultures.

Traumatic/Dry Lumbar Punctures

- Interpretation of traumatic or dry taps can be difficult. In general, traumatic lumbar punctures (LPs) are defined as greater than 500 RBCs/hpf and correcting with ratios can be inaccurate. The decision regarding whether or not to treat for meningitis in these situations is influenced by degree of fever, degree of illness, other laboratory studies, cultures, age of the infant, and other factors.

Neonatal Herpes Simplex Virus (HSV)[14,15]

- See algorithm on *page 2*
- Early diagnosis and treatment improves outcomes; untreated infections often result in death or serious morbidity
- The vast majority of neonatal HSV cases occur in infants less than 28 days, with few cases reported greater than 6 weeks of age
- Skin, eye, and mucous membrane infection typically presents at 7-14 days of age, CNS infection at 14-21 days, and disseminated disease at 5-12 days

Meningitis Encephalitis Panel (MEP)

- MEP rapidly tests CSF for 14 common causes of central nervous system (CNS) infection but does not rule out meningitis due to other pathogens.
- MEP should be ordered if concern for HSV and enterovirus/parechovirus. If only suspicious of a single organism (or MEP unavailable), consider PCR testing for individual organism(s).
- Consider MEP for enterovirus and parechovirus testing regardless of CSF white blood cell count (WBC) (as most lack pleocytosis).

Viral Testing[13]

Viral testing indicated in select infants based on season and clinical presentation and *only* if results will change management.

- Consider flu PCR during influenza season.
- Consider Gastrointestinal Pathogen Panel if bloody diarrhea.

Additional diagnostic studies if indicated:

- Basic metabolic profile (BMP) if concern of dehydration, electrolyte disturbance or if starting acyclovir

THERAPEUTICS

Antibiotic Recommendations

- Obtain all cultures prior to antibiotic administration if possible
- IV route of antibiotic administration is preferred
- If enterovirus or parechovirus is identified in a well-appearing infant, you can discontinue antibiotics
- Duration of antibiotic therapy varies based on diagnosis, culture results, and clinical improvement of the infant

	Focus	Age 0-28 days	Age 29-60 days
EMPIRIC THERAPY	Suspected UTI or SBI	ampicillin (see dosing below) ***AND*** gentamicin (see dosing below)	ceftriaxone (see dosing below)
	Suspected Meningitis or abnormal CSF	ampicillin (see dosing below) ***AND*** cefotaxime (see dosing below)	vancomycin (see dosing below) ***AND*** ceftriaxone (see dosing below)
	Suspected HSV	acyclovir (see dosing below)	

- Dosing Recommendations (updated 12/2019):
    - Ampicillin:
        - Suspected UTI/SBI:
            - Body weight greater than 2 kg
                - 0-28 days: 50 mg/kg every 8 hours
                - 29-60 days: 50 mg/kg every 6 hours
        - Suspected meningitis or abnormal CSF:
            - Less than or equal to 7 days: 100 mg/kg/dose every 8 hours
            - 8-60 days: 75 mg/kg/dose every 6 hours
    - Gentamicin:
        - 35+ weeks
            - Less than or equal to 7 days: 4 mg/kg every 24 hours
            - 8-60 days: 5 mg/kg every 24 hours

- Cefotaxime:
  - 50 mg/kg/dose at the following intervals:
    - q8-12 h: Less than/equal to 7 days old
    - q6-8h: Greater than 7 days old
- Vancomycin:
  - > 28 weeks
    - SCr < 0.7: 15 mg/kg q12
    - SCr 0.7-0.9: 20 mg/kg q24
    - SCr 1-1.2: 15 mg/kg q24
    - SCr 1.3-1.6: 10 mg/kg q24
    - SCr > 1.6: 15 mg/kg Q48
- Ceftazidime:
  - 50 mg/kg/dose at the following intervals:
    - q8-12h: Less than/equal to 7 days old
    - q8h: Greater than 7 days old
- Ceftriaxone:
  - Infant must be older than 28 days to use
    - Sepsis/UTI: 50 mg/kg Q24H
    - Meningitis/Abnormal CSF: 100 mg/kg Q24H -**OR-** 50 mg/kg Q12H
- Acyclovir:
  - 20 mg/kg/dose every 8 hours

Alternative to cefotaxime during medication shortage for infants less than or equal to 28 days old: ceftazidime 50 mg/kg/dose every 8 hours, max 2000 mg/dose

Outpatient Antibiotic Recommendations for Urinary Tract Infection (UTI)

- For neonates and infants less than 2 months of age with presumed UTI, initiate empiric parenteral antibiotics. Neonates less than 1 month of age must receive parenteral therapy, due to inadequate drug absorption, immature immune system and increased dissemination of infection[18]. Bacteremia secondary to acute pyelonephritis occurs in 6.1-22.7% of children less than 2 months of age[19].
  - For infants 29-60 days old with uncomplicated bacterial UTI and close follow-up, parenteral antibiotics may be switched to oral antibiotics at the discretion of the provider after clinical improvement.
  - Oral antibiotics should be chosen based on gram stain, culture results and local antibiotic susceptibility patterns.

Additional Antibiotic Considerations

- 29-60 days: Antibiotics are not indicated if laboratory results are within normal limits, no concern of SBI/sepsis, or high index suspicion of viral etiology[20,13]. Select site-specific treatment for minor focal infection in well-appearing child

DISPOSITION

Admission

- See Admission Algorithm on *page 3*
- Additional considerations for admission:
  - Unable to confirm follow up in less than 24 hours
  - Lack of telephone or transportation
  - Inadequate home resources
  - Caretaker unable to provide care
  - Notify primary care provider (PCP) and admitting physician

Discharge Home

- If the patient is diagnosed with a treatable infection, then manage as appropriate
- Discharge home with good follow up if patient is well-appearing and cultures negative at 24-36 hours, workup for age and appearance is complete and reassuring (including HSV if appropriate).
  - If well appearing infant greater than 7 days with enterovirus or parechovirus identified, can discharge earlier

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Clinical Care Guideline and Measures Review Committee – January 9th, 2018
Pharmacy and Therapeutics Committee – February 1st, 2018

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LAST DATE OF REVIEW OR REVISION	February 1, 2018
APPROVED BY	 Lalit Bajaj, MD, MPH Medical Director, Clinical Effectiveness

REVIEW/REVISION SCHEDULE

Scheduled for full review on February 1, 2022.

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