



Refer to the NM Antimicrobial Stewardship Website at <https://asp.nm.org> under Antimicrobial Resources to find the **Allergy Toolkit**. Includes: 1) Provider Education: Penicillin Allergy, 2) Cross Reactivity Chart: Beta-lactams, 3) Allergy Risk Assessment and Clinical Pathway, 4) Patient Education: Penicillin Allergy, and 5) Graded Challenge Guidance Document.

Graded Challenge hours of operations:

M-F 8am to 4pm. Consult the Antimicrobial Stewardship Program (ASP) by paging 5-5955 with each order.

All graded challenge orders must have an Antimicrobial Stewardship representative present during administration. Any order requests where implementation of a graded challenge would occur during off-hours will be processed for administration the following business day.

GRADED CHALLENGES

A. Criteria

1. Recommended to verify penicillin tolerance in non-critically ill in-patients with a **low-risk for a true IgE-mediated** reaction using a β -lactam with a dis-similar R1 side chain. (Refer to the [Allergy Risk Assessment and Clinical Pathway](#) in Allergy Toolkit).
2. To decrease the risk for a reaction, the graded challenge will be performed with a different β -lactam class, carrying a dissimilar side chain. (Refer to the [Cross Reactivity Chart: Beta-lactams](#) in the Allergy Toolkit).
3. The graded challenge is only used to test a patient's reaction to the challenged β -lactam. Patients do not need to increase their level of care during the graded challenge. Graded challenges may be performed on the general medical floors; no ICU admission necessary.
4. Patient allergy history profiles in EPIC should be updated, indicating tolerance or intolerance to the graded challenge. The graded challenge is not a method of de-labeling the penicillin allergy history.
 - a. Ex. update in EPIC allergy profile: *Tolerated ceftriaxone graded challenge on 7.17.19*

B. Order-set process

1. Graded challenge orders in EPIC

**Antimicrobial / Anti-infective Graded Challenge – NMH. (Order Set)
ANTIBIOTIC/ANTI-INFECTIVE IVPB GRADED CHALLENGE PANEL (Order Panel)
ANTIBIOTIC/ANTI-INFECTIVE ORAL GRADED CHALLENGE PANEL (Order Panel)**

2. Emergency medications will be ordered with each β -lactam graded challenge. Medications are available in designated unit Omnicells called: [Allergy Test Emergency Kit](#). **If any of the following medications is required, immediately stop test dose protocol.**
 - a. EPINEPHrine (ADRENALIN) 1 mg/mL (1:1,000) injection; Dose: 0.3 mg IM ONCE and call Rapid Response
 - b. MethylPREDNISolone sodium succinate (SOLU-MEDROL) injection; Dose: 125 mg IV Push ONCE and call Rapid Response
 - i. Epinephrine and Methylprednisolone are to be used if systemic symptoms during graded challenge administration are experienced that are indicative of anaphylaxis, such as full body flushing, hives, severe nausea, vomiting, diarrhea, chest pain, shortness of breath, wheezing, or hypotension.
 - c. DiphenhydrAMINE (BENADRYL) injection; Dose: 50 mg IV Push PRN for 72 hours if used alone for mild symptoms
 - i. Diphenhydramine is to be used if mild symptoms during graded challenge administration are experienced, such as new onset runny nose, itching, congestion, mild nausea/discomfort, shortness of breath or a few scattered hives. These symptoms may signify impending anaphylaxis, especially if the symptoms occur within minutes of drug administration.

3. Step-by-step order process and screen shots

Order and Order Set Search

GRADED CHALLENGE

Browse Preference List Facility List Database

Order Sets & Panels

Name	User Version Name	Type
Antimicrobial / Anti-infective Graded Challenge - NMH		Order Set
ANTIBIOTICS/ANTI-INFEKTIVE IVPB GRADED CHALLENGE PANELS		Order Panel
ANTIBIOTICS/ANTI-INFEKTIVE ORAL GRADED CHALLENGE PANELS		Order Panel

Medications

Name	Dose	Route	Frequency	Code
AMOXICILLIN (AMOXIL) 50 MG IN 1 ML ORAL SUSPENSION (10% TOTAL DOSE PO GRADED CHALLENGE...)				221891
AMOXICILLIN (AMOXIL) 450 MG IN 9 ML ORAL SUSPENSION (90% TOTAL DOSE PO GRADED CHALLENGE...)				221889
AMPICILLIN 10 MG/100 ML NS IVPB (GRADED CHALLENGE)	10 mg	IVPB	ONCE	408520

Order Sets

Orders

Order Sets

Antimicrobial / Anti-infective Graded Challenge - NMH Personalize

Clear All Orders

General

- Vital Signs - During Graded Challenge Process
Routine, Per Policy, starting today at 0829, Until Specified
Check vital signs (blood pressure, heart rate, and respiratory rate) prior to beginning the first graded challenge dose (time 0) and every 60 minutes thereafter until the procedure is complete. At each check, if no symptoms indicative of an allergic reaction are noted, then advance to the next dose.
- Notify Provider - Graded Challenge
Routine, UNTIL DISCONTINUED, starting today at 0829, Until Specified
If patient requires epinephrine or diphenhydramine or methylprednisolone, IMMEDIATELY stop protocol and contact the primary service, and Antimicrobial Stewardship (pager: 55955). Signs and Symptoms of mild or systemic reaction: MILD SYMPTOMS: such as new onset runny nose, itching, congestion, mild nausea/discomfort or a few scattered hives require that the patient be monitored closely. These symptoms may signify impending anaphylaxis. Administer an antihistamine such as diphenhydramine 50 mg intravenously immediately, SYSTEMIC SYMPTOMS: such as full body flushing, hives, severe nausea, vomiting, diarrhea, chest pain, shortness of breath, wheezing, or hypotension accompanied by irritability and confusion are indicative of anaphylaxis. Administer Epinephrine 0.3 mg (1:1000) IM. Diphenhydramine intravenously (50 mg IV for adults) and methylprednisolone intravenously (125 mg IV for adults) may be given with epinephrine if needed. NOTE: diphenhydramine and methylprednisolone should not substitute the use of epinephrine as a first-line agent for SYSTEMIC SYMPTOMS suggestive of anaphylaxis. IF NECESSARY, repeat epinephrine intramuscularly every 5 minutes as necessary up to 3 times total. **If patient requires epinephrine or diphenhydramine or methylprednisolone, immediately stop protocol and contact the primary service and Antimicrobial Stewardship Team (pager: 55955)**

Medications

- IV Fluid
- Treatment Medications
 - Antibiotics/Anti-infective IVPB Graded Challenge Panels
 - Antibiotics/Anti-infective ORAL Graded Challenge Panels
- Treatment of Mild and Systemic Symptoms
 - diphenhydramine (BENADRYL) injection 50 mg
50 mg, IV/Push, PRN, hypersensitivity reaction, starting today at 0828, For 72 hours
Give once as needed for MILD symptoms, such as new onset runny nose, itching, congestion, mild nausea/discomfort or a few scattered hives require that the patient be monitored closely. These symptoms may signify impending anaphylaxis. If this medication is required, IMMEDIATELY stop protocol.
 - EPINEPHRINE (ADRENALIN) injection 0.3 mg
0.3 mg, Intramuscular, PRN, other, anaphylaxis, starting today at 0828, For 72 hours
Give once as needed for SYSTEMIC symptoms such as full body flushing, hives, severe nausea, vomiting, diarrhea, chest pain, shortness of breath, wheezing, or hypotension accompanied by irritability and confusion are indicative of anaphylaxis and require Epinephrine 0.3 mg (1:1000) intramuscularly. If this medication is required, immediately stop protocol
 - EPINEPHRINE
Duration of 3 days exceeds recommended maximum of 1 days
 - methylPREDNISolone sodium succinate (PF) (SOLU-MEDROL) injection 125 mg
125 mg, IV/Push, PRN, anaphylaxis, starting today at 0828, For 72 hours
Give once as needed for SYSTEMIC symptoms such as full body flushing, hives, severe nausea, vomiting, diarrhea, chest pain, shortness of breath, wheezing, or hypotension accompanied by irritability and confusion are indicative of anaphylaxis. If this medication is required, immediately stop protocol.

Notes Patient

Manage Orders

Providers New i-Vent Interactions

Place new orders or orc Telephone with readba

This patient has acti

Orders from Or

Antimicrobial / A NMH

Vital Signs - During Routine, Per Policy, sta Check vital signs (bloo rate) prior to beginnin (time 0) and every 60 r is complete. At each c allergic reaction are nc

Notify Provider - Gc Routine, UNTIL DISCO Specified If patient requires epir methylprednisolone. If contact the primary se Stewardship (pager: 5 systemic reaction: MIL runny nose, itching, co few scattered hives, rec closely. These sympto anaphylaxis. Administ diphenhydramine 50 n SYSTEMIC SYMPTOMS severe nausea, vomitir breath, wheezing, or h and confusion are indi Epinephrine 0.3 mg (1: intravenously (50 mg I intravenously (125 mg epinephrine if needed, methylprednisolone of epinephrine as a first-l suggestive of anaphylt aminadhrine intramus

Pend Ord

Remove All

Antibiotics/Anti-infective IVPB Graded Challenge Panels

Accept

Providers New i-Vent Interactions

Telephone with readback

This patient has active treatment/therapy plans.

New Orders

Antibiotics/Anti-infective IVPB Graded Challenge Panels

cefTRIAxone (ROCEPHIN) 10 mg in sodium chloride 0.9 % 100 mL IVPB (1% Total Dose Graded Challenge)
10 mg, IVPB, Administer over 30 Minutes, ONCE, today at 0845, For 1 dose
Dose #1 of Graded Challenge
Allergy/Contraindication: Cefazolin Reactions: Shortness Of Breath, Rash

cefTRIAxone (ROCEPHIN) 100 mg in sodium chloride 0.9 % 100 mL IVPB (10% Total Dose Graded Challenge)
100 mg, IVPB, Administer over 30 Minutes, ONCE, today at 0945, For 1 dose
Dose #2 of Graded Challenge
Allergy/Contraindication: Cefazolin Reactions: Shortness Of Breath, Rash

cefTRIAxone (ROCEPHIN) 890 mg in sodium chloride 0.9 % 100 mL IVPB (89% Total Dose Graded Challenge)
890 mg, IVPB, Administer over 30 Minutes, ONCE, today at 1045, For 1 dose
Dose #3 of Graded Challenge
Allergy/Contraindication: Cefazolin Reactions: Shortness Of Breath, Rash

ertapenem (INVANZ) graded challenge dosing

meropenem (MERREM) graded challenge dosing

oxacillin graded challenge dosing

penicillin G sodium graded challenge dosing

piperacillin - tazobactam (ZOSYN) graded challenge dosing

Pend Orders Sign & Hold Sign Orders

Remove All Sign & Verify

Antibiotics/Anti-Infective IVPB Graded Challenge Panels

ceftazidime (FORTAZ) graded challenge dosing

cefTRIAxone (ROCEPHIN) graded challenge dosing

cefTRIAxone (ROCEPHIN) 10 mg in sodium chloride 0.9 % 100 mL IVPB (1% Total Dose Graded Challenge) Accept Cancel

Allergy/Contraindication: Cefazolin **Reactions:** Shortness Of Breath, Rash

Dose: mg mg

Administer Dose: 10 mg
Administer Amount: 10 mg

Route:

Frequency:

Starting: 8/2/2019 At: 0845

First Dose: **Today 0845** Number of doses: 1

Scheduled Times: 08/02/19 0845

Administer Over: Minutes

Base: sodium chloride 0.9 % mL

Priority:

Treatment reason:

Treatment indication:

Other comments:

Admin. Inst.:

Prod. Admin. Inst.:

Note to Pharmacy:

Indications:

Self Administered Patient supplied: doses

Notes: Patient Chart, Orders

Manage Orders Order Sets Options

Providers New I-Vent Interactions

Place new orders or order sets

Telephone with readback

This patient has active treatment/therapy plans.

New Orders

Antibiotics/Anti-Infective IVPB Graded Challenge Panels

cefTRIAxone (ROCEPHIN) 10 mg in sodium chloride 0.9 % 100 mL IVPB (1% Total Dose Graded Challenge)
10 mg IVPB, Administer over 30 Minutes, ONCE, today at 0845, For 1 dose
Dose #1 of Graded Challenge
Allergy/Contraindication: Cefazolin
Reactions: Shortness Of Breath, Rash

cefTRIAxone (ROCEPHIN) 100 mg in sodium chloride 0.9 % 100 mL IVPB (10% Total Dose Graded Challenge)
100 mg IVPB, Administer over 30 Minutes, ONCE, today at 0945, For 1 dose
Dose #2 of Graded Challenge
Allergy/Contraindication: Cefazolin
Reactions: Shortness Of Breath, Rash

cefTRIAxone (ROCEPHIN) 890 mg in sodium chloride 0.9 % 100 mL IVPB (89% Total Dose Graded Challenge)
890 mg IVPB, Administer over 30 Minutes, ONCE, today at 1045, For 1 dose
Dose #3 of Graded Challenge
Allergy/Contraindication: Cefazolin
Reactions: Shortness Of Breath, Rash

Antibiotics/Anti-Infective ORAL Graded Challenge Panels

penicillin V potassium (VEETIDS) ORAL graded challenge dosing

amoxicillin (AMOXIL) ORAL graded challenge dosing

amoxicillin (AMOXIL) 50 mg in 1 mL oral suspension (10% Total Dose PO Graded Challenge) Accept Cancel

amoxicillin (AMOXIL) 250 mg/5 mL oral suspension 50 mg Accept Cancel

Allergy/Contraindication: Cefazolin **Reactions:** Shortness Of Breath, Rash

Report:	Creatinine Clearance	Serum creatinine	Time Elapsed	Patient Height
	61.85 mL/min/1.73m2 (A)	0.37 mg/dL (L)	6 hours (08/02/19 0137)	67 in.

Lab Test Results

Component	Time Elapsed	Value	Range	Status
Creatinine	6 hours (08/02/19 0137)	0.37 (L)	0.60 - 1.30 mg/dL	Final result
	1 day (08/01/19 0435)	0.32 (L)	0.60 - 1.30 mg/dL	Final result

Dose: mg mg mg

Administer Dose: 50 mg
Administer Amount: 1 mL

Route:

Frequency:

Starting: 8/2/2019 At: 0900

First Dose: **Today 0900** Number of doses: 1

Scheduled Times: 08/02/19 0900

Priority:

Treatment reason:

Treatment indication:

Other comments:

Admin. Inst.:

Prod. Admin. (none)

Notes: Patient Chart, Orders

Manage Orders Order Sets Options

Providers New I-Vent Interactions

Place new orders or order sets

Telephone with readback

This patient has active treatment/therapy plans.

New Orders

Antibiotics/Anti-Infective ORAL Graded Challenge Panels

amoxicillin (AMOXIL) 50 mg
50 mg Oral, ONCE, today at 0900, For 1 dose
Dose #1 of graded challenge
Allergy/Contraindication: Cefazolin
Reactions: Shortness Of Breath, Rash

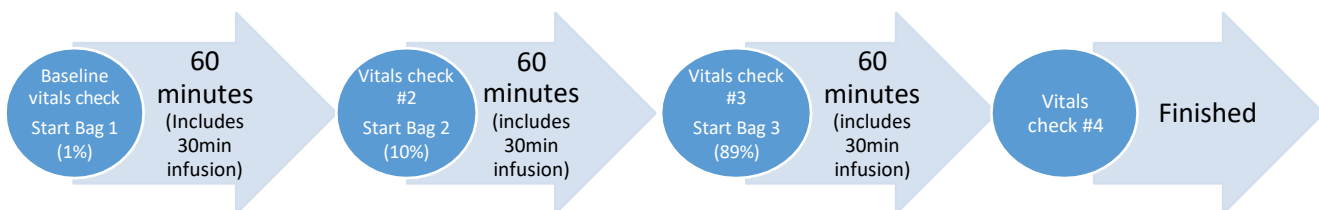
amoxicillin (AMOXIL) 450 mg
450 mg Oral, ONCE, today at 0900, For 1 dose
Dose #2 of graded challenge
Indications: Dose # 2 of graded challenge
Allergy/Contraindication: Cefazolin
Reactions: Shortness Of Breath, Rash

C. Administration

All graded challenge orders must have an antimicrobial stewardship representative present during administration. Graded Challenge hours of operations: M-F 8am to 4pm. Page the ASP pager with each order: 55955

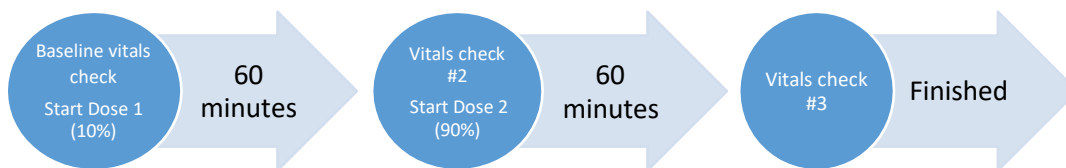
1. IV administration

- a. 4 vitals checks; 60 minute observation periods (includes 30 minute infusion using primary tubing); 180 min total process
- b. Procedure for IV dosing: perform vitals checks and administer doses as shown in the figure below.
 - i. Administer 1% of the dose, then in 30-60 minutes administer 10% of the dose, then in 30-60 minutes administer the remainder of the dose (89%).
- c. Upon completion of the 180min procedure, if no signs of an allergic reaction are observed and vitals are normal, then the graded challenge is complete and the patient can safely receive the full dose of the drug at regularly scheduled intervals as ordered per the team.
- d. Document (in)tolerance in patient allergy history profile



2. PO administration

- a. 3 vitals checks; 60 minute observation periods; 120 min total process
- b. Procedure for PO dosing: perform vitals checks and administer doses as shown in the figure below.
 - i. Administer 10% of the dose, and then in 60 minutes give the remainder of the dose (90%).
- c. Upon completion of the 120 minute procedure, if no signs of an allergic reaction are observed and vitals are normal, then the graded challenge is complete and the patient can safely receive the full dose of the drug at regularly scheduled intervals as ordered per the team.
- d. Document (in)tolerance in patient allergy history profile



3. Monitoring

Runny nose	Full body flushing
Itching	Chest Pain
Congestion	Shortness of breath/ Wheezing
Mild nausea/discomfort	Hypotension
Hives	Confusion

ORAL GRADED CHALLENGES

Refer to the [Graded Challenge Pharmacy Dosing Recipes](#) for preparation details

Antimicrobials Oral suspension/solution	STOCK SOLUTION	Stock Concentration (mg/mL)	10% total dose Syringe 1	90% total dose Syringe 2
Penicillin VK	500 mg (10 mL)	50	50 mg/1mL	450 mg/9mL
Amoxicillin	500 mg (10 mL)	50	50 mg/1mL	450 mg/9mL
Amoxicillin-clavulanate	875 mg (17.5 mL)	50	87.5 mg/1.75mL	787.5 mg/15.75mL
Cephalexin (1 st gen) (Keflex)	500 mg (10 mL)	50	50 mg/1mL	450 mg/9mL
Cefuroxime (2 nd gen) (Ceftin)	500 mg (10 mL)	50	50 mg/1mL	450 mg/9mL
Cefixime (3 rd gen) (Suprax)	400 mg (20 mL)	20	40 mg/2mL	360 mg/18mL

IV GRADED CHALLENGES

Refer to the [Graded Challenge Pharmacy Dosing Recipes](#) for preparation details

IV Antimicrobials	STOCK BAG (empty viaflex, TV bag)		Diluent	Final Conc. Stock Bag	1% total dose Bag 1	10% total dose Bag 2	89% total dose Bag 3
Ampicillin	1000 mg	TV 100 mL	NS	10 mg/mL	10 mg/100mL	100 mg/100mL	890 mg/100mL
Amp-sulbactam	1500 mg	TV 100 mL	NS	15 mg/mL	15 mg/100mL	150 mg/100mL	1335 mg/100mL
Cefazolin	1000 mg	TV 100 mL	NS	10 mg/mL	10 mg/100mL	100 mg/100mL	890 mg/100mL
Cefepime	1000 mg	TV 100 mL	NS	10 mg/mL	10 mg/100mL	100 mg/100mL	890 mg/100mL
Ceftazidime	1000 mg	TV 100 mL	NS	10 mg/mL	10 mg/100mL	100 mg/100mL	890 mg/100mL
Ceftriaxone	1000 mg	TV 100 mL	NS	10 mg/mL	10 mg/100mL	100 mg/100mL	890 mg/100mL
Ertapenem	1000 mg	TV 100 mL	NS	10 mg/mL	10 mg/100mL	100 mg/100mL	890 mg/100mL
Meropenem	1000 mg	TV 100 mL	NS	10 mg/mL	10 mg/100mL	100 mg/100mL	890 mg/100mL
Oxacillin	1 gram	TV 100 mL	NS	0.01 g/mL	0.01 g/100mL	0.1 g/100mL	0.89 g/100mL
PCN G -K	1 Million Units (Mu)	TV 100 mL	NS	0.01 Mu/mL	0.01 Mu/100mL	0.1 Mu/100mL	0.89 Mu/100mL
Pip-tazobactam	3.375 gram	TV 100 mL	NS	0.0338 g/mL	0.0338 g/100mL	0.3375 g/100mL	3.003 g/100mL

TV = Total Volume; NS = Normal Saline (0.9% Sodium Chloride)