

### Inclusion Criteria

- Signs and symptoms of anaphylaxis\* and /or received epinephrine prior to arrival for presumed anaphylaxis

### Exclusion Criteria

- Symptoms clearly attributed to other cause

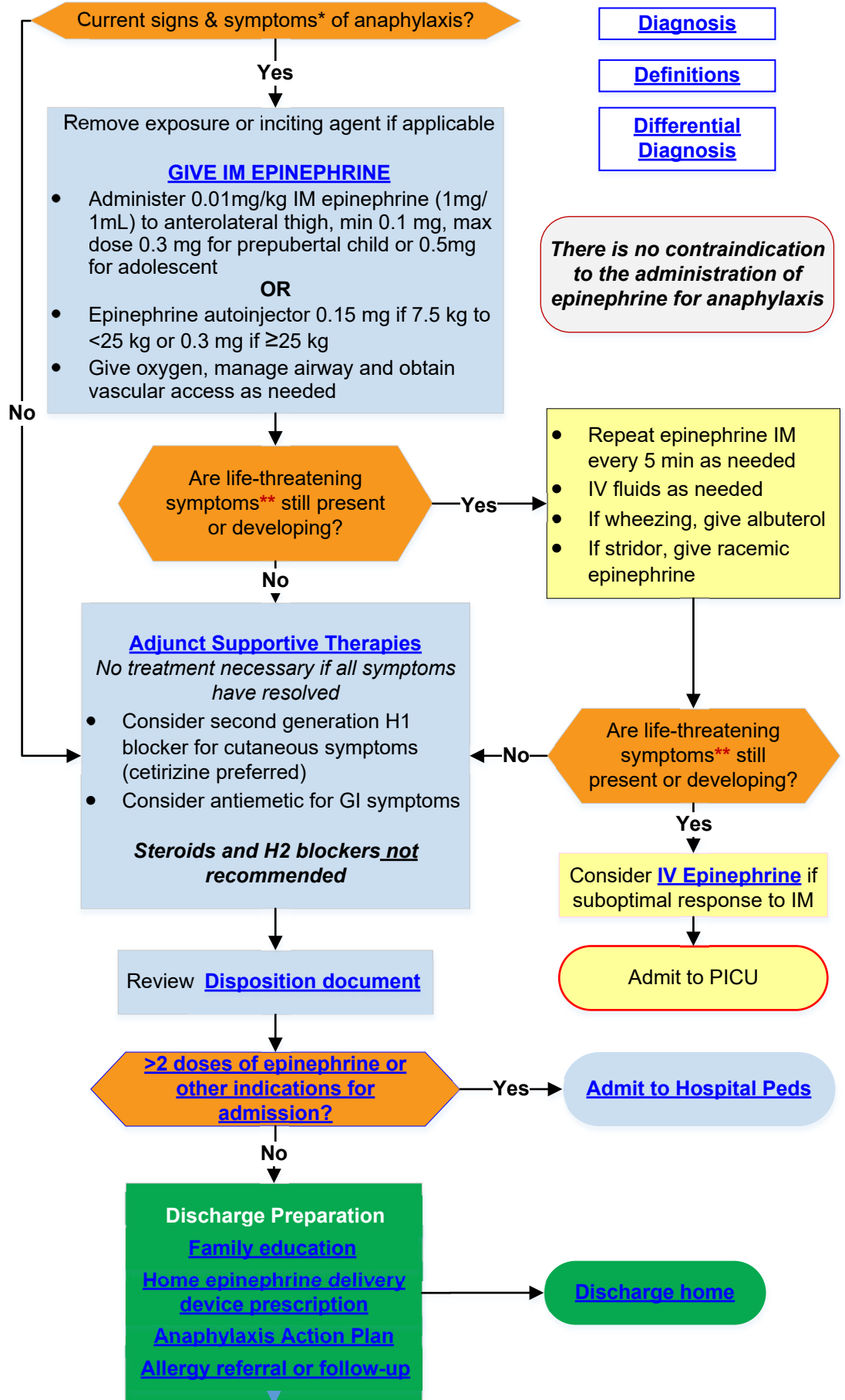
### \*Anaphylaxis Signs & Symptoms

1. **Acute onset** of symptoms with involvement of skin and/or mucosa AND either respiratory compromise or decreased blood pressure/end organ dysfunction  
**OR**
2. **Two or more** of the following that **occur rapidly** after exposure to a **likely** allergen
  - **Skin/mucosa involvement** (pruritus, flushing, hives, angioedema)
  - **Respiratory compromise** (dyspnea, wheeze, hoarseness, stridor, tachypnea, cyanosis)
  - **Decreased BP** or associated symptoms
  - **Persistent GI symptoms** (vomiting, diarrhea, abdominal pain)**OR**
3. Decreased blood pressure for age after exposure to a **known** allergen for that patient

**\*\*Life-threatening symptoms can include: respiratory distress, stridor, hypotension, altered mental status**

### Disposition

- Most patients will be eligible for early discharge from the ED (1 hour post epinephrine)
- [Disposition](#)



[Diagnosis](#)

[Definitions](#)

[Differential Diagnosis](#)

**There is no contraindication to the administration of epinephrine for anaphylaxis**

- Repeat epinephrine IM every 5 min as needed
- IV fluids as needed
- If wheezing, give albuterol
- If stridor, give racemic epinephrine

Are life-threatening symptoms\*\* still present or developing?

Consider **IV Epinephrine** if suboptimal response to IM

Admit to PICU

Admit to Hospital Peds

Discharge home

# Anaphylaxis

## Urgent Care

[Diagnosis](#)

[Definitions](#)

[Differential Diagnosis](#)

### Inclusion Criteria

- Signs and symptoms of anaphylaxis\* and /or received epinephrine prior to arrival for presumed anaphylaxis

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### \*Anaphylaxis Signs & Symptoms

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OR

2. **Two or more** of the following that **occur rapidly** after exposure to a **likely** allergen

- **Skin/mucosa involvement** (pruritus, flushing, hives, angioedema)
- **Respiratory compromise** (dyspnea, wheeze, hoarseness, stridor, tachypnea, cyanosis)
- **Decreased BP** or associated symptoms
- **Persistent GI symptoms** (vomiting, diarrhea, abdominal pain)

OR

3. Decreased blood pressure for age after exposure to a **known** allergen for that patient

**\*\*Life-threatening symptoms can include: respiratory distress, stridor, hypotension, altered mental status**

### Disposition

- Most patients will be eligible for early discharge from the UC (1 hour post epinephrine)
- [Disposition](#)

Current signs & symptoms\* of anaphylaxis?

Yes

Remove exposure or inciting agent if applicable

### GIVE IM EPINEPHRINE

- Administer 0.01mg/kg IM epinephrine (1mg/1mL) to anterolateral thigh, min 0.1 mg, max dose 0.3 mg for prepubertal child or 0.5mg for adolescent
- Give oxygen, manage airway and obtain vascular access as needed

**There is no contraindication to the administration of epinephrine for anaphylaxis**

No

Are life-threatening symptoms\*\* still present or developing?

Yes

- Initiate EMS transfer to MCED
- Repeat epinephrine IM every 5 min as needed
- If wheezing, give albuterol
- If stridor, give racemic epinephrine
- Consider IV access and fluids as needed

No

### Adjunct Supportive Therapies

No treatment necessary if all symptoms have resolved

- Consider second generation H1 blocker for cutaneous symptoms (cetirizine preferred)
- Consider antiemetic for GI symptoms

**Steroids and H2 blockers not recommended**

### † Indications for Transfer

- Required other supportive therapy (albuterol, rac epi, etc)
- Nonverbal, difficult airway, current asthma exacerbation, other comorbidities
- Social concerns (family comfort, access to care, etc)
- Required more than one dose of IM epinephrine

Review [Disposition document](#)

- Monitor for one hour if patient meets early discharge criteria

>2 doses of epinephrine or other indications for admission?

Yes

[Transfer to MCED](#)†

No

### Discharge Preparation

[Family education](#)  
[Home epinephrine delivery device prescription](#)  
[Anaphylaxis Action Plan](#)  
[Allergy referral or follow-up](#)

[Discharge home](#)

# Disposition

## Early Discharge Criteria for ED/UC (1 hour post epinephrine)

- Significant symptoms have resolved after one dose of epinephrine and patient feels well
- Home epinephrine device available on hand or at home
- If prior history of anaphylaxis, no biphasic reaction
- No other **Red Flags** or social concerns

## Prolonged Observation in ED or as inpatient (4-6 hours post last dose of epinephrine)

\*If ANY of the following are present

- Received 2 doses of epinephrine
- Required supportive therapy with IV fluids, racemic epinephrine or albuterol
- Presence of other **Red Flags**, clinical, or social concerns

## Red Flags for Prolonged Observation ED or inpatient

- Non-verbal (does not include pre-verbal patients), difficult airway, or other significant comorbidities
- Current asthma exacerbation
- Any signs of **Airway swelling** with current episode
- Patient lives greater distance away

## Admission Criteria/Considerations

- Severe or protracted anaphylaxis (**Definitions**)
- Patient received more than 2 doses of epinephrine
- Patient specific medical or social concerns (ex. family discomfort, lack of access to epinephrine autoinjector, unable to establish safe plan for discharge)

[ED Algorithm](#)

[UC Algorithm](#)

[Inpatient  
Algorithm](#)

# Signs/Symptoms of Airway Swelling

**Includes:**

- Stridor
- Voice changes
- Difficulty managing secretions
- Any other clear indications of respiratory distress such as tripodding or hypoxia

**Does not include:**

- Cough
- Lip swelling
- Scratchy throat

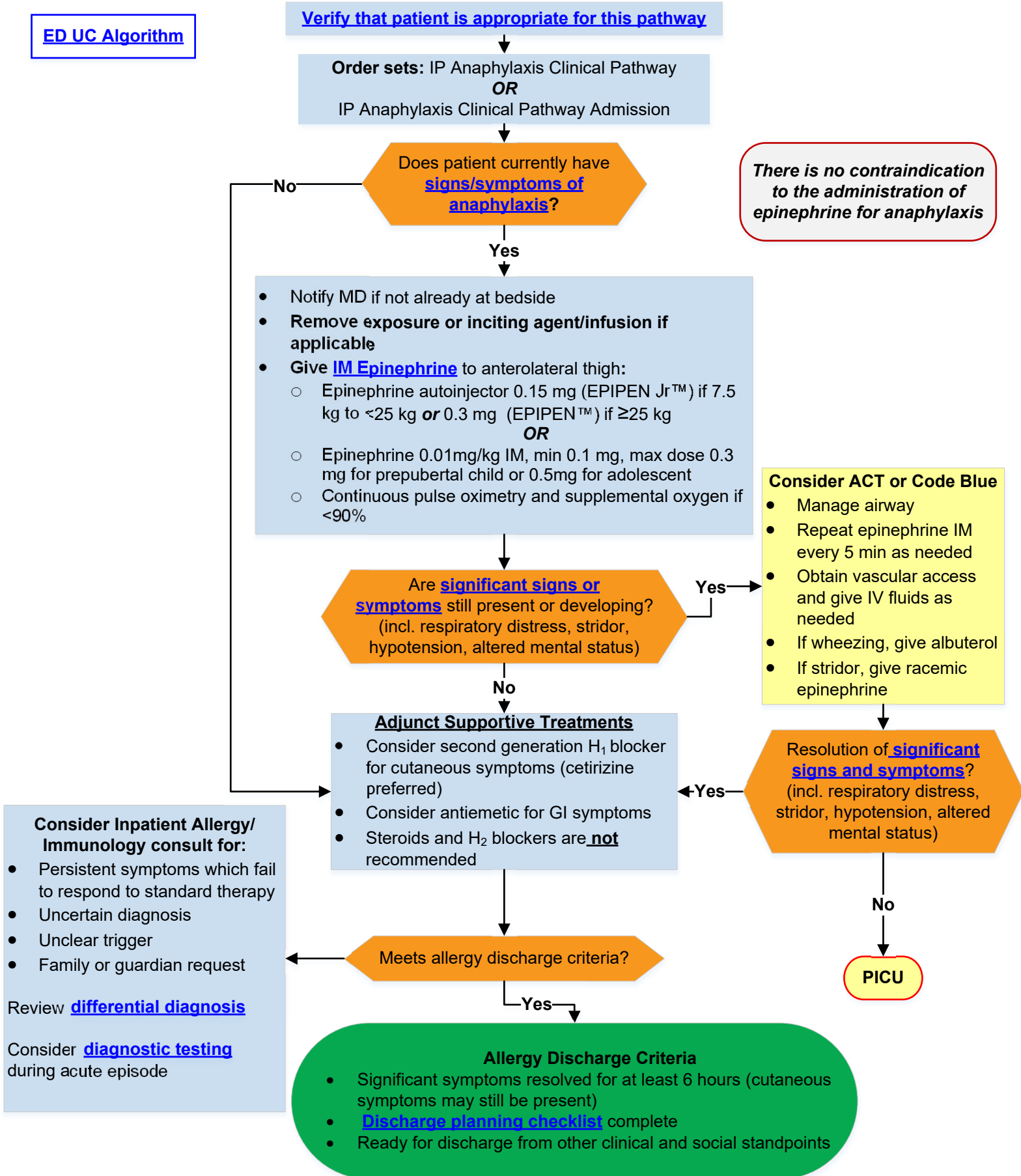
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[UC Algorithm](#)

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# Anaphylaxis Inpatient

**ED UC Algorithm**



*There is no contraindication to the administration of epinephrine for anaphylaxis*

**Consider ACT or Code Blue**

- Manage airway
- Repeat epinephrine IM every 5 min as needed
- Obtain vascular access and give IV fluids as needed
- If wheezing, give albuterol
- If stridor, give racemic epinephrine

**Consider Inpatient Allergy/ Immunology consult for:**

- Persistent symptoms which fail to respond to standard therapy
- Uncertain diagnosis
- Unclear trigger
- Family or guardian request

Review [differential diagnosis](#)

Consider [diagnostic testing](#) during acute episode

**Allergy Discharge Criteria**

- Significant symptoms resolved for at least 6 hours (cutaneous symptoms may still be present)
- [Discharge planning checklist](#) complete
- Ready for discharge from other clinical and social standpoints

# Pre-Pathway Validation

## Is this Anaphylaxis?

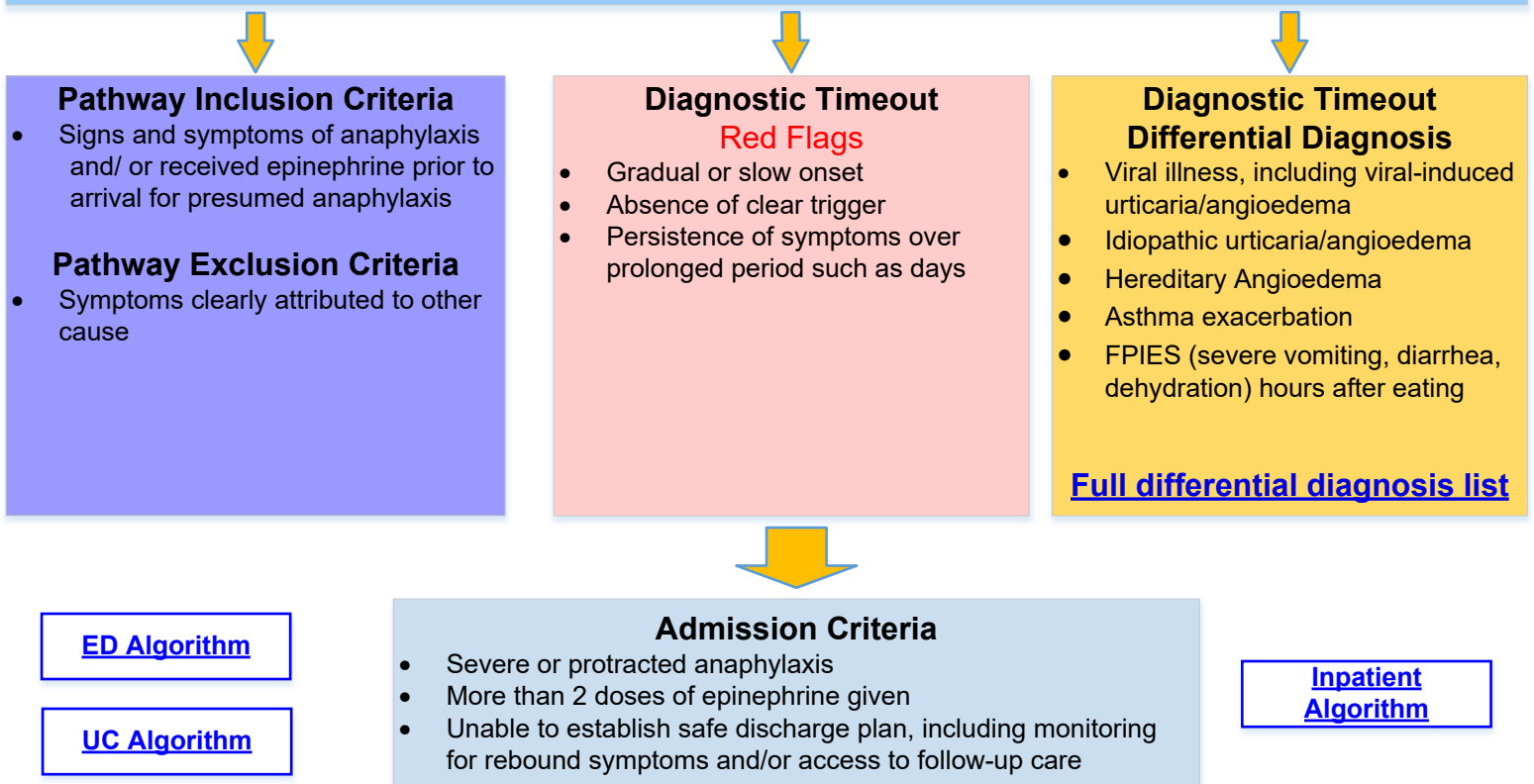
Anaphylaxis is an acute, potentially life-threatening and rapidly progressive systemic allergic reaction for which epinephrine is the only first-line treatment. It is a clinical diagnosis that should not rely upon diagnostic testing. Anaphylaxis can range widely in severity and may be resolving with or without epinephrine by the time clinical evaluation occurs.

### Presentation:

- **Rapid onset of:**
  - **Severe symptoms**, including one or more of the following:
    - **Lungs/Breathing:** shortness of breath, wheeze, repetitive cough, hoarseness, stridor, dyspnea, tachypnea
    - **Mouth/Throat:** tongue swelling, throat tightness, closing or fullness, dysphagia
    - **Heart/Circulation:** pale, blue/cyanosis, faint, weak pulse, tachycardia, hypotension
    - **GI:** repetitive or severe vomiting
    - **Skin:** severe swelling or extensive hives, generalized pruritus, flushing
    - **CNS:** lightheaded, confusion, feeling of “doom”, syncope
  - **Or combination of symptoms** from two body areas:
    - **Skin:** hives, angioedema (e.g., eyes, lips)
    - **GI:** mild nausea/discomfort
- Exposure to known allergen
- Cutaneous manifestations including urticaria and angioedema are the most common, but may be absent in about 20% of cases

### NIAID Diagnostic Criteria for anaphylaxis

Definitions of uniphasic, biphasic, protracted and refractory anaphylaxis



#### Pathway Inclusion Criteria

- Signs and symptoms of anaphylaxis and/ or received epinephrine prior to arrival for presumed anaphylaxis

#### Pathway Exclusion Criteria

- Symptoms clearly attributed to other cause

#### Diagnostic Timeout

##### Red Flags

- Gradual or slow onset
- Absence of clear trigger
- Persistence of symptoms over prolonged period such as days

#### Diagnostic Timeout Differential Diagnosis

- Viral illness, including viral-induced urticaria/angioedema
- Idiopathic urticaria/angioedema
- Hereditary Angioedema
- Asthma exacerbation
- FPIES (severe vomiting, diarrhea, dehydration) hours after eating

[Full differential diagnosis list](#)

[ED Algorithm](#)

[UC Algorithm](#)

#### Admission Criteria

- Severe or protracted anaphylaxis
- More than 2 doses of epinephrine given
- Unable to establish safe discharge plan, including monitoring for rebound symptoms and/or access to follow-up care

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Algorithm](#)

# Diagnosis

Anaphylaxis is a rapidly progressive systemic allergic reaction. It is a clinical diagnosis that should not rely upon diagnostic testing. This clinical pathway provides treatment recommendations for anaphylaxis from any cause, including indications for escalation of therapy when necessary. Anaphylaxis can range widely in severity and may be resolving with or without epinephrine by the time clinical evaluation occurs. As such, global assessment of severity, current clinical status, and treatment administered should be considered for subsequent monitoring duration and interventions once the patient is stable.

## Typical presentation:

- Rapid onset
- Exposure to **known** allergen
- Cutaneous manifestations including urticaria and angioedema are the most common, but may be absent in about 20% of cases

## Diagnostic Criteria for anaphylaxis

- In 2006 the NIAID and Food Allergy and Anaphylaxis Network established criteria to serve as a framework to facilitate the diagnosis of anaphylaxis. This is the mostly commonly used criteria.
- Anaphylaxis is likely when 1 of 3 criteria is fulfilled:
  1. **Acute onset** of an illness (minutes to hours) with involvement of the skin, mucosal tissue or both with either respiratory involvement or reduced blood pressure and/or associated symptoms of end-organ involvement
  2. **Two or more** of the following that **occur rapidly** after exposure to a likely allergen for the patient:
    - **Skin/mucosal involvement**
    - **Respiratory compromise**
    - **Decreased blood pressure** or associated symptoms
    - **Persistent GI symptoms**
  3. Reduced blood pressure as result of exposure to a **known** allergen trigger

**NOTE: Criteria should not replace clinical judgment and epinephrine administration is not limited to those meeting the criteria**

## Consider other alternate clinical problem and diagnosis when:

- None of the diagnostic criteria are met
- Slow or gradual onset of symptoms
- Persistence of symptoms over prolonged period (ex. days)
- Absence of clear trigger

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[Pre-Pathway  
Validation](#)

# Definitions

## **Anaphylaxis**

- Serious allergic reaction that is usually rapid in onset and may cause death

## **Uniphasic Anaphylaxis**

- Most common type
- Peaks within hours after symptom onset and then resolves within several hours

## **Biphasic Anaphylaxis (5%)**

- Recurrence of anaphylaxis that develops within 1 to 72 hours following the apparent resolution of the initial anaphylactic episode with no additional exposure to the causative agent
- Typically occurs within 12 hours
- Risk factors include:
  - More severe initial presentation (hypotension)
  - >1 dose epinephrine required for resolution of initial episode
  - Unknown trigger
  - History of biphasic reaction
  - Reaction to drug

## **Protracted Anaphylaxis**

- Persistent reactions lasting hours or days without resolving completely (persist at least 4 hours)
- Very uncommon

## **Refractory anaphylaxis**

- Continued symptoms of anaphylaxis despite appropriate epinephrine dosing and symptom-directed treatment
- > 3 doses of epinephrine or initiation of epinephrine infusion suggested by expert panel

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Algorithm](#)

[Disposition](#)

[Pre-Pathway  
Validation](#)

# Differential Diagnosis

## Consider other alternate clinical problem and diagnosis when:

- None of the diagnostic criteria are met
- Slow or gradual onset of symptoms
- Persistence of symptoms over prolonged period (ex. days)
- Absence of clear trigger

## Differential Diagnosis:

- Skin or mucosal
  - Idiopathic or physical urticaria and angioedema
  - Pollen Food Allergy Syndrome (just oral symptoms)
  - Hereditary Angioedema (hives typically absent)
- Endocrine
  - Hypoglycemia
  - Thyrotoxic crisis
  - Carcinoid syndrome
  - Vasointestinal peptide tumors
  - Pheochromocytoma
- Pulmonary
  - Asthma exacerbation
  - Acute laryngotracheitis
  - Obstruction (ex. foreign body, vocal cord dysfunction)
- Neuro/Psych
  - Hyperventilation syndrome
  - Anxiety and panic disorder
  - Somatoform disorder
  - Dissociative disorder and conversion
  - Epilepsy
  - Cerebrovascular event
  - Psychosis
  - Factitious disorder
- Cardiovascular
  - Vasovagal syncope
  - Pulmonary embolism
  - Myocardial infarction
  - Cardiac arrhythmias
  - Cardiogenic shock
- Other
  - Drugs: ethanol, opiates
  - Histamine (scombroid fish poisoning)
  - Food Protein Induced Enterocolitis (FPIES; delayed onset severe vomiting, typically 2-3 hours after eating. Patient may also have diarrhea and dehydration)

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# First Line Therapy

FIRST LINE THERAPIES			
Medication	Dose	Route	Frequency
<b>Epinephrine IM</b>	0.01 mg/kg using 1mg/1mL to anterolateral thigh, min 0.1 mg, max dose 0.3 mg for prepubertal child or 0.5mg for adolescent  OR  Epinephrine autoinjector 0.15 mg if 7.5 kg to <25 kg or 0.3 mg if $\geq$ 25 kg	IM	Every 5-15 minutes as needed
<b>Epinephrine IV</b>	0.1 mcg/kg/minute (0.05-0.2 mcg/kg/min); titrate to response	IV	Continuous

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# Adjunct Therapies

ADJUNCT THERAPIES			
Medication	Dose	Route	Frequency
<b>Albuterol</b>	1.25 mg or 2.5 mg	inhalation	PRN wheezing, per provider
<b>Racemic Epinephrine</b> (Racpinephrine) 2.25% solution	0.5 mL diluted in 2 to 3 mL normal saline	inhalation	PRN stridor, per provider
<b>IV Fluids</b> (LR or NS)	20 ml/kg bolus Max: 1000ml	IV	Once
<b>Ondansetron</b> (Zofran™)	8-15 kg: 2 mg >15-30 kg: 4 mg >30 kg: 8 mg	PO	Once
<b>Ondansetron</b> (Zofran™)	0.15mg/kg with max of 8mg	IV	Once
<b>Cetirizine</b> *preferred over first generation antihistamine	< 6mo: 1.25 mg 6-24 mo: 2.5 mg 2-5 yrs: 5 mg >5 yrs: 10 mg	PO	Once daily, can increase to twice daily
<b>Diphenhydramine</b> (if unable to take PO or second-generation antihistamine not available)	1 mg/kg/dose, max dose 50 mg	IV/PO	Every 6 hours
H <sub>2</sub> blockers	Not recommended; not supported by evidence		
Systemic corticosteroids	Not recommended for acute management; consider in cases of concurrent asthma exacerbation; previous belief that steroids decrease biphasic or prolonged reactions is not supported by evidence		
<b>Glucagon</b>	Consider if no response to IM epinephrine and patient on beta-blocker		

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# Diagnostic Testing

- There are no laboratory tests available in an emergency department or clinic setting to confirm a diagnosis of anaphylaxis in real time
- However, laboratory tests (ex. serum tryptase level) obtained during or shortly after symptom onset can help to support the clinical diagnosis of anaphylaxis, particularly when the diagnosis is uncertain

## **Total Serum Tryptase**

- Tryptase is a mediator released by mast cells and basophils during anaphylaxis
- Tryptase level should ideally be drawn 30-120 minutes after onset of symptoms (but may remain elevated for several hours)
- Elevated levels of total tryptase in serum may be useful for distinguishing anaphylaxis from other conditions in the differential diagnosis
- The PPV of an elevated tryptase is higher than the NPV value of a normal tryptase
- Total tryptase levels are less often elevated in food-induced anaphylaxis

## **Summary**

- **Tryptase** should **not** be used to diagnose anaphylaxis in real time but can be supportive after the event
- **Tryptase** may **not** be used to guide acute management of anaphylaxis
- Consider obtaining a tryptase level when anaphylaxis is on the differential. Elevations can support the diagnosis of anaphylaxis, but normal levels do not necessary exclude it, especially if related to food or if drawn after 3 hours

## **Additional testing**

- Follow-up allergy evaluation (ex. skin testing or serum specific IgE level) is important for confirmation or identification of allergens. Allergy follow-up recommended.

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# Patient & Caregiver Education

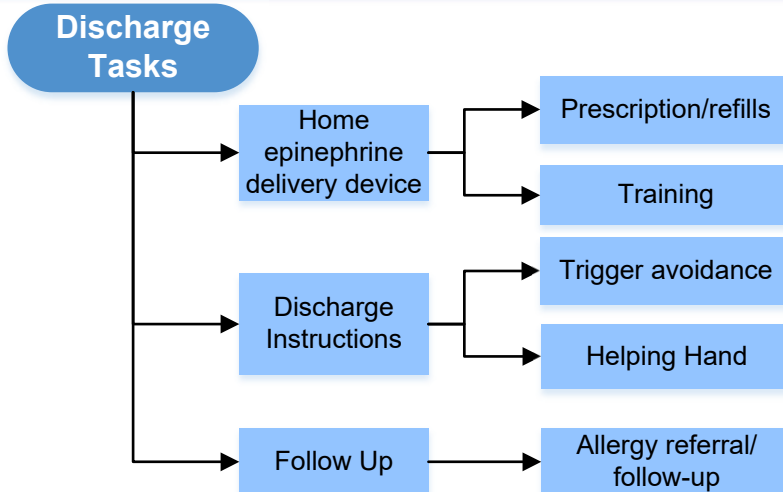
- Caregivers and patient to participate in demonstration with autoinjector trainers, if indicated
- Provide caregiver or patient education documents:
  - Helping Hands on home epinephrine delivery device
  - Emergency Action Plan (EAP)
- Physician or other provider reviews trigger avoidance with caregivers and patient
- Review signs and symptoms concerning for biphasic anaphylaxis if discharging from ED/Urgent care

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# Discharge Planning



## Prescriptions: Home epinephrine delivery device:

### **Epinephrine autoinjector (prescribe 2 two-packs)**

7.5 kg to <25 kg Epinephrine auto injector **0.15 mg/0.3ml** Use PRN severe reaction. Inject IM into anterolateral thigh.

≥25 kg Epinephrine auto injector **0.30 mg/0.3 ml** Use PRN severe reaction. Inject IM into anterolateral thigh.

\*some patients with known allergy may have existing prescription for Auvi-Q device, with additional dosing option of 0.1mg

**OR** (if available)

### **Intranasal epinephrine spray (Neffy)**

Children ≥4 years and Adolescents:

≥15 kg to <30 kg: **1 mg/0.1 mL** spray: Intranasal: 1 spray (1 mg) in one nostril once; if symptoms persist or worsen after first dose, may repeat dose in 5 minutes in the same nostril.

≥30 kg: **2 mg/0.1 mL** spray: Intranasal: 1 spray (2 mg) in one nostril once; if symptoms persist or worsen after first dose, may repeat dose in 5 minutes in the same nostril.

## Prescriptions: Cetirizine

Once daily as needed for itching or few hives (not to replace use of epinephrine for severe or rapidly spreading hives concerning for anaphylaxis)

< 6 mo	Cetirizine 1.25 mg
6-24mo	Cetirizine 2.5 mg
2-5 years	Cetirizine 5 mg
> 5 years	Cetirizine 10 mg

## Prescriptions: Albuterol

If confirmed or suspected asthma, also give albuterol MDI, 2-4 puffs Q4H PRN with spacer

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# Anaphylaxis Action Plan

## Allergy/Anaphylaxis EMERGENCY ACTION PLAN (EAP)

Any **SEVERE SYMPTOMS** after suspected or known exposure such as :

**One or more** of the following:

**LUNG:** short of breath, wheeze, repetitive cough

**THROAT:** tightness, closing or fullness, trouble breathing or swallowing

**HEART:** pale, blue, faint, weak pulse, lightheaded, feeling of “doom”, passing out

**MOUTH:** tongue swelling

**GUT:** repetitive or severe vomiting

**SKIN:** severe swelling or many hives over body

**1. INJECT EPINEPHRINE IMMEDIATELY**

2. Call 911

3. Begin monitoring (see box below)

4. Give additional medications:  
Antihistamine for itching/hives  
Albuterol for asthma symptoms

5. Stay with child

**Or combination** of mild symptoms from two body areas:

**SKIN:** hives, swelling (e.g., eyes, lips)

**GUT:** mild nausea/discomfort

**MILD SYMPTOMS ONLY** such as:

**MOUTH:** itchy mouth

**SKIN:** few hives around mouth/face, mild itch

**GUT:** mild nausea/discomfort

1. GIVE ANTIHISTAMINE

2. Stay with person; alert healthcare professions and parent

3. If symptoms progress (see above): USE EPINEPHRINE

4. Begin monitoring (see box below)

Monitoring:

- Stay with person; alert parent. Tell rescue squad that epinephrine was given
- Have person lay on back if possible (or side if vomiting) - **DO NOT HAVE THEM STAND UP**
- Note time epinephrine given; give second dose in 5-10 minutes if symptoms return or don't improve

[Epinephrine Auto Injector Helping Hand](#)

[ED Algorithm](#)

[UC Algorithm](#)

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# Helping Hands

## Epinephrine Auto-Injectors for Severe Allergic Reaction (Adrenaclick® , Auvi-Q® , EpiPen® , Symjepi®)

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# Quality Metrics

## Outcome Measures

### Emergency Department:

1. ED length of stay
2. Time from arrival to IM epinephrine administration
3. Rate of patients who received IM epinephrine first when other anaphylaxis medications (diphenhydramine, cetirizine, loratadine, steroids) were also administered.
4. Rate of enteral diphenhydramine use
5. Admission rate

### Urgent Care:

1. UC length of stay
2. Time from arrival to IM epinephrine administration
3. Rate of patients who received IM epinephrine first when other anaphylaxis medications (diphenhydramine, cetirizine, loratadine, steroids) were also administered.
4. Rate of enteral diphenhydramine use
5. Transfer rate

### Inpatient:

1. Utilization rate of IM epinephrine for anaphylaxis
2. Rate of patients who received IM epinephrine first when other anaphylaxis medications (diphenhydramine, cetirizine, loratadine, steroids) were also administered within an hour before or after epinephrine.
3. IP length of stay

## Process Measures

1. ED/UC Order Set & Smart Set utilization
2. IP Order Set utilization

## Balance Measures

1. 24hr ED/UC return rate

[ED Algorithm](#)

[UC Algorithm](#)

[Inpatient  
Algorithm](#)

# References

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[ED Algorithm](#)

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Algorithm](#)

# Pathway Team & Process

## Pathway Development Team

### Leader(s):

Allergy/Immunology:  
Kasey Strothman, MD

### Members:

Allergy/Immunology:  
Margaret Redmond, MD  
Rebecca Scherzer, MD  
Kristina Roth, MD

### Urgent Care:

Luciana Berg, MD  
Jerry Stultz, MD

### Emergency Medicine:

Daniel Scherzer, MD  
Betsy Schmerler, MD

### Hospital Pediatrics:

Sofia Davila, MD

### PICU:

Jennifer Macdonald, MD, PhD

## Clinical Pathways Program:

Medical Director – Emergency Medicine:

Aarti Gaglani, MD

Medical Director – Hospital Pediatrics:

Gerd McGwire, MD, PhD

Medical Director – Clinical Informatics & Emergency Medicine:

Laura Rust, MD, MPH

Business & Development Manager:

Rekha Voruganti, MBOE, LSSBB

Program Coordinators:

Tahje Brown, MBA

Tara Dinh, BS

Clinical Pathway Approved

Medical Director – Associate Chief Quality Officer,  
Center for Clinical Excellence:

Ryan Bode, MD, MBOE

Advisory Committee Date: *November, 2022*

Origination Date: *November, 2022*

Last Revision Date: *January, 2026*

Next Revision Date: *January, 2031*

## Clinical Pathway Development

This clinical pathway was developed using the process described in the NCH Clinical Pathway Development Manual Version 6, 2022. Clinical Pathways at Nationwide Children's Hospital (NCH) are standards which provide general guidance to clinicians. Patient choice, clinician judgment, and other relevant factors in diagnosing and treating patients remain central to the selection of diagnostic tests and therapy. The ordering provider assumes all risks associated with care decisions. NCH assumes no responsibility for any adverse consequences, errors, or omissions that may arise from the use or reliance on these guidelines. NCH's clinical pathways are reviewed periodically for consistency with new evidence; however, new developments may not be represented, and NCH makes no guarantees, representations, or warranties with respect to the information provided in this clinical pathway.

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**For more information about our pathways and program please contact:  
[ClinicalPathways@NationwideChildrens.org](mailto:ClinicalPathways@NationwideChildrens.org)**

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