

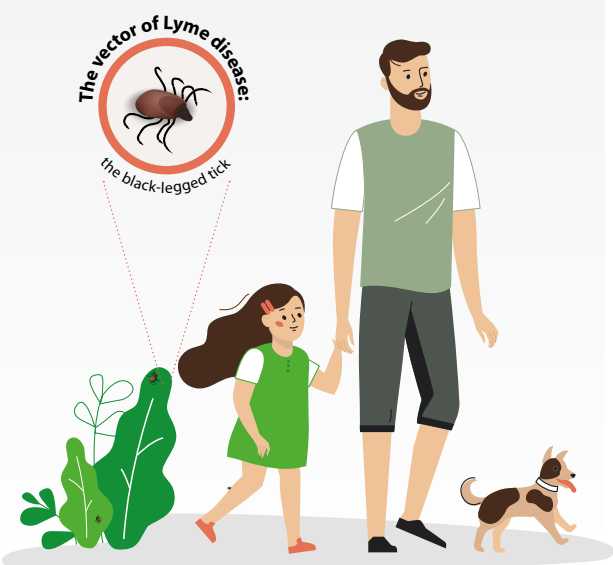


This optimal use guide is intended mainly for primary care clinicians. It is provided for information purposes only and should not replace the judgement of the clinician who performs reserved activities by an act or a regulation. The recommendations were developed using a systematic process and are supported by the scientific literature and the knowledge and experience of Québec clinicians, experts and patients. For further details, go to the section "INESSS's Guides" on its website (inesss.qc.ca).

GENERAL INFORMATION

WHAT IS LYME DISEASE?

- Lyme disease is an infectious disease caused by bacterial genospecies of *Borrelia burgdorferi*, which are transmitted to humans by black-legged ticks that are carriers.
- It is a notifiable disease (MADO) and is on the increase in Québec.
- It can affect several anatomical systems at the same time.



WHAT ARE THE DIFFERENT STAGES OF THE DISEASE ?

Localized stage (sometimes called the early stage): **Beginning of the infection before dissemination of the bacteria in the bloodstream.**

- Main manifestation observed:



- Not always present or noticed.
- If present, usually appears 3 to 30 days after infection but can appear up to 3 months post-bite.

Isolated cutaneous manifestation
(isolated erythema migrans)

Early disseminated stage

Bacterial dissemination via the bloodstream

- Generally occurs when the local infection has not been detected or has not been treated effectively.
- Occurs a few days after isolated erythema migrans and to a few weeks after infection (usually up to 6 months post-bite).
- Can include general systemic symptoms.
- Main manifestations observed:



Cutaneous
(multiple erythema migrans)



Neurological
(neuroborreliosis)



Cardiac
(Lyme carditis)

Late disseminated stage

Complication of the early disseminated stage.

- Occurs a few weeks or even a few months after infection (usually up to a year post-bite).
- Main manifestation observed in North America:



Articular
(Lyme arthritis)

RISK FACTORS

- ▶ The risk of tick exposure:
 - Depends on lifestyle, outdoor activities (recreation or work), places visited or place of residence, and being around pets that have been outdoors;
 - Is present throughout the year but is negligible in the winter in Québec, except for people who travel to areas where the climate is favourable for ticks ([Québec](#), [other Canadian provinces](#), the [United States](#), [Europe](#)).


! Since the bite is painless and the tick is small, the patient will often not have any recollection of having been bitten.

! Non-tick transmission of the bacterium is poorly documented in the scientific literature and probably rare.

PRESENTATION

- ▶ The diagnostic process should include:
 - A tick exposure risk assessment;
 - A thorough physical examination that includes a neurological examination and a search for erythema migrans and manifestations of the disseminated stage;
 - Considering other possible clinical conditions (consult the [nonexhaustive list of differential diagnoses](#)).
- ▶ The clinical manifestations of Lyme disease are not mutually exclusive. The presentation, the severity of the manifestations, their duration and the speed of progression of the disease from one stage to the next vary from patient to patient.
- ▶ Refer to the [Lyme disease diagnostic support tool](#) to view the recommended algorithm and for information on when serological tests are indicated and how to interpret them.

MAIN MANIFESTATIONS OF LYME DISEASE (other systems may be affected)¹

	Symptoms ²	Signs and presentation
Cutaneous manifestations 	Little or no pain or itching.	Isolated erythema migrans Multiple erythema migrans
Neurological manifestations	<ul style="list-style-type: none"> • Facial palsy (sometimes bilateral); • Facial numbness; • Deafness; • Diplopia. 	Cranial neuritis (especially facial palsy, but other involvement of the cranial nerves is possible).
	<ul style="list-style-type: none"> • Lower motor neuron-type weakness affecting one or more nerve or root territories; • Paresthesia or hypoesthesia affecting one or more nerve or root territories; • Abolition of one or more deep tendon reflexes. 	<ul style="list-style-type: none"> • Mononeuropathy; • Multiple mononeuritis; • Radiculopathy with no other cause; • Plexopathy.
	<ul style="list-style-type: none"> • Headache; • Nuchal pain or stiffness; • Photophobia; • Nausea; • Vomiting. 	Aseptic meningitis.
Cardiac manifestations (more rare in children)	<ul style="list-style-type: none"> • Chest pain; • Palpitations • Dyspnea; • Syncope; • Dizziness. 	<ul style="list-style-type: none"> • Atrioventricular block; • Nonspecific arrhythmia; • Pericardial syndrome (with or without block) • Heart failure.
Articular manifestations	<ul style="list-style-type: none"> • Joint swelling often worse than the pain and the other associated symptoms; • In most cases, the knee is affected. 	<ul style="list-style-type: none"> • Swelling of one or more joints (mainly the knee, but other, smaller joints can be affected); • Possible flare-ups of arthritis alternating with periods of remission without treatment.

1. Examples of other manifestations: non-neurological ocular manifestations (uveitis, keratitis, conjunctivitis, episcleritis, retinitis and choroiditis).

2. General systemic symptoms may also be present: fever and chills, malaise, fatigue, muscle pain, joint pain, concentration and memory problems, headaches, isolated lymphadenopathy, flu-like syndrome (consistent with Lyme disease, particularly if it occurs during the summer), mononucleosis syndrome (consistent with Lyme disease, particularly if it occurs during the summer), asthenia, lethargy and anorexia.

Legend:

 Photos available as a diagnostic aid.

TREATMENT PRINCIPLES


- ▶ In a patient who presents with a cutaneous manifestation with no other manifestations suggestive of the disseminated stage:
 - If there is some hesitation between a diagnosis of infectious cellulitis and one of erythema migrans of Lyme disease, opt for a treatment that would cover both diseases (e.g., amoxicillin-clavulanate).
- ▶ As soon as a diagnosis of erythema migrans is made, antibiotic therapy can be initiated immediately (serological tests are not indicated in this case).
- ▶ After diagnosing a manifestation attributable to Lyme disease (e.g., isolated erythema migrans), the clinician should always check for signs and symptoms of involvement in other anatomical systems in order to choose the appropriate antibiotic therapy.
- ▶ In situations where neurological, cutaneous (multiple erythema migrans), cardiac or articular manifestations might be attributed to Lyme disease, based on the clinical presentation, and while waiting for the laboratory test results, antibiotic therapy could be initiated after a discussion with one or more medical specialists or an experienced colleague.
- ▶ Doxycycline and beta-lactams are the preferred treatments for the main manifestations of Lyme disease. In the event that these drugs cannot be prescribed (e.g., an absolute contraindication, a history of very severe allergic reaction to penicillins), macrolides can be used to treat isolated erythema migrans. However, for the other clinical manifestations, the choice of antibiotic should be discussed with a medical specialist.

ANTIBIOTIC THERAPY

IMPORTANT INFORMATION ON THE USE OF DOXYCYCLINE IN CHILDREN UNDER 8 YEARS OF AGE

- ▶ The available scientific safety data suggest that the use of doxycycline at doses ranging from 2 to 10 mg/kg/d and for average total durations of between 6 and 20 days would have no effect in terms of tooth staining or a change in the colour of permanent teeth.
- ▶ Since 2018, the American Academy of Pediatrics has recommended the use of doxycycline, regardless of the child's age, for treating the manifestations of Lyme disease that need to be treated for at most 14 days.
- ▶ Because of its lipophilic properties, doxycycline has a good ability to cross the blood-brain barrier.

CUTANEOUS MANIFESTATIONS WITH OR WITHOUT GENERAL SYSTEMIC SYMPTOMS

	1 ST LINE		OTHER OPTIONS	
	Antibiotic and dosage	Duration ¹	Antibiotic and dosage	Duration ¹
 <p>Isolated erythema migrans with no general systemic symptoms</p>	Doxycycline PO² 4,4 mg/kg/d divided into 2 doses (max.: 100 mg/dose)	10 days (10-14 days)	Amoxicillin PO 50 mg/kg/d divided into 3 doses (max.: 500 mg/dose) or Cefuroxime axetil PO³ 30 mg/kg/ into 2 doses (max.: 500 mg/dose)	14 days (14-21 days)
<p>Isolated erythema migrans with general systemic symptoms or Multiple erythema migrans ± general systemic symptoms</p>		<p>! If < 8 years of age: <i>Prescribe only after an informed discussion with the patient's parent (or legal representative)</i></p>		14 days (14-21 days)

Reasons for consulting, or referring the patient to, one or more medical specialists:

- Neurological, cardiac or articular manifestations occur during treatment.
- Symptoms persist post-treatment.
- The antibiotic therapy fails, or the attribution of the cutaneous manifestations with or without general systemic symptoms to Lyme disease needs to be re-examined.

1. The time intervals proposed for the durations of treatment are based on the selected primary studies, clinical practice recommendations and guidelines.
2. There is no commercially available pediatric formulation of doxycycline. However, if need be, an individualized formulation can be prepared by the pharmacy (e.g., a compounded oral suspension).
3. Cefuroxime axetil suspension is little used because of its unpleasant taste. See the product monograph for suggestions on how to improve the taste.

NEUROLOGICAL MANIFESTATIONS (NEUROBORRELIOSIS)

LYME DISEASE
IN CHILDREN

	1 ST LINE		OTHER OPTIONS	
	Antibiotic and dosage	Duration ¹	Antibiotic and dosage	Duration ¹
Peripheral nervous system involvement (e.g., cranial mononeuritis or multiple mononeuritis, plexopathy or radiculopathy)	Doxycycline PO² 4,4 mg/kg/d divided into 2 doses (max.: 100 mg/dose) ! If < 8 years of age: <i>Prescribe only after an informed discussion with the patient's parent (or legal representative)</i>	14 days (14-21 days)	Amoxicillin PO 50 mg/kg/d divided into 3 doses (max.: 500 mg/dose) or Cefuroxime axetil PO³ 30 mg/kg/d divided into 2 doses (max.: 500 mg/dose)	14 days (14-21 days)
Central nervous system involvement (including optic neuritis) or Meningitis	Ceftriaxone IV 75 - 100 mg/kg/d as a single dose (max.: 2 g)	14 days (10-28 days)	Cefotaxime IV 225 - 300 mg/kg/d divided into 3 or 4 doses (max.: 12 g/d) or Penicillin G IV 200 000 - 400 000 U/kg/d divided every 4 hrs (max.: 18 - 24 million U/d)	14 days (10-28 days)

Reasons for consulting, or referring the patient to, one or more medical specialists:

- Suspicion of neuroborreliosis (clinical evaluation and decision to be made regarding 1st-line antibiotic therapy).
- The occurrence of articular manifestations during treatment. In such case, consideration might be given to prolonging the treatment to 28 days.
- Symptoms persist post-treatment.
- The antibiotic therapy fails, or the attribution of the neurological manifestations to neuroborreliosis needs to be re-examined.

CARDIAC MANIFESTATIONS (LYME CARDITIS)



	1 ST LINE		OTHER OPTIONS	
	Antibiotic and dosage	Duration ¹	Antibiotic and dosage	Duration ¹
1st degree AV block with PR interval < 300 ms⁵	Doxycycline PO² 4,4 mg/kg/d d divided into 2 doses (max.: 100 mg/dose) ! If < 8 years of age: <i>Prescribe only after an informed discussion with the patient's parent (or legal representative)</i>	14 days (14-21 days)	Amoxicillin PO 50 mg/kg/d into 3 doses (max.: 500 mg/dose) or Cefuroxime axetil PO³ 30 mg/kg/d divided into 2 doses (max.: 500 mg/dose)	14 days (14-21 days)
<ul style="list-style-type: none"> • 1st degree AV block with PR interval > 300 ms⁵ • High-degree AV block⁵ (2nd or 3rd degree) 	Ceftriaxone IV 75 - 100mg/kg/d as a single dose (max.: 2 g)		Cefotaxime IV 150-200 mg/kg/d divided into 3 or 4 doses (max.: 6 g/d) or Penicillin G IV 200 000 - 400 000 U/kg/d divided every 4 hours (max.: 18 - 24 million U/d)	
Myocarditis or pericarditis (with or without block)⁵				



Reasons for consulting, or referring the patient to, one or more medical specialists:

- Suspicion of Lyme carditis (clinical evaluation and decision to be made regarding 1st-line antibiotic therapy).
- Examining the possibility of switching to the PO route.
- The occurrence of neurological or articular manifestations during treatment. In such case, consideration might be given to changing the antibiotic or the duration of treatment.
- Symptoms persist post-treatment.
- The antibiotic therapy fails, or the attribution of the cardiac manifestations to Lyme carditis needs to be re-examined.

1. The time intervals proposed for the durations of treatment are based on the selected primary studies, clinical practice recommendations and guidelines.
2. There is no commercially available pediatric formulation of doxycycline. However, if need be, an individualized formulation can be prepared by the pharmacy (e.g., a compounded oral suspension).
3. Cefuroxime axetil suspension is little used because of its unpleasant taste. See the product monograph for suggestions on how to improve the taste.
4. PO therapy should be accompanied by serial ECGs for monitoring purposes.
5. Cardiac monitoring should be done in cases where treatment is administered intravenously.

ARTICULAR MANIFESTATIONS (LYME ARTHRITIS)

LYME DISEASE
IN CHILDRENStay up to date at inesss.qc.ca

	Age	1 ST LINE		OTHER OPTIONS	
		Antibiotic and dosage	Duration ¹	Antibiotic and dosage	Duration ¹
Lyme arthritis	≥ 8 years	Doxycycline PO² 4,4 mg/kg/ d divided into 2 doses (max.: 100 mg/dose)	28 days	Amoxicillin PO 50 mg/kg/d divided into 3 doses (max.: 500 mg/dose) or Cefuroxime axetil PO³ 30 mg/kg/d divided into 2 doses (max.: 500 mg/dose)	28 days
	< 8 years	Amoxicillin PO 50 mg/kg/d divided into 3 doses (max.: 500 mg/dose) or Cefuroxime axetil PO³ 30 mg/kg/ d divided into 2 doses (max.: 500 mg/dose)		<i>If history of very severe allergy to penicillins and after an informed discussion with the patient's parent (or legal representative)</i>  Doxycycline PO² 4,4 mg/kg/d divided into 2 doses (max.: 100 mg/dose)	
Recurrence of Lyme arthritis	≥ 8 years	Doxycycline PO² 4,4 mg/kg/d divided into 2 doses (max.: 100 mg/dose)	28 days	Amoxicillin PO 50 mg/kg/d divided into 3 doses (max.: 500 mg/dose) or Cefuroxime axetil PO³ 30 mg/kg/d divided into 2 doses (max.: 500 mg/dose)	28 days
		Ceftriaxone IV 75 - 100 mg/kg/d as a single dose (max.: 2 g)	14-28 days	Ceftriaxone IV 150-200 mg/kg/d divided into 3 or 4 doses (max.: 6 g/d) or Penicillin G IV 200 000 - 400 000 U/kg/d divided every 4 hrs (max.: 18 - 24 million U/d)	14-28 days
	< 8 years	Amoxicillin PO 50 mg/kg/d divided into 3 doses (max.: 500 mg/dose) or Cefuroxime axetil PO³ 30 mg/kg/d divided into 2 doses (max.: 500 mg/dose)	28 days	<i>If history of very severe allergy to penicillins and after an informed discussion with the patient's parent (or legal representative)</i>  Doxycycline PO² 4,4 mg/kg/d divided into 2 doses (max.: 100 mg/dose)	28 days
		Ceftriaxone IV 75 - 100 mg/kg/d as a single dose (max.: 2 g)	14-28 days	Cefotaxime IV 150- 200 mg/kg/d divided into 3 or 4 doses (max.: 6 g/d) or Penicillin G IV 200 000 - 400 000 U/kg/d divided every 4 hrs (max.: 18 - 24 million U/d)	14-28 days

Reasons for consulting, or referring the patient to, one or more medical specialists:


- Suspicion of Lyme arthritis (clinical evaluation and decision to be made regarding 1st-line antibiotic therapy).
- The antibiotic therapy fails, or the attribution of the arthritis to Lyme disease needs to be re-examined.
- Symptoms persist post-treatment despite two courses of antibiotic (the decision not to prescribe a new antibiotic should be made on a case-by-case basis).

Additional information:

- ! The use of corticosteroids should be avoided when treating Lyme arthritis with antibiotics.
- Consideration may be given to using nonsteroidal anti-inflammatories (NSAIDs) for the PRN treatment of pain, in addition to antibiotics.
- An intra-articular corticosteroid injection or the use of a disease-modifying antirheumatic drug might be considered after appropriate antibiotic therapy. If need be, the opinion of a medical specialist or an experienced colleague should be sought.

1. The time intervals proposed for the durations of treatment are based on the selected primary studies, clinical practice recommendations and guidelines.
 2. There is no commercially available pediatric formulation of doxycycline. However, if need be, an individualized formulation can be prepared by the pharmacy (e.g., a compounded oral suspension).
 3. Cefuroxime axetil suspension is little used because of its unpleasant taste. See the product monograph for suggestions on how to improve the taste.

HISTORY OF ALLERGIC REACTION TO PENICILLINS

CONFIRMED ALLERGY TO PENICILLINS	CROSS-ALLERGIES TO DISSIMILAR CEPHALOSPORINS							
Of 100 people who report a history of allergy to a penicillin, a diagnosis of allergy will be confirmed in:	Of 100 people with a confirmed allergy to penicillins, a cross-reaction with a “dissimilar” cephalosporin may be observed in:							
<p>Fewer than 6 children</p> <p><i>Mainly observed reactions: mostly non-severe, delayed rashes</i></p>	<p>1 or 2 of them</p> <table border="1"> <tr> <td>Cefotaxime</td> <td>1.08 (0.27; 4.22)</td> <td rowspan="3">Absolute risk (95% confidence interval)</td> </tr> <tr> <td>Ceftriaxone</td> <td>0.43 (0.07; 2.62)</td> </tr> <tr> <td>Cefuroxime axetil</td> <td>0.79 (0.18; 3.33)</td> </tr> </table>	Cefotaxime	1.08 (0.27; 4.22)	Absolute risk (95% confidence interval)	Ceftriaxone	0.43 (0.07; 2.62)	Cefuroxime axetil	0.79 (0.18; 3.33)
Cefotaxime	1.08 (0.27; 4.22)	Absolute risk (95% confidence interval)						
Ceftriaxone	0.43 (0.07; 2.62)							
Cefuroxime axetil	0.79 (0.18; 3.33)							
<p>Carefully assess the patient’s allergy status during the visit before considering an antibiotic other than a “dissimilar” cephalosporin.</p>								
<p>Click here  to view the algorithm specific to Lyme disease.</p>								

INFORMATION TO BE GIVEN TO THE PATIENT’S PARENT (OR LEGAL REPRESENTATIVE)

ASK THE PARENT (OR LEGAL REPRESENTATIVE):

- ▶ To watch for Lyme disease symptoms in the child during the observation period as well as during and after treatment (refer to the [follow-up sheet](#));
- ▶ To take a photo including a measuring device, if applicable, of the redness if doubt persists as to it being attributed to Lyme disease.
- ▶ To contact a health professional, if necessary.

INFORM THE PARENT (OR LEGAL REPRESENTATIVE):

- ▶ That the child can take an antipyretic/analgesic (e.g., acetaminophen or ibuprofen) in addition to their antibiotic therapy to relieve the pain and general systemic symptoms.
- ▶ That a Jarisch-Herxheimer reaction could occur after antibiotic therapy is initiated. This systemic inflammatory reaction can occur when treating an infection caused by spirochete bacteria, such as those in the *Borrelia burgdorferi* group.
 - **However**, it should not result in the antibiotic being discontinued. If in doubt, a health professional must be contacted.

ADVISE THE PARENT (OR LEGAL REPRESENTATIVE):

- ▶ That, as a general rule, the child should recover completely after the antibiotic therapy, especially if they are treated early and for erythema migrans.
- ▶ That for certain manifestations of the disseminated stages (e.g., facial palsy and arthritis), symptoms may persist for weeks or even months after appropriate antibiotic therapy, hence a possible significant impact on their quality of life.
- ▶ To consult a health professional if the symptoms do not improve or if they recur after the end of treatment.

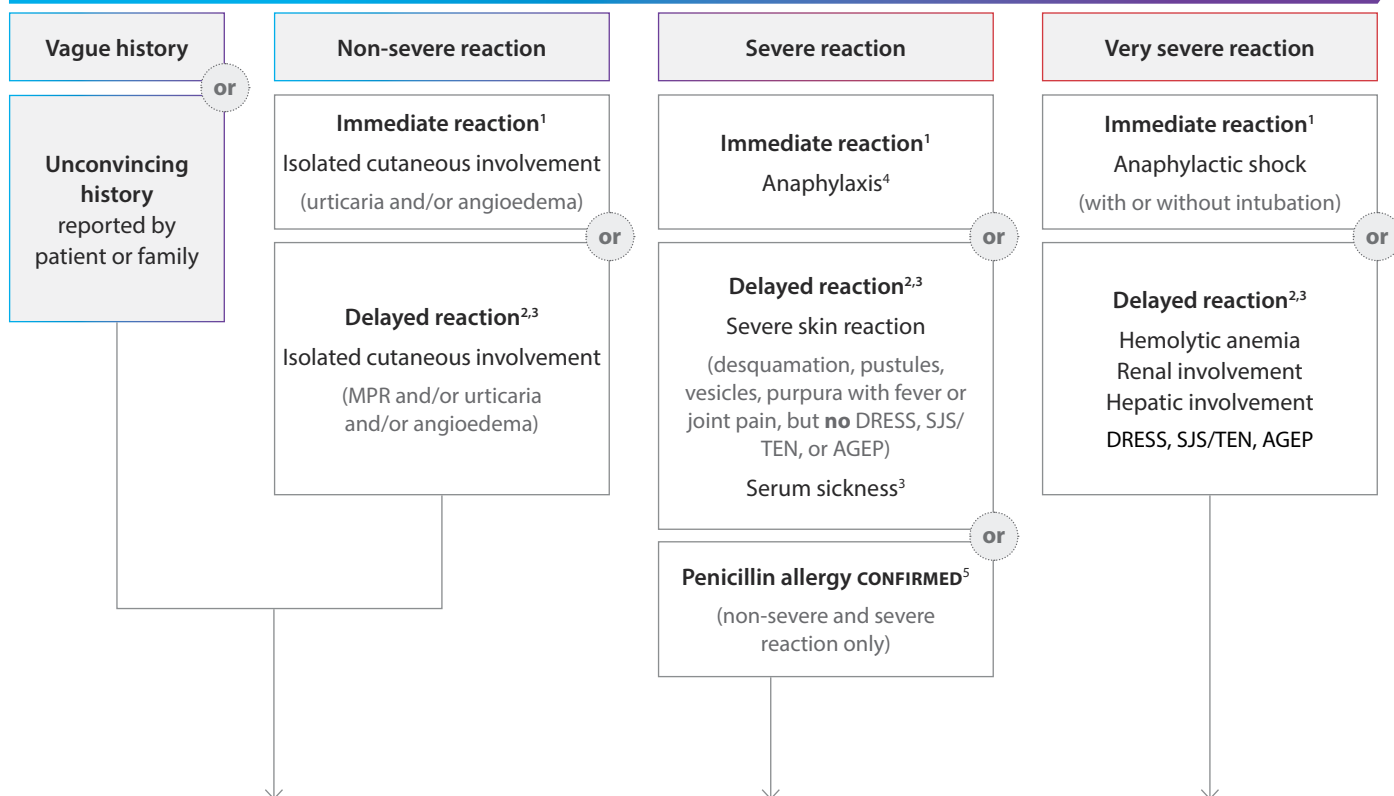
MONITORING

- ▶ The clinical condition of a patient diagnosed with Lyme disease who experiences persistent symptoms after antibiotic therapy should be reevaluated jointly with one or more medical specialists, depending on the symptoms, if severity and duration of the symptoms since the end of treatment seem unusual and cannot be explained by other likely clinical conditions.
 - ! Serological tests are not indicated for monitoring the effectiveness of antibiotic therapy.

LYME DISEASE IN CHILDREN

SEVERITY OF PREVIOUS ALLERGIC REACTION TO PENICILLIN ANTIBIOTICS

ASSESS THE SEVERITY OF THE INITIAL REACTION AND ASSESS THE RISKS INVOLVED




THE FOLLOWING CAN BE PRESCRIBED SAFELY:

 **DISSIMILAR cephalosporins**

**Cefuroxime axetil OR Ceftriaxone IV*
OR Cefotaxime IV***

* IV administration if the PO option is not tolerated.

PRESCRIBE THE FOLLOWING WITH CAUTION:


 **Amoxicillin
Penicillin**

The 1st dose should **always** be administered under medical supervision.

If history of:

- **Immediate reactions**, a drug provocation test should be performed;
- **Delayed reactions**, the patient or his/her family should be informed of the possible risk of recurrence in the days following initiation of the antibiotic.

PRESCRIBE THE FOLLOWING WITH CAUTION:

 **DISSIMILAR cephalosporins**

**Cefuroxime axetil OR Ceftriaxone IV*
OR Cefotaxime IV* ONLY**

if history of recent non-severe reactions as an adult **OR** of serum sickness-type reactions during childhood³.

* IV administration if the PO option is not tolerated.

The 1st dose should **always** be administered under medical supervision.

If history of:

- **Immediate reactions**, a drug provocation test should be performed;
- **Delayed reactions**, the patient or his/her family should be informed of the possible risk of recurrence in the days following initiation of the antibiotic.

AVOID PRESCRIBING:

 **Beta-lactam⁶**

Choose another class of antibiotics.

If strong indication of a beta-lactam, obtain a consultation with specialized services.

IF NEITHER DOXYCYCLINE NOR A BETA-LACTAM⁶ CAN BE ADMINISTERED, THE FOLLOWING CAN BE PRESCRIBED:


 **Azithromycin⁷
Clarithromycin** **To treat isolated EM**

1. Immediate reaction (type I or IgE-mediated): usually occurs within 1 hour after taking **the first dose** of a drug.
2. Delayed reaction (type II, III or IV): may occur at any time from one hour after the administration of a drug.
3. Delayed skin reactions and serum sickness-like reactions that occur in children on antibiotic therapy are generally nonallergic and may be of viral origin.
4. Anaphylaxis without shock or intubation requires an extra level of vigilance.
5. With no recommendations concerning other beta-lactams.
6. Penicillins, cephalosporins and carbapenems.
7. Unless the patient has a heart defect due to possible QT interval prolongation.

For further information on the clinical manifestations, consult the [interactive tool](#).

AGEP: acute generalized exanthematous pustulosis;
DRESS: drug reaction with eosinophilia and systemic symptoms;
EM: erythema migrans;
MP R: maculopapular rash;
SJS: Stevens–Johnson syndrome;
TEN: toxic epidermal necrolysis.

AVOID PRESCRIBING:

 **Amoxicillin
Penicillin**

IF NEITHER DOXYCYCLINE NOR A BETA-LACTAM⁶ CAN BE ADMINISTERED, THE FOLLOWING CAN BE PRESCRIBED:

 **Azithromycin⁷
Clarithromycin** **To treat isolated EM**

DECISION-MAKING FOR ADMINISTERING A NEW BETA-LACTAM

LYME DISEASE IN CHILDREN

Alternatives if neither doxycycline nor a beta-lactam can be administered to treat isolated erythema migrans

Antibiotic	Daily dosage	Maximum dosage	Duration
Azithromycin ¹	10 mg/kg/day PO	500 mg/day	7-10 days
Clarithromycin	15 mg/kg/day PO ÷ BID	500 mg/dose	14-21 days

1. Unless the patient has a heart defect due to possible QT interval prolongation.

MAIN REFERENCES

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