INCRELEX® (mecasermin)

Non-Discrimination Statement and Multi-Language Interpreter Services information are located at the end of this document.

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Medical Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Medical Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as “Description” defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as “Criteria” defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Medical Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Medical Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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INCRELEX (mecasermin) (cont.)

Description:

Increlex (mecasermin) is an injectable solution of human insulin-like growth factor-1 produced by recombinant DNA technology. Increlex is used for the treatment of growth failure in children with severe primary insulin-like growth factor (IGF-1) deficiency, also referred to as primary IGFD. These children have normal or elevated levels of growth hormone but due to lack of IGF-1, are unable to utilize the growth hormone resulting in extremely short stature.

Severe primary IGF-1 deficiency is defined by:

- Height standard deviation score less than or equal to –3.0 for age and sex of the individual
- Basal IGF-1 standard deviation score less than or equal to –3.0 for age and sex of the individual
- Normal or elevated growth hormone

Increlex is also used in children with a growth hormone (GH) gene deletion who have developed neutralizing antibodies to GH.

Increlex is not a substitute for GH for approved GH indications.

Criteria:

- FDA-approved dosage of Increlex for the long-term treatment of growth failure in individuals 2 through 17 years of age\(^1\) with severe primary IGF-1 deficiency (IGFD) is considered **medically necessary** with documentation of **ALL** of the following:

  1. Height standard deviation score equal to or less than –3.0 for age and sex of the individual
  2. Basal IGF-1 standard deviation score equal to or less than –3.0 for age and sex of the individual\(^2\)
  3. Normal or elevated growth hormone level
  4. No evidence of **ANY** of the following:

    - Closed epiphyses (growth plates)
    - Active or suspected neoplasia
    - Chromosome aberrations
    - Malnutrition
    - Secondary forms of IGF deficiency (e.g., growth hormone deficiency, hypothyroidism, chronic treatment with systemic anti-inflammatory steroids)

  5. Dosage is not greater than 0.04 to 0.08 mg/kg (40 to 80 µ/kg) twice daily given subcutaneously for at least one week and, if well tolerated, increased by 0.04 mg/kg per dose to the maximum dose of 0.12 mg/kg given subcutaneously twice daily\(^3\).
INCRELEX (mecasermin) (cont.)

Criteria: (cont.)

- FDA-approved dosage of Increlex in individuals 2 through 17 years of age\(^1\) with the growth hormone gene deletion who have developed neutralizing antibodies to growth hormone is considered medically necessary with documentation of ALL of the following:

1. Growth hormone levels are normal or low
2. IGF-1 levels are on the lowest 25% of reference laboratory's range\(^2\)
3. No evidence of ANY of the following:
   - Closed epiphyses (growth plates)
   - Active or suspected neoplasia
   - Chromosome aberrations
   - Malnutrition
   - Secondary forms of IGF deficiency (e.g., growth hormone deficiency, hypothyroidism, chronic treatment with systemic anti-inflammatory steroids)

4. Dosage is not greater than 0.04 to 0.08 mg/kg (40 to 80 µ/kg) twice daily given subcutaneously for at least one week and, if well tolerated, increased by 0.04 mg/kg per dose to the maximum dose of 0.12 mg/kg given subcutaneously twice daily\(^3\)

- Increlex for all other indications not previously listed or if above criteria not met is considered experimental or investigational based upon:

1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
2. Insufficient evidence to support improvement of the net health outcome, and
3. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives.

\(^1\) Increlex has not been studied in children less than 2 years of age or in adults.
\(^2\) The laboratory performing the test should include their specific reference range for age and sex of the individual to determine the basal serum IGF-1 level deviation.
\(^3\) Review by the clinical pharmacist and/or medical director(s) and/or clinical advisor(s) is required if medication dosages differ from those listed above.
INCRELEX (mecasermin) (cont.)

Resources:

Literature reviewed 03/14/17. We do not include marketing materials, poster boards and non-published literature in our review.

1. CenterWatch. Drugs Approved by the FDA Drug Name: Increlex (mecasermin). Updated 06/20/2008

FDA Product Approval Information for Increlex:
INCRELEX (mecasermin) (cont.)

Resources: (cont.)

Increlex Package Insert:

- FDA-approved indication and dosage:

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<thead>
<tr>
<th>Indication</th>
<th>Recommended Dose</th>
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<td>INCRELEX (mecasermin [rDNA origin] injection) is indicated for the treatment of growth failure in children with severe primary IGF-1 deficiency (Primary IGFD) or with growth hormone (GH) gene deletion who have developed neutralizing antibodies to GH. Severe Primary IGFD is defined by height standard deviation score ≤ –3.0 and basal IGF-1 standard deviation score ≤ –3.0 and normal or elevated growth hormone (GH). Severe Primary IGFD includes classical and other forms of growth hormone insensitivity. Patients with Primary IGFD may have mutations in the GH receptor (GHR), post-GHR signaling pathway including the IGF-1 gene. They are not GH deficient, and therefore, they cannot be expected to respond adequately to exogenous GH treatment. INCRELEX is not intended for use in subjects with secondary forms of IGF-1 deficiency, such as GH deficiency, malnutrition, hypothyroidism, or chronic treatment with pharmacologic doses of anti-inflammatory steroids. Thyroid and nutritional deficiencies should be corrected before initiating INCRELEX treatment. INCRELEX is not a substitute for GH treatment.</td>
<td>Preprandial glucose monitoring is recommended at treatment initiation and until a well-tolerated dose is established. If frequent symptoms of hypoglycemia or severe hypoglycemia occur, preprandial glucose monitoring should continue. The dosage of INCRELEX should be individualized for each patient. The recommended starting dose of INCRELEX is 0.04 to 0.08 mg/kg (40 to 80 μg/kg) twice daily by subcutaneous injection. If well-tolerated for at least one week, the dose may be increased by 0.04 mg/kg per dose, to the maximum dose of 0.12 mg/kg given twice daily. Doses greater than 0.12 mg/kg given twice daily have not been evaluated in children with Primary IGFD and, due to potential hypoglycemic effects, should not be used. If hypoglycemia occurs with recommended doses, despite adequate food intake, the dose should be reduced. INCRELEX should be administered shortly before or after (± 20 minutes) a meal or snack. If the patient is unable to eat shortly before or after a dose for any reason, that dose of INCRELEX should be withheld. Subsequent doses of INCRELEX should never be increased to make up for one or more omitted dose.</td>
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INCRELEX (mecasermin) (cont.)

Non-Discrimination Statement:

Blue Cross Blue Shield of Arizona (BCBSAZ) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability or sex. BCBSAZ provides appropriate free aids and services, such as qualified interpreters and written information in other formats, to people with disabilities to communicate effectively with us. BCBSAZ also provides free language services to people whose primary language is not English, such as qualified interpreters and information written in other languages. If you need these services, call (602) 864-4884 for Spanish and (877) 475-4799 for all other languages and other aids and services.

If you believe that BCBSAZ has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability or sex, you can file a grievance with: BCBSAZ’s Civil Rights Coordinator, Attn: Civil Rights Coordinator, Blue Cross Blue Shield of Arizona, P.O. Box 13466, Phoenix, AZ 85002-3466, (602) 864-2288, TTY/TDD (602) 864-4823, crc@azblue.com. You can file a grievance in person or by mail or email. If you need help filing a grievance BCBSAZ’s Civil Rights Coordinator is available to help you. You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at: U.S. Department of Health and Human Services, 200 Independence Avenue SW., Room 509F, HHH Building, Washington, DC 20201, 1–800–368–1019, 800–537–7697 (TDD). Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html

Multi-Language Interpreter Services:

Spanish: Si usted, o alguien a quien usted está ayudando, tiene preguntas acerca de Blue Cross Blue Shield of Arizona, tiene derecho a obtener ayuda e información en su idioma sin costo alguno. Para hablar con un intérprete, llame al 602-864-4884.

Navajo: Díí kwe’é atah nílníigíí Blue Cross Blue Shield of Arizona haadá yít’éego bina’ídilkidgo éi docdago Háida bíjá aniyeedííí ńíilaa doo hóló díí t’a házadk’ehí háká a’doowolgo bee hazi’doó baqáh ilínígódí. A’ła’ halné’iiziní kojí bich’íi’ hodililííí 877-475-4799.

Chinese: 如果您，或者您正在协助的对象，有关插入项目的名称 Blue Cross Blue Shield of Arizona 方面的问题，您有权免费以您的母语得到帮助和讯息。洽询一位翻译员，请拨电话 在此插入数字 877-475-4799。

Vietnamese: Nếu quý vị, hay người mà quý vị đang giúp đỡ, có câu hỏi về Blue Cross Blue Shield of Arizona quý vị sẽ có quyền được giúp và có thêm thông tin bằng ngôn ngữ của mình miễn phí. Để nói chuyện với một thợ dịch viên, xin gọi 877-475-4799.

Arabic: إن كان لديك أو أدى شخص تساعده أسئلة بخصوص Blue Cross Blue Shield of Arizona الضرورية بلغتك من دون أية تكلفة، للتحدث مع مترجم اتصل ب 877-475-4799.
INCRELEX (mecasermin) (cont.)

Multi-Language Interpreter Services: (cont.)

Tagalog: Kung ikaw, o ang iyong tinutulungan, ay may mga katanungan tungkol sa Blue Cross Blue Shield of Arizona, may karapatan ka na makakauhag tungkol at impormasyon sa iyong wika ng walang gastos. Upang makaasap ang isang tagasalin, tumawag sa 877-475-4799.

Korean: 만약 귀하 또는 귀하가 돌보는 어떤 사람이 Blue Cross Blue Shield of Arizona에 관해서 질문이 있다면 귀하의 그릴한 도움과 정보를 귀하의 외국어로 이용 부담없이 얻을 수 있는 권리가 있습니다. 그렇게 통역사와 얘기하기 위해서는 877-475-4799로 전화하십시오.

French: Si vous, ou quelqu’un que vous êtes en train d’aider, a des questions à propos de Blue Cross Blue Shield of Arizona, vous avez le droit d’obtenir l’aide et l’information dans votre langue à aucun coût. Pour parler à un interprète, appelez 877-475-4799.

German: Falls Sie oder jemand, dem Sie helfen, Fragen zum Blue Cross Blue Shield of Arizona haben, haben Sie das Recht, kostenlose Hilfe und Informationen in Ihrer Sprache zu erhalten. Um mit einem Dolmetscher zu sprechen, rufen Sie bitte die Nummer 877-475-4799 an.

Russian: Если у вас или лица, которому вы помогаете, имеется вопросы по поводу Blue Cross Blue Shield of Arizona, то вы имеете право на бесплатное получение помощи и информации на вашем языке. Для разговора с переводчиком позвоните по телефону 877-475-4799.

Japanese: ご本人様、またはお客様の身の回りの方でも、Blue Cross Blue Shield of Arizonaについてご質問がございましたら、ご希望の言語でサポートを受けたり、情報を入手したりすることができます。料金はかかりません。通訳とお話される場合、877-475-4799までお電話ください。

Farsi: اگر شما، یا کسی که شما به آن کمک می‌کنید، سوال در مورد اطلاعات به زبان خود را به طور رایگان دریافت نمایید 877-475-4799.

Assyrian: Blue Cross Blue Shield of Arizona، دەناسرا بە ئین رەداری کە کەم و خەڵکی شەوەیە. 877-475-4799.

Serbo-Croatian: Ukoliko Vi ili neko kome Vi pomažete ima pitanje o Blue Cross Blue Shield of Arizona, imate pravo da besplatno dobijete pomoć i informacije na Vašem jeziku. Da biste razgovarali sa prevodicom, nazovite 877-475-4799.

Thai: หากคุณหรือคนที่คุณช่วยเหลือในภาษาอังกฤษ Blue Cross Blue Shield of Arizona
คุณสามารถติดต่อได้โดยความสะดวกและไม่มีค่าใช้จ่าย พร้อมสอบถาม โทร 877-475-4799