NONINVASIVE TECHNIQUES FOR EVALUATION AND MONITORING OF CHRONIC LIVER DISEASE

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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NONINVASIVE TECHNIQUES FOR EVALUATION AND MONITORING OF CHRONIC LIVER DISEASE (cont.)

**Description:**

Multianalyte Assays:
Multianalyte assays with algorithmic analyses (MAAAs) use the results from multiple assays of various types in an algorithmic analysis to determine and report a numeric score(s) or probability. MAAAs have been investigated as a substitute for biopsy in the screening, evaluation and monitoring of individuals with chronic liver disease including fibrosis, steatosis or steatohepatitis in individuals with hepatitis C, alcoholic liver disease and non-alcoholic fatty liver disease. The results of individual component assays are not reported separately. Assays include ASH FibroSure®, FibroSpect II®, HCV FibroSure®, HepaScore®, and NASH FibroSure®.

ASH FibroSure (ASH Test):
Combination of 10 serum biochemical markers of liver function together with age, gender, height and weight in a proprietary algorithm exclusively offered by LabCorp. Test is proposed to provide surrogate markers for liver fibrosis, hepatic steatosis, and alcoholic steatohepatitis (ASH). Biochemical markers include:

1. Alpha-2 macroglobulin
2. Alanine aminotransferase (ALT)
3. Apolipoprotein A1
4. Aspartate aminotransferase (AST)
5. Bilirubin, total
6. Cholesterol, total
7. Gamma glutamyl transpeptidase (GGT)
8. Glucose, fasting
9. Haptoglobin
10. Triglycerides

FibroSpect II:
Combination of 3 serum biochemical markers that directly measure fibrogenesis of the liver analyzed using a patented algorithm exclusively by Prometheus® laboratories. Biochemical markers include:

1. Alpha-2 macroglobulin
2. Hyaluronic acid
3. TIMP-1
NONINVASIVE TECHNIQUES FOR EVALUATION AND MONITORING OF CHRONIC LIVER DISEASE (cont.)

Description: (cont.)

HCV FibroSure (FibroTest):
Combination of 6 serum biochemical indirect markers of liver function plus age and gender, analyzed with a patented algorithm exclusively offered by LabCorp, to generate a measurement of fibrosis and necro-inflammatory activity in the liver. Biochemical markers include:

1. Alanine aminotransferase (ALT)
2. Alpha-2 macroglobulin
3. Apolipoprotein A1
4. Bilirubin, total
5. Gamma glutamyl transpeptidase (GGT)
6. Haptoglobin

HepaScore:
Combination of 4 serum biochemical markers, analyzed using a patented algorithm exclusively offered by Quest Diagnostics, to generate a measurement to determine the degree of hepatic fibrosis. Biochemical markers include:

1. Alpha-2 macroglobulin
2. Bilirubin, total
3. Gamma glutamyl transpeptidase (GGT)
4. Hyaluronic acid

NASH FibroSure (NASH Test):
Combination 10 serum biochemical markers of liver function together with age, gender, height, and weight, analyzed with a proprietary algorithm exclusively offered by LabCorp. Proposed to provide surrogate markers for liver fibrosis, hepatic steatosis, and Nonalcoholic steatohepatitis (NASH). Biochemical markers include:

1. Alpha-2 macroglobulin
2. Alanine aminotransferase (ALT)
3. Apolipoprotein A1
4. Aspartate aminotransferase (AST)
5. Bilirubin, total
6. Cholesterol, total
7. Gamma glutamyl transpeptidase (GGT)
8. Glucose, fasting
9. Haptoglobin
10. Triglycerides
NONINVASIVE TECHNIQUES FOR EVALUATION AND MONITORING OF CHRONIC LIVER DISEASE (cont.)

Description: (cont.)

Noninvasive Imaging Technologies:
Noninvasive imaging technologies to detect liver fibrosis or cirrhosis in individuals with chronic liver disease have been investigated as an alternative to liver biopsy. Noninvasive imaging technologies include transient elastography, magnetic resonance elastography, acoustic radiation force impulse imaging and real-time tissue elastography. Elastography refers to the measurement of elastic properties of tissues and is based on the principle that malignant tissue is harder than benign tissue. Elastography examines the viscoelastic properties of tissue and has been investigated as a technique to increase ultrasound (US) and magnetic resonance (MR) specificity.

Acoustic Radiation Force Impulse Imaging (ARFI):
ARFI uses an ultrasound probe to produce an acoustic ‘push’ pulse, which generates shear waves that propagate in tissue to assess liver stiffness. ARFI elastography evaluates the wave propagation speed to assess tissue stiffness. The faster the shear wave speed, the harder the object. ARFI elastography can be performed at the same time as a liver sonographic evaluation, even in individuals with a significant amount of ascites. ARFI technologies include Virtual Touch™ Quantification and Siemens Acuson S2000™ system.

Magnetic Resonance Elastography (MRE):
MRE combines MR imaging (MRI) with sound waves to create a visual map (elastogram) showing the stiffness of body tissues. MRE advantages over ultrasound elastography include: 1) analyzing larger liver volumes; 2) analyzing liver volumes of obese individuals or individuals with ascites; and 3) precise analysis of viscoelasticity using a 3-dimensional displacement vector.

Real-Time Tissue Elastography (RTE):
RTE is a type of strain elastography which uses a combined autocorrelation method to measure tissue strain caused by manual compression or an individual’s heartbeat. The relative tissue strain is displayed on conventional color B mode ultrasound images in real time. This technology does not perform as well in severely obese individuals. RTE technologies includes HI VISION™ Preirus™.

Shear Wave Elastography:
Shear wave elastography uses ultrasound beams that are transmitted continuously to tissue at different depths at high speed. The restorative force of the tissue propagates laterally, generating shear waves. The velocity of the waves is measured and a two-dimensional image is created. The waves propagate quickly through hard tissue and more slowly through soft tissue, which allows for the calculation of tissue elasticity. Shear wave technologies include the Aixplorer® MultiWave™ Ultrasound System.
NONINVASIVE TECHNIQUES FOR EVALUATION AND MONITORING OF CHRONIC LIVER DISEASE (cont.)

**Description:** (cont.)

Transient Elastography:
Vibration controlled transient elastography (VCTE) uses a mechanical vibrator to produce mild amplitude and low-frequency (50 Hz) waves, inducing an elastic shear wave that propagates throughout the liver. Ultrasound tracks the wave, measuring its speed, which correlates with liver stiffness. Increases in liver fibrosis also increase liver stiffness and resistance of liver blood flow. Transient elastography technologies include FibroScan.

**Criteria:**

For elastography for other than liver disease, see BCBSAZ Medical Coverage Guideline #O848, “Elastography”.

- A single FibroSURE multianalyte assay for the evaluation of individuals with chronic liver disease are considered medically necessary.

- FibroSURE multianalyte assay for the monitoring of individuals with chronic liver disease are considered *experimental or investigational* based upon:
  1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcome, 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.

- Other multianalyte assays with algorithmic analyses for the evaluation or monitoring of individuals with chronic liver disease for all other indications not previously listed or if above criteria not met are considered *experimental or investigational* based upon:
  1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcome, 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.

These tests include, *but are not limited to*:

- FibroSpect
- HepaScore
NONINVASIVE TECHNIQUES FOR EVALUATION AND MONITORING OF CHRONIC LIVER DISEASE  (cont.)

Criteria: (cont.)

➢ Use of the following noninvasive shear wave elastography imaging techniques for the evaluation or monitoring of individuals with chronic liver disease is considered medically necessary.

   1. Acoustic radiation force impulse imaging
   2. Real-time tissue elastography
   3. Shear wave elastography/Aixplorer
   4. Transient elastography/FibroScan/Vibration Controlled Transient Elastography (VCTE)

➢ Use of the following noninvasive imaging techniques for the evaluation or monitoring of individuals with chronic liver disease is considered experimental or investigational based upon:

   1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcome, 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, and
   4. Insufficient evidence to support improvement outside the investigational setting.

   Imaging techniques include, but are not limited to:

   ▪ Magnetic resonance elastography

Resources:

Literature reviewed 12/19/17. We do not include marketing materials, poster boards and non-published literature in our review.

The BCBS Association Medical Policy Reference Manual (MPRM) policy is included in our guideline review. References cited in the MPRM policy are not duplicated on this guideline.


NONINVASIVE TECHNIQUES FOR EVALUATION AND MONITORING OF CHRONIC LIVER DISEASE (cont.)

Resources: (cont.)


NONINVASIVE TECHNIQUES FOR EVALUATION AND MONITORING OF CHRONIC LIVER DISEASE (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: Díi kwe’e atah níilníi’í Blue Cross Blue Shield of Arizona haada yiit’éego bina’íílídikíígo el dodo Háída bíí aniyeedíí’í t’áadó le’e’ yína’íílídikíígo beeñáah’áaníí hóóq díí t’áa hazaak’eehí hák’í a’doowolgo bee haza’q doo báah ilínígóó. Ata’ halné’ígíí kojí’ bích’íjí hodilíihí 877-475-4799.

Chinese: 如果您，或是您正在协助的对像，有关于插入项目的名称Blue Cross Blue Shield of Arizona方面的问

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

Arabic: إن كان لديك أو لدى شخص تساعدك سؤالا عن بخصم، Blue Cross Blue Shield of Arizona

ENGLISH: You have the right to ask a question and receive additional information in your language free of charge. To speak with a translator, call 877-475-4799.
NONINVASIVE TECHNIQUES FOR EVALUATION AND MONITORING OF CHRONIC LIVER DISEASE (cont.)

Multi-Language Interpreter Services: (cont.)

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

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

French: Si vous, 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 de 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 Doimetscher zu sprechen, rufen Sie bitte die Nummer 877-475-4799 an.

Russian: Если у вас или лица, которому вы помогаете, имеются 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。料金はありません。通訳とお話される場合、877-475-4799 までお電話ください。

Farsi:

آگر شما یا کسی که شما با او کمک می‌کنید، سوال‌ها مورد اطلاعات در مورد Blue Cross Blue Shield of Arizona را بپرسید، اطلاعات به زبان خود را به طور رایگان دریافت کنید. دریافت تمایل 975-4799-4797.

Assyrian:

Blue Cross Blue Shield of Arizona

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 prevodiocem, nazovite 877-475-4799.

Thai: หากคุณหรือคนที่คุณช่วยเหลืออยู่มีคำถามเกี่ยวกับ Blue Cross Blue Shield of Arizona คุณสามารถจะได้รับความช่วยเหลือและข้อมูลในภาษาของคุณโดยไม่เสียค่าใช้จ่าย โปรดติดต่อที่ 877-475-4799