harliku™
(nitisinone) Tablets

Step towards a brighter future, let's go!

This guide will support you in taking HARLIKU™ (nitisinone) Tablets, and managing alkaptonuria (AKU). It also contains useful information about Cycle Vita™, our dedicated patient support program, which delivers individualized support* at every step.

This brochure is intended for patients and caregivers in the US who have been prescribed HARLIKU. It is provided for information purposes only. It is not intended to be, and should not be used as, a substitute for medical advice.

Indications: HARLIKU™ (nitisinone) Tablets is indicated for the reduction of urine homogentisic acid (HGA) in adult patients with alkaptonuria (AKU).

Please see the Important Safety Information on page 2 and full Prescribing Information at harliku.com/pi/.

NOT AN ACTUAL PATIENT

Important Safety Information

Indications

HARLIKU™ (nitisinone) Tablets is indicated for the reduction of urine homogentisic acid (HGA) in adult patients with alkaptonuria (AKU).

Important Safety Information

Do not take HARLIKU if you are allergic to nitisinone or any of the other ingredients. Tell your healthcare provider about any health problems, and if you are pregnant or planning to become pregnant and/or breastfeeding, before starting treatment.

Serious Adverse Reactions:

Eye Symptoms and Skin Changes Due To Elevated Plasma Tyrosine Levels:

Inadequate restriction of tyrosine and phenylalanine intake can result in elevated levels of plasma tyrosine, which may lead to keratitis (eye problems) and hyperkeratotic plaques (thickening of the skin on the soles and palms).

- Your healthcare provider will obtain a slit-lamp examination prior to initiating HARLIKU treatment, regularly during treatment and may reexamine you if you develop symptoms or if you develop high plasma tyrosine levels.
- Your HARLIKU treatment may be temporarily interrupted until symptoms have resolved.

Changes in Blood Profile:

- You may develop leukopenia (reduction in the number of white blood cells, which form part of the immune system) and severe thrombocytopenia (abnormally low levels of platelets, which help the blood to clot).
- Your healthcare provider will monitor platelet and white blood cell counts during HARLIKU therapy.

Common Adverse Reactions:

The most common adverse reactions (≥1%) reported in patients with AKU taking nitisinone in the clinical trials were elevated tyrosine levels, low platelets (thrombocytopenia) and inflammation of the cornea, eye irritation, eye pain and photophobia (keratitis).

Drug Interactions:

Nitisinone can interfere with the effect of other medicines. Tell your healthcare provider or pharmacist if you are taking, have recently taken or might take any other medicines.

Please see the full Prescribing Information at harliku.com/pi/.

Use in Specific Populations:

Pregnancy: The safety of this medicine has not been studied in pregnancy. Tell your healthcare provider immediately if you become pregnant or are planning to become pregnant.

Lactation: The safety of this medicine has not been studied in breastfeeding women. Tell your healthcare provider immediately if you plan to breastfeed.

Pediatric Use: The safety of this medicine have not been studied in pediatric patients with AKU.

Geriatric Use: Clinical studies of HARLIKU did not include a sufficient number of patients 65 years of age and older, to determine whether they respond differently from younger adult patients. Elderly patients should be cautious reflecting any decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

If you get any side effects, talk to your healthcare provider. This includes possible side effects not listed above.

For more detailed information, please refer to the full Prescribing Information at harliku.com/pi/

To report SUSPECTED ADVERSE REACTIONS, contact Cycle Pharmaceuticals at 1-855-831-5413, or the FDA at: 1-800-FDA-1088 or www.fda.gov/medwatch.

You should expect to receive calls from the Cycle Vita team to support you in your treatment.

It is important you answer our calls to avoid delays in receiving your medication.

Save the Cycle Vita number in your phone:
888-360-8482

Welcome from Cycle Vita

CYCLE VITA™
Support *for life*

At Cycle Vita, we understand that as a patient living with a rare disease you may need additional support to manage your condition.

That's why HARLIKU, the first FDA-approved treatment for use in AKU, has your needs in mind. Through Cycle Vita, our dedicated patient support* program, we can help give you the product and process support that you need at every step of your journey. Whether that's help accessing HARLIKU from your insurance provider, continuous product support, assistance with nutrition or resources about how to stay active with AKU.

Whatever stage you are at, we are here to help you step towards a brighter future with HARLIKU. Let's go!

Best Wishes,

Cycle Vita

Important Safety Information

Do not take HARLIKU if you are allergic to nitisinone or any of the other ingredients. Tell your healthcare provider about any health problems, and if you are pregnant or planning to become pregnant and/or breastfeeding, before starting treatment.

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What is AKU?

AKU is an extremely rare genetic condition that is estimated to affect approximately one in 1,000,000 in the US.[2] Patients with AKU have trouble breaking down a chemical called homogentisic acid (HGA), an intermediate product in the digestion of protein.[2] Over time, HGA deposits in the bones and cartilage, turning them black, where the name of Black Bone Disease comes from.[3]

The earliest signs of AKU are dark-stained diapers caused by black/brown urine. These symptoms can be missed if the urine has not had time to interact with oxygen in the air. Due to the slow progression of AKU, more noticeable symptoms typically appear in adulthood.

Common symptoms include:

- Discoloration in the eyes, ears, around the nose (ochronosis)
- Joint pain starting from the back, knee, then hip and shoulder (osteoarthritis)
- Kidney and bladder stones
- Complications in the heart and connective tissue[3]

AKU is not known to affect life span,[4] however **the sooner appropriate diagnosis and care can be given, the greater the chance of slowing down the progression of non-reversible symptoms.[5]**

Important Safety Information

Serious Adverse Reactions: Eye Symptoms and Skin Changes Due To Elevated Plasma Tyrosine Levels: Inadequate restriction of tyrosine and phenylalanine intake can result in elevated levels of plasma tyrosine, which may lead to keratitis (eye problems) and hyperkeratotic plaques (thickening of the skin on the soles and palms).

Living with AKU

HARLIKU, an FDA-approved treatment for AKU is now available to reduce urinary HGA levels.[1]

For symptom management, your healthcare provider may recommend anti-inflammatory medication and pain relief, while more severe cases may require surgery and joint replacement.[4] Staying active with light exercise can help slow down the progression of osteoarthritis.[6]

You can do some gentle exercise to improve joint flexibility, and build muscle strength, for example:

- Pilates
- Tai Chi
- Cycling
- Yoga
- Walking
- Swimming

Try these Pilates exercises from the AKU Society here

You should **avoid** high impact sports or exercises that put additional strain on the joints, such as:

- Baseball
- Football
- Basketball
- Soccer

Please consult your healthcare provider before beginning any new exercise program. Cycle Pharmaceuticals accepts no liability for injuries or health issues arising from participation in these activities.

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Your healthcare provider will obtain a slit-lamp examination prior to initiating HARLIKU treatment, regularly during treatment and may reexamine you if you develop symptoms or if you develop high plasma tyrosine levels. Your HARLIKU treatment may be temporarily interrupted until symptoms have resolved.

Introducing HARLIKU

HARLIKU is indicated for the reduction of urine HGA in adult patients with AKU.[1]

The first and only FDA-approved treatment for AKU[1]

Reduces urinary HGA levels by up to 97%,[1] which may slow down AKU progression[7]

Accompanied by Cycle Vita, where you can find one-to-one support*

NOT ACTUAL PATIENTS

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Changes in Blood Profile: You may develop leukopenia (reduction in the number of white blood cells, which form part of the immune system) and severe thrombocytopenia (abnormally low levels of platelets, which help the blood to clot). Your healthcare provider will monitor platelet and white blood cell counts during HARLIKU therapy.

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HARLIKU

The effects of nitisinone, the active ingredient in HARLIKU, have been studied in clinical trials and shown to benefit adult patients with AKU.[7,8]

Based on the results from the studies, in which patients were treated with nitisinone for up to three years, HARLIKU helped patients by:

- Improving quality of life in the areas of pain, energy levels, and physical functioning[8]
- Improving their performance in a walking test[8]
- Slowing further AKU progression[7]

NOT AN ACTUAL PATIENT

Step towards a brighter future with HARLIKU, let's go!

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Taking HARLIKU

Take **one tablet** (2 mg nitisinone) orally, once a day, every day.

You have the flexibility to take HARLIKU **with or without food.**

If you miss a dose, **take the next dose at the scheduled time.** Do NOT take two doses at once to make up for the missed dose.

Throughout your treatment, your healthcare provider may monitor your blood tyrosine levels regularly. If your tyrosine levels are high, your healthcare provider may recommend diet adjustments or pause your HARLIKU treatment.

Important Safety Information

Drug Interactions: Nitisinone can interfere with the effect of other medicines. Tell your healthcare provider or pharmacist if you are taking, have recently taken or might take any other medicines.

Cycle Vita – Dedicated Support for You

CYCLE VITA™
Support *for life*

We know that life-changing treatments need a support system which is tailored to the unique challenges you might be facing. That's why we created Cycle Vita, our dedicated patient support program, which delivers individualized product and process support* at every step, including:

Bridge Program: A free supply of HARLIKU allows you to begin therapy immediately while Cycle Vita secures appropriate Benefit Verification and assists with Prior Authorization. The Bridge Program is also available if you are experiencing a temporary lapse in insurance. Bridge duration is driven by the active pursuit of insurance coverage by your clinic.

Co-Pay Assistance Program: Commercially insured eligible patients may pay as little as $0.

Reimbursement Research Support: The Cycle Vita team are experts in assisting with securing coverage, and can support you throughout the process, including Benefit Investigations and Prior Authorization assistance. Where an appeal is needed, Cycle Vita will work with your insurer to understand the requirements and help with any reimbursement gaps.

Continuous Clinical Product Support: Cycle Vita provides you with product support to help manage every aspect of the HARLIKU therapeutic routine, such as onboarding onto therapy, clinical education and ongoing support with adherence. Additional support with nutrition and managing the physical aspects of AKU are available on request.

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The Cycle Vita Team

CYCLE VITA™
Support *for life*

The Cycle Vita team is just a phone call away. Throughout your HARLIKU treatment, you can expect to hear from two different types of people at Cycle Vita.

Clinical Education Managers

provide you with clinical education, product support, and nutritional support (when necessary).*

Access Specialists

help you access HARLIKU through enrollment, financial and pharmacy support.*

A friendly and familiar team is here at Cycle Vita

888-360-8482 | hello@cyclevita.life | www.cyclevita.life

Important Safety Information

Use in Specific Populations:

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Visit harliku.com for more Information.

Visit harliku.com/pi/ for the full Prescribing Information.

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References
1. HARLIKU (nitisinone) Tablets. Prescribing Information. Cycle Pharmaceuticals Ltd 2. Introne WJ, Perry M, Chen M. 2003 (updated 2021). Alkaptonuria. Available at: https://www.ncbi.nlm.nih.gov/sites/books/NBK1454/ [Accessed May 29 2025] 3. AKU Society. Symptoms. Available at https://akusociety.org/symptoms/ [Accessed May 9 2025] 4. NORD. 2017. Alkaptonuria. Available at https://rarediseases.org/rare-diseases/alkaptonuria/ [Accessed May 12 2025] 5. Rudebeck M, Scott C, Sireau N, Ranganath L. 2020. A patient survey on the impact of alkaptonuria symptoms as perceived by the patients and their experiences of receiving diagnosis and care. JIMD Rep. 53(1):71-79. doi:10.1002/jmd2.12101 6. AKU Society. Self-Management. Available at https://akusociety.org/self-management/ [Accessed May 12 2025] 7. Ranganath LR, Khedr M, Milan AM, et al. 2018. Nitisinone arrests ochronosis and decreases rate of progression of Alkaptonuria: Evaluation of the effect of nitisinone in the United Kingdom National Alkaptonuria Centre. Mol Genet Metab. 125(1-2):127-134. doi:10.1016/j.ymgme.2018.07.011 8. Spears KR, Rossignol F, Perry MB, et al. 2024 Patient-reported outcomes and functional assessments of patients with Alkaptonuria in a 3-year Nitisinone treatment trial. Mol Genet Metab. 143(1-2),108562. doi:10.1016/j.ymgme.2024.108562

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*Some areas of support may not be accessible to all patients. Eligibility criteria may apply to ensure compliance with all applicable federal and state requirements, and benefits may be limited to commercially insured patients only. For more detailed information about eligibility, terms and conditions, please contact the Cycle Vita team at 888-360-8482.

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