Clinical Policy: Methoxsalen (Uvadex)

Reference Number: HIM.PA.17
Effective Date: 12.01.18
Last Review Date: 11.22
Line of Business: HIM

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Methoxsalen (Uvadex®) is a naturally occurring photoactive substance that belongs to a group of compounds known as psoralens or furocoumarins.

FDA Approved Indication(s)

Uvadex is indicated for extracorporeal administration with the THERAKOS® UVAR XTS® or THERAKOS® CELLEX® Photopheresis System in the palliative treatment of the skin manifestations of cutaneous T-cell lymphoma (CTCL) that is unresponsive to other forms of treatment.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Uvadex is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Cutaneous T-Cell Lymphoma (must meet all)**:**

1. Diagnosis of CTCL;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Failure of at least 2 of the following therapies (*see Appendix B*), unless clinically significant adverse effects are experienced or all are contraindicated:
   a. External beam radiation therapy;
   b. PUVA/UVB phototherapy;
   c. Systemic retinoid;
   d. Interferon-alpha or interferon-gamma;
   e. Methotrexate;
   f. Mechlorethamine;
   g. Istodax® or Zolinza®;
   h. Adcetris®;
   i. Poteligeo®;
   j. Folotyn®;
   k. Gemcitabine;
   l. Liposomal doxorubicin;
   m. Keytruda®;

n. Alemtuzumab (*note: credit can be given for prior use of this agent, but members should not be redirected to it as it is no longer commercially available*);

**Prior authorization may be required for Istodax, Zolinza, Adcetris, Poteligeo, Folotyn, and Keytruda*

5. Request meets one of the following (a or b):*
   a. Dose does not exceed treatment volume (mL) x 0.017 per treatment;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months (7 treatment cycles)

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: HIM.PA.154 for health insurance marketplace.

II. Continued Therapy

A. Cutaneous T-Cell Lymphoma (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Uvadex for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. Member has not yet received a total of 7 treatment cycles;
4. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed treatment volume (mL) x 0.017 per treatment;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: up to a total of 6 months (up to a total of 20 treatment cycles)

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: HIM.PA.154 for health insurance marketplace.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – HIM.PA.154 for health insurance marketplace.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CTCL: cutaneous T-cell lymphoma
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
mechlorethamine, nitrogen mustard	0.2 mg/kg or 6 mg/m^2 given as a single IV dose on day 1, or on days 1 and 8 of a regimen. Alternatively, it may be given as 0.1 mg/kg IV once daily for 4 successive days every 3—6 weeks	0.4 mg/kg/dose or 6 mg/m^2/dose
interferons (interferon-alpha-2b, interferon-gamma-1b)	Varies	Varies
methotrexate	25 to 50 mg PO every week	50 mg/week
retinoids (e.g., Targretin® [bexarotene], all-trans retinoid acid, isotretinoin, [13-cis-retinoic acid, acitretin])	Varies	Varies
Adcetris® (brentuximab vedotin)	1.8 mg/kg IV every 3 weeks until disease progression or a maximum of 16 cycles	180 mg/dose
Poteligeo® (mogamulizumab)	1 mg/kg IV on days 1, 8, 5, and 22 in cycle 1, then 1 mg/kg IV on days 1 and 15 in subsequent cycles until disease progression.	1 mg/kg/dose

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
HDAC-inhibitors (e.g., Istodax® [romidepsin], Zolinza® [vorinostat])	Varies	Varies
PUVA/UVB	Varies **There are no disease-specific guidelines for phototherapy used to treat mycosis fungoides and Seezary syndrome (MF/SS) despite the fact that efficacy in many cases equals or surpasses that of systemic medications*	Varies
Electron beam radiation therapy	8 to 12 Gy for individual plaque and tumor lesions; 24 to 30 Gy for unilesional presentation; or 12 to 36 Gy (4 to 6 Gy per week) of total skin electron beam therapy to cover the entire cutaneous surface	Undetermined
Folotyn® (pralatrexate)	30 mg/m^2 IV once weekly for 6 weeks; repeat cycles every 7 weeks until disease progression	See regimen
gemcitabine	1,200 mg/m^2 IV over 30 minutes on days 1, 8, and 15 repeated every 28 days for 3 to 6 cycles	See regimen
liposomal doxorubicin (Doxil®)	20 or 40 mg/m^2 IV once every 4 weeks for up to 8 cycles	See regimen
Keytruda® (pembrolizumab)	2 mg/kg every 3 weeks for up to 24 months	See regimen
alemtuzumab (Campath®)	30 mg IV 3 times weekly	See regimen

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): idiosyncratic or hypersensitivity reactions to methoxsalen, other psoralen compounds or any of the excipients; photosensitivity; aphakia; contraindicated to photopheresis procedure
- Boxed warning(s): methoxsalen should be used only by physicians who have special competence in the diagnosis and treatment of cutaneous T-cell lymphoma and who have special training and experience in the THERAKOS CELLEX Photopheresis System. Please consult the CELLEX Operator's Manual before using this product.

Appendix D: General Information

- CTCLs are a group of non-Hodgkin's lymphoma of mature T-cells that primarily present in the skin, and at times progress to involve lymph nodes, blood, and visceral organs. Mycosis fungoides is the most common subtype with primary cutaneous involvement and Sezary syndrome is an erythrodermic, leukemic variant of CTCL that is characterized by significant blood involvement and lymphadenopathy.

- There is no clinical evidence to show that treatment with Uvadex beyond 6 months or using a different schedule provides additional benefit.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Palliative treatment of CTCL	Calculate the dosage according to treatment volume as follows: • Treatment volume X 0.017 = mL of methoxsalen per treatment. Refer to the THERAKOS UVAR XTS or THERAKOS CELLEX Photopheresis System Operator's Manual. Each treatment involves collection of leukocytes, photoactivation, and reinfusion of photoactivated cells; methoxsalen is injected into the recirculation bag prior to the photoactivation phase. Treatment is given on 2 consecutive days every 4 weeks for at least 7 treatment cycles (approximately 6 months). In patients who have an increased skin score (from baseline) at the fourth treatment assessment (at approximately 3 months), an accelerated treatment schedule may be administered consisting of 2 consecutive treatments every 2 weeks for a maximum of 20 cycles. Resume the regular treatment schedule if there is a 25% improvement in the skin score after 4 consecutive weeks on the accelerated treatment schedule. There is no clinical evidence of additional treatment benefit beyond 6 months or with a different schedule.	Not established

VI. Product Availability

Single-use vial: 20 mcg/mL in 10 mL

VII. References

1. Uvadex Prescribing Information. West Chester, PA: Therakos, Inc.; March 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/020969s010lbl.pdf. Accessed July 27, 2022.
2. National Comprehensive Cancer Network. Primary Cutaneous Lymphomas Version 2.2022. Available: https://www.nccn.org/professionals/physician_gls/pdf/primary_cutaneous.pdf. Accessed July 27, 2022.

3. Olsen EA, Hodak E, Anderson T, et al. Guideline for phototherapy of mycosis fungoides and Sezary syndrome: a consensus statement of the United States Cutaneous Lymphoma Consortium. J Am Acd Dermatol. 2016; 74(1):27-58. http://dx.doi.org/10.1016/j.jaad.2015.09.033
4. Zackheim HS, Kashani-Sabet M, and Hwang ST. Low-dose methotrexate to treat erythrodermic cutaneous T-cell lymphoma: results in twenty-nine patients. J Am Acad Dermatol 1996;34:626-31.
5. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2022. Available at: http://www.clinicalpharmacology-ip.com/. Accessed July 27, 2022.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	09.04.18	11.18
4Q 2019 annual review: no significant changes; updated NCCN dosing per new template; references reviewed and updated.	08.28.19	11.19
4Q 2020 annual review: no significant changes; updated maximum methotrexate dose in Appendix B Therapeutic Alternatives per updated NCCN guideline recommendations; references reviewed and updated.	07.13.20	11.20
4Q 2021 annual review: no significant changes; BBW info updated; HIM.PHAR.21 changed to HIM.PA.154; references reviewed and updated.	06.25.21	11.21
4Q 2022 annual review: no significant changes; per NCCN, added Folotyn, gemcitabine, liposomal doxorubicin, Keytruda, and alemtuzumab as alternative prior therapy options; references reviewed and updated. Template changes applied to other diagnoses/indications.	07.27.22	11.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy,

contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.