

January 8, 2025

Analysis of 25.0547.02000 Step Therapy Protocol Limitations on Associated Conditions of Metastatic Cancer

Prepared for the North Dakota Legislative Council Pursuant to North Dakota Century Code 54-03-28

Amanda Rocha Richard Cadwell, ASA, MAAA Donna Novak, FCA, ASA MAAA



Table of Contents

I.	Evaluation of Proposed Mandated Health Insurance Services
II.	Process
III. Sym	Mandated Prohibition of Step Therapy Protocols on Drugs Used to Treat aptoms or Side Effects of Metastatic Cancer Benefits
В	ackground
	Condition
	Treatment
P	revalence of Coverage
	State Employee Retiree Group Health Insurance
	Essential Health Benefits Benchmark Plan and Commercial Coverage7
	nalyses Concerning Mandated No Step Therapy for Drugs Used to Treat Symptoms Associated Conditions of Metastatic Cancer
IV.	Other State Step Therapy Laws Regarding Metastatic Cancer Drugs 11
V.	Limitations
VI.	Reliance and Qualifications
App	endix A: Definitions
App	endix B: NovaRest Assumptions and Methodology
	endix C: List of prescription drug(s) identified to treat symptoms or side effects of astatic cancer
Refe	erences



I. Evaluation of Proposed Mandated Health Insurance Services

The North Dakota Legislative Council (NDLC) was asked to perform a cost benefit analysis of 25.0547.02000¹ (Draft Bill or the Bill) for the standing Legislative Assembly pursuant to the North Dakota Century Code (NDCC) 54-03-28. The Draft Bill amend and reenact section 19-02.1-16.3 of the NDCC, provides for a report; provides for an application; and provides an expiration date.

The Draft Bill 25.0547.02000, as proposed, states that "the recommended prescription drug, or sequence of prescription drugs, is prescribed to treat the individual's diagnosis of metastatic cancer or an associated condition." An associated condition is specified to mean a symptom or side effect associated with metastatic cancer or its treatment, and which further jeopardizes the health of an individual if left untreated per the judgement of a health care practitioner.

NovaRest, Inc. has been contracted as the NDLC's consulting actuary, and has prepared the following evaluation of the elimination of step therapy protocols for drugs used to treat symptoms or associated conditions of metastatic cancer.

This report includes information from several sources to provide more than one perspective on the proposed mandate to provide an unbiased report. As a result, there may be some conflicting information within the contents. Although we only used sources that we considered credible, we do not offer any opinions regarding whether one source is more credible than another.

NovaRest was asked to provide estimates for the North Dakota Public Employee Retirement System (NDPERS), as well as the impact if the Draft Bill was expanded to the commercial market. We were provided information on four plans administered by NDPERS, 1. Grandfathered PPO/Basic Plan, 2. Non-Grandfathered PPO/Basic Plan, 3. High Deductible Health Plan (HDHP), and 4. Dakota Retiree Plan. For the commercial market we used information from the National Association of Insurance Commissioners Supplemental Health Care Exhibit (SHCE) for individual, small group, and large group markets. Generally, when considering benefits for the individual and small group we considered the Affordable Care Act (ACA) single-risk pool plans, and for large group we considered a sample of plans from the largest three insurers in the North Dakota market.



The NDPERS non-Medicare plans use the same Sanford Health Plan formulary, and we did not identify step therapy on any of the identified prescription drug(s) used to treat symptoms or side effects of metastatic cancer. See Appendix C for the list of prescription drugs identified to treat symptoms or side effects of metastatic cancer.

The NDPERS Humana Insurance Company Medicare prescription drug plan uses a different formulary and only applies step therapy to brand versions of Imiquimod, also known as Zyclara. The generic version of Imiquimod, and all other identified prescription drug(s) used to treat symptoms or side effects of metastatic cancer are not subject to step therapy but they are subject to cost-sharing and Zyclara is a higher tier drug that requires significantly more member out-of-pocket costs. Therefore, we expect little increase in the utilization of Zyclara as the generic version is significantly less expensive, and we estimate there will be no impact on NDPERS Medicare from this proposed mandate.

In the commercial market, all insurers, with the exception of Medica, do not require step therapy for prescription drug(s) used to treat symptoms or side effects of metastatic cancer. Therefore, NovaRest estimates that additional percentage impact of eliminating step therapy protocols for drugs used to treat symptoms or associated with metastatic cancer to health care costs and premiums is 0.00% on a percent of premium basis and \$0.00 - \$0.03 on a per member per month (PMPM) basis for NDPERS and the individual, small group, and large group markets based on the insurer formularies. Please see Appendix B for NovaRest's assumptions and methodology.

Although there is no estimated impact, passing this mandate would ensure that future insurers or products in the market do not implement step therapy on current or future prescription drug(s) used to treat symptoms or side effects of metastatic cancer

II. Process

NovaRest was charged with addressing the following analyses regarding this proposed mandate:

- The extent to which the coverage will increase or decrease the cost of the service;
- The extent to which the coverage will increase the appropriate use of the service;
- The extent to which the coverage will increase or decrease the administrative expenses of insurers, including health maintenance organizations, or other organizations authorized to provide health benefit plans in the State, and the premium and administrative expenses of policyholders and contract holders; and
- The impact of this coverage on the total cost of health care.

NovaRest reviewed literature (including reports completed for other states that were either considering or have passed similar legislation) and developed an independent estimate of the proposed mandate's impact on premiums.



III. Mandated Prohibition of Step Therapy Protocols on Drugs Used to Treat Symptoms or Side Effects of Metastatic Cancer Benefits

The Draft Bill would mandate no step therapy protocols for prescription drug(s) used to treat symptoms or side effects of metastatic cancer. It does not require coverage of a nonformulary prescription drug, which is important considering each formulary we reviewed do not include the identified drugs on their formulary. Additionally, many of the drugs identified also include other utilization management such as prior authorization or prescription quantity limits even where step therapy is not included. These other utilization management methods are not impacted by the Draft Bill.

Background

Condition

Metastasis is when cancer spreads to areas of the body other than where it started. Metastatic cancer is also called metastatic tumor, metastasis (one cancerous tumor), metastases (more than one cancerous tumor), advanced cancer, secondary, cancer, or stage IV cancer.² Almost all cancers have the potential to metastasize but whether it does or not depends on the type, size, and location of the cancer among other factors.³

Metastatic cancer happens when cancer cells break off from the original tumor where they originated. There are three ways in which metastases can occur. One way is that cancer cells can grow directly into the tissue surrounding the primary tumor, they can travel through the bloodstream to other locations like other organs or bones, and they can move through the lymphatic system to other lymph nodes.⁴

There are currently 623,405 people living with the most common metastatic cancers in the United States.⁵ With a total population of 340,110,988⁶ in the United States, this translates to approximately 0.2% of the population living with metastatic cancer.

There are not always symptoms experienced with metastatic cancer. Some general signs and symptoms of advanced and metastatic cancer can include loss of energy and feeling tired and/or weak, unexpected weight loss, pain, shortness of breath or trouble breathing, and finding a new lump or swollen lymph node.⁷ If there are more serious symptoms, it would depend on where the cancer has spread. Some common symptoms are pain and fractures when cancer has spread to the bone, headache, seizures, or dizziness when cancer has spread to the brain, shortness of breath when cancer has spread to the lung, and jaundice or swelling in the belly when cancer has spread to the liver.⁸ Some of the most common sites of metastases are adrenal glands, bones, brain, liver, lungs, liver, and peritoneum.⁹



Treatment

There are many treatments for metastatic cancer that are determined by the type of cancer, where it has spread, and any of the patient's other health issues. Systemic therapy is commonly used for metastatic cancers. This may be intravenous or oral and is beneficial since it can address visible and microscopic cancer throughout the body.¹⁰ Other treatments can include radiotherapy, chemotherapy, hormonal therapies, targeted therapies, surgery, and palliative care.¹¹

The drugs used to treat symptoms of metastatic cancer also depend on the type of cancer and where it has spread. For example, bone metastases where cancer has spread to the bone, are commonly treated with bisphosphonates. Bisphosphonates are drugs that help slow the breakdown of bone and are used to help manage and prevent problems like hypercalcemia, bone pain, and broken bones.¹² The National Cancer Institute (NIH) has compiled a list of drugs approved by the FDA for some conditions caused by the cancer or its treatment.¹³ Please see the list of drugs in Appendix C.

Prevalence of Coverage

State Employee Retiree Group Health Insurance

The formulary for the NDPERS non-Medicare plans do not require step therapy for drugs used to treat symptoms of metastatic cancer. The most recent Sanford NDPERS Dakota Plan Members Formulary¹⁴ was checked for the drugs listed in the table in Appendix C.

The formulary for the NDPERS Medicare prescription drug plan included step therapy on brand versions of Imiquimod. Our understanding is that the generic version of Imiquimod would currently be required to be used first, prior to "stepping" to the brand version (Zyclara) which would not be permitted by the Draft Bill. The most recent Humana NDPERS prescription drug plan formulary was checked for the drugs listed in the table in Appendix C.¹⁵



Essential Health Benefits Benchmark Plan and Commercial Coverage

There are three insurers who offer the majority of the individual, small group, and large group insurance in North Dakota, per the 2023 SHCE, – Sanford Health Plan, BlueCross BlueShield North Dakota, and Medica Insurance Company. The drugs listed in the table above were searched for in each insurer's formularies. Below are the formularies where we did not identify any step therapy for the drugs listed in Appendix C:

- Sanford ACA Compliant Individual/Small Group 4-Tier Formulary¹⁶
- Sanford ACA Compliant Individual/Small Group 6-Tier Formulary¹⁷
- Sanford Commercial 3-Tier (Large Group/Self-Funded) Formulary¹⁸
- Sanford Commercial 5-Tier (Large Group/Self-Funded) Formulary¹⁹
- Sanford Commercial 6-Tier (Large Group/Self-Funded) Formulary²⁰
- BCBSND Health Ins. Market Individual Small Group 4-Tier Formulary²¹
- BCBSND Health Ins. Market Individual Small Group 6-Tier Formulary²²
- BCBSND Large Group Drug Formulary²³

Please note that the bill does not require coverage of nonformulary prescription drugs. So, not all the drugs listed in the table above are covered by each insurer, but if they are, they do not require step therapy.

The only insurer in the commercial who required step therapy for some of these drugs on their formulary was Medica. Medica's 2025 Commercial Drug List with ACA Preventive Drugs²⁴ requires step therapy for the following drugs used to treat symptoms associated with metastatic cancer:

- Dexamethasone oral tablets, dose pack
 - We note that Dexamethasone is available as a generic for many forms tablets, intensol, elixir, and oral solution without step therapy. Only the dose pack is subject to step therapy.
- Relistor subcutaneous solution
- Relistor subcutaneous syringe



Analyses Concerning Mandated No Step Therapy for Drugs Used to Treat Symptoms or Associated Conditions of Metastatic Cancer

The extent to which the coverage will increase or decrease the cost of the service.

There is expected to be no impact on the cost of the service for NDPERS non-Medicare plans. There are no step therapy protocols currently implemented for drugs used to treat symptoms or associated conditions of metastatic cancer. The proposed bill would not change that.

The NDPERS Medicare plan would likely remove the step therapy on brand versions of Imiquimod for the Humana prescription drug plan, which may increase the usage of brand versions of Imiquimod (particularly Zyclara) and may impact the cost. We expect a \$0 impact in the cost of Zyclara, due to the small amount of membership in the NDPERS Medicare plan, and the availability of the generic.

If the bill is expanded to include the commercial market, we would expect little to no impact as most insurers, with the exception of Medica, do not require step therapy for these drugs.

For Medica step therapy is applied to the Dexamethasone oral tablet dose pack, while a generic for many forms including tablets, intensol, elixir, and oral solution are available without step therapy. We expect a \$0 impact to the cost of the Dexamethasone oral tablet dose pack, based on potential utilization compared to the market size.

Medica also has step therapy on Relistor, which is included in Appendix C for constipation. Relistor is an expensive brand drug which we expect would only be used in select circumstances. We expect a \$0 impact on the cost due to additional usage likely being very small.



The extent to which the coverage will increase the appropriate use of the service.

For NDPERS non-Medicare we do not expect an increase in the use of any drugs, as all formulary drugs identified are already not subject to step-therapy.

For NDPERS Medicare there may be an increase in usage of Zyclara, however, as the generic version is less expensive and currently available without step therapy and we expect the increase in usage to be de minimis.

If the bill is expanded to include the commercial market, there may be a slight increase in the use of Dexamethasone oral tablet dose pack and Relistor which are subject to step therapy on Medica's formulary, however, Medica's market share is small and therefore we believe the increase in usage to be de minimis.

The extent to which the coverage will increase or decrease the administrative expenses of insurers, including health maintenance organizations, or other organizations authorized to provide health benefit plans in the State, and the premium and administrative expenses of policyholders and contract holders.

The formulary for the NDPERS non-Medicare plans do not require step therapy for drugs used to treat symptoms of metastatic cancer, and therefore we expect a \$0.00 PMPM or 0.0% impact to administrative expenses or premiums as a result of the Draft Bill.

The formulary for the NDPERS Medicare prescription drug plan included step therapy on brand versions of Imiquimod. The removal of step-therapy on drugs may result in a slight decrease in administrative costs on the NDPERS Medicare prescription drug plan only if the Draft Bill is passed, but we believe the decrease is de minimis.

Regarding the premium impact, our understanding is that the generic version of Imiquimod would currently be required to be used first, prior to "stepping" to the brand versions which would not be permitted by the Draft Bill. However, we assume most prescriptions would be for the generic version, and while there is a significant difference in cost, we believe the impact would be very small. All other drugs identified, including other drugs in the same category of Imiquimod, are not subject to step therapy. Therefore, the impact on premiums is the number of prescriptions for the brand version of one formulary drug, where the generic was not prescribed. We believe this impact is de minimis, and therefore expect a \$0.00 PMPM or 0.0% impact to premiums.

If expanded to the commercial market, only Medica would be impacted. As with NDPERS Medicare, removal of step-therapy may decrease administrative costs. We estimate a de minimis impact, however.

Regarding the premium impact to the commercial market, we did not identify any drugs used to treat metastatic cancer associated conditions subject to step therapy on the Sanford Health Plan or Blue Cross Blue Shield North Dakota plan formularies. Therefore we estiamte a \$0.00 PMPM or 0.0% of premium impact.



Medica is the only insurer who requires step therapy for drugs used to treat symptoms of cancer (Dexamethasone oral tablet dose pack and Relistor). Medica has membership in the small group and large group markets per the 2023 SHCE. Dexamethosone is available generic in many forms without step therapy, so the difference in cost of the dose pack would be the only impact. For Relistor, we estimated the increase in usage. We estimate a \$0.00 to \$0.03 PMPM increase to premiums or 0.00% (with rounding to the hundredth decimal place) increase to premiums to Medica only if language is expanded to the commercial market.

The impact of this coverage on the total cost of health care.

Changes to the cost of the service or utilization of the service would impact the total cost of health care in North Dakota. We do not anticipate any significant increase in the cost per drug, but the utilization of the services would likely increase slightly since these drugs would be offered to members without having to try other drugs as required by step therapy protocols. We estimate a \$0 increase in the total cost of health care with the passage of the Draft Bill to the NDPERS plans.

If the Draft Bill language is expanded to the North Dakota commercial market, we estimate less than a \$2,600 increase to the total cost of health care in North Dakota due to Medica removing step therapy on the Dexamethasone oral tablet dose pack and Relistor.



IV.Other State Step Therapy Laws Regarding Metastatic Cancer Drugs²⁵

There are many states who have passed laws regarding step therapy protocols. There are even fewer who prohibit step therapy for cancer drugs and none who prohibit step therapy for associated conditions of metastatic cancer. Below are the states who have passed laws limiting step therapy for cancer drugs:

Arkansas – Arkansas Code § 23-99-1114: Step therapy protocols must be created by either a multidisciplinary panel of experts following research and medical practice or in accordance with peer reviewed publications; insurer must follow and publish a clear and convenient process to request exemptions; exemption must be granted if protocol required drug is contraindicated or will likely cause serious adverse reaction, the drug is expected to be ineffective based on the known characteristics of the patient and drug, the patient has previously tried the drug or a similar drug, the drug is not in the best interest of the patient, or the patient is experiencing a positive therapeutic outcome on their current prescribed drug; determination required within seventy-two hours for nonurgent exemption requests and twenty-four hours for urgent exemption requests; insurers may not require step therapy for patients with metastatic cancer unless use of the preferred drug is consistent with FDA approved indications, the National Comprehensive Cancer Network indications, or peerreviewed recognized medical literature.

Colorado – Colorado Revised Statutes: § 10-16-145: Prohibits step therapy requirements for patients with stage four advanced metastatic cancer unless the preferred drug is consistent with FDA approved indications, the National Comprehensive Cancer Network indications, or peer-reviewed recognized medical literature; insurers may not require step therapy when the patient has tried the step-therapy-required drugs under current or previous health insurance plan and drugs were discontinued for lack of efficacy or adverse effects.

Connecticut – Connecticut General Statutes § 38a-510 and § 38a-544: Prohibits insurers from requiring step therapy for longer than sixty days or for any stage IV metastatic cancer prescription drug; requires insurers to have override process for step therapy regimens if the patient's health care provider deems the step therapy drug regimen clinically ineffective after sixty days of use.

Hawaii Proposed HB 2194²⁶: Prohibits a health insurer from requiring an insured diagnosed with stage two through stage five cancer to undergo step therapy prior to covering the insured for certain drugs prescribed by the insured's health care provider, under certain conditions.

Louisiana – Louisiana Revised Statute § 22:1053: Insurer must make step therapy override process easily accessible on their website; insurer must grant step therapy override request if the patient's provider can demonstrate that: the required drug has been ineffective in treating the patient, the required drug is reasonably expected to be ineffective based on the



known characteristics of the patient and drug, the preferred drug is contraindicated or will likely cause harm to the patient, the patient is currently receiving a positive therapeutic outcome for the condition under consideration, or the required drug is not in the best interest of the patient based on medical necessity; prohibits step therapy protocols for the treatment of stage-four advanced metastatic cancer or associated condition if the patient's current drug has an FDA or National Comprehensive Cancer Network indication, or is supported by medical literature; requires determination within seventy-two hours for nonurgent requests and twenty-four hours for urgent requests.

Maryland – Maryland Code, Insurance § 15-142: Prohibits insurers from imposing step therapy requirements if: the required drug has not been approved by FDA for the medical condition, or the patient's provider shows that the current prescription drug was ordered with the past 180 days and was effective in treating the patient's condition; prohibits insurers from imposing step therapy requirements for FDA approved drugs for treatment of patient's stage four advanced metastatic cancer when use of prescription drug is consistent with FDA approved indication or the National Comprehensive Cancer Network indication.

Minnesota – Minnesota Statutes Chapter 62Q § 62q.184: Requires insurers to make step therapy override process easily accessible on website; insurers must grant step therapy exception request if: the required drug is contraindicated or likely to harm the patient or likely to decrease the functional daily ability of the patient, the patient has tried the required drug and it was discontinued by the patient's provider for ineffectiveness or an adverse event, the patient is currently receiving a drug with a positive therapeutic outcome and the patient's provider indicated that a change is likely to be ineffective or cause harm; prohibits step therapy requirements for patients with stage four advanced metastatic cancer or associated conditions if use of the drug is consistent with FDA or National Comprehensive Care Network indications; requires determination within five days for nonurgent requests and seventy-two hours for urgent requests.

Nevada – 2021 Senate Bill 290 § 1: Requires insurers to permit patients with stage three or stage four cancer to apply for exemptions from step therapy protocols by having their provider present the clinical rationale for the exemption; requires insurers to grant step therapy protocol exemptions for patients with stage three or stage four cancer if the required drug has not been effective in treating the cancer, the delay of effective treatment would have severe of irreversible consequences for the patient, the required treatment is contraindicated or is likely to cause the patient harm or is likely to prevent the patient from engaging in daily living activities, or the condition of the patient is stable on their current drug.

North Dakota – North Dakota Century Code § 19-02.1-16.3: Insurers or pharmacy benefits managers may not require step therapy protocols for coverage of FDA approved prescription drugs for the treatment of cancer and usage of the drug is consistent with FDA approved indications or is supported by peer-reviewed medical literature.



V.Limitations

NovaRest has prepared this report in conformity with its intended use by persons technically competent to evaluate our estimate regarding Draft Bill No. 25.0547.02000. Any judgments as to the data contained in the report or conclusions about the ramifications of that data should be made only after reviewing the report in its entirety, as the conclusions reached by review of a section or sections on an isolated basis may be incorrect. Appropriate staff is available to explain and/or clarify any matter presented herein. It is assumed that any user of this report will seek such explanations as to any matter in question.

NovaRest did not have access to actual insurer claims data by service type or reimbursement rates. NovaRest also did not perform an insurer data request for the commercial market, or have access to the most recent rate filings in North Dakota. NovaRest has developed projections in conformity with what we believe to be the current and proposed operating environments and are based on best estimates of future experience within such environments. It should be recognized that actual future results may vary from those projected in this report. Factors that may cause the actual results to vary from the projected include new insurance regulations, differences in implementation of the required coverage by NDPERS, changes in medical treatments and practices, accounting practices, changes in federal and/or local taxation, external economic factors such as inflation rates, investment yields and ratings, and inherent potential for normal random fluctuations in experience.

VI. Reliance and Qualifications

We are providing this report to you solely to communicate our findings and analysis of Draft Bill 25.0547.02000. The reliance of parties other than the North Dakota Legislative Council (NDLC) on any aspect of our work is not authorized by us and is done at their own risk.

To arrive at our estimate, we made use of information provided by Sanford Health Plan for NDPERS, carrier rate filings and other public sources including census data and National Association of Insurance Commissioners financial data. We did not perform an independent investigation or verification. If this information was in any way inaccurate, incomplete, or out of date, the findings and conclusions in this report may require revision.

This memorandum has been prepared in conformity with the applicable Actuarial Standards of Practice.

We have no conflicts of interest in performing this review and providing this report.

We are members of the American Academy of Actuaries and meet that body's Qualification Standards to render this opinion. We meet the Qualification Standards promulgated by these professional organizations to perform the analyses and opine upon the results presented in this Actuarial Report.



Appendix A: Definitions

- a) "Associated condition" means a symptom or side effect associated with metastatic cancer or its treatment and which, in the judgment of the health care practitioner, further jeopardizes the health of an individual if left untreated.
- b) "Metastatic cancer" means cancer that has spread from the primary or original site to lymph nodes, nearby tissues, or other parts of the body.
- c) "Pharmacy benefits manager" has the same meaning as in section 19-03.6-01.
- d) "Step therapy protocol" means a protocol requiring an individual use a drug, or sequence of drugs, other than the prescription drug, or sequence of prescription drugs, the individual's health care provider recommend for the individual's treatment, before the pharmacy benefits manager or health plan allows coverage for the recommended prescription drug, or sequence of prescription drugs.



Appendix B: NovaRest Assumptions and Methodology Data

- NDPERS provided the premiums, claims, membership, and age distribution in NDPERS for 2023.
- The age and gender proportions of North Dakota's population are based on the 2023 Vintage population estimates.²⁷
- Health premiums and member months for the individual, small group, and large group markets are based on the 2023 Supplemental Health Care Exhibit (SHCE).

Assumptions

- We relied on the National Cancer Institute's list of the drugs approved to treat associated conditions of cancer.²⁸
- The formularies for Sanford, Medica, and BlueCross BlueShield of North Dakota's formularies were used to determine if the approved drugs are covered and if there are any limitations on those drugs.
- Zyclara was identified as requiring step therapy in the NDPERS Medicare prescription drug plan, while the generic version Imiquimod is available without step therapy. Member cost sharing for Imiquimod is significantly lower than for Zyclara and we believe due to the cost a very small percentage of people would opt for Zyclara, therefore we assumed a de minimis impact.
- The drugs that require step therapy in the commercial market are dexamethasone oral tablets, dose pack and Relistor. Dexamethasone is used to treat anemia, drug toxicity, and high blood calcium. The percentage of cancer patients who experience these symptoms is 22.7% 90% for anemia²⁹, 19% 53% for drug toxicity³⁰, and 10% 20% for high blood calcium³¹. Relistor is prescribed to patients who experience constipation which accounts for about 43% 58% of cancer patients.³²

Methodology

- We only expect an additional cost for the commercial market, where we applied the percentage of people with metastatic cancer to Medica's small group and large group populations since they are the only insurer to require step therapy for drugs used to treat symptoms of metastatic cancer.
- Calculated the number of these cancer patients who experience anemia, drug toxicity, high blood calcium, and constipation. These are the symptoms that are treated with dexamethasone and Relistor.
- Found costs for dexamethasone and Relistor and compared them to alternative drugs for them. We assumed no cost for the dexamethasone oral tablets since other options for dexamethasone are covered in the formulary with no restrictions. They are dexamethasone intensol, dexamethasone oral elixir, dexamethasone oral solution, and dexamethasone oral tablet. As an alternative to Relistor we compared the cost with Movantik.
- Calculated the difference between the drugs that require step therapy and alternative drugs who do not, which resulted in a 0.00% impact to premium (rounded to the nearest hundredth).



Appendix C: List of prescription drug(s) identified to treat symptoms or side effects of metastatic cancer³³

Condition	Medication
Actinic Keratosis	Aminolevulinic Acid (Ameluz, Levulan Kerastick)
	Fluorouracil (5-FU) Topical (Carac, Efudex, Fluoroplex, Tolak)
	Imiquimod (Aldara, Zyclara)
Aggressive Systemic	Imatinib Mesylate (Gleevec)
Mastocytosis	Midostaurin (Rydapt)
Anemia (Low Red Blood	Darbepoetin Alfa (Aranesp)
Cells)	Dexamethasone
	Epoetin Alfa (Epogen, Procrit, Retacrit)
	Lenalidomide (Revlimid)
	Luspatercept-aamt (Reblozyl)
Consideration of the second	Prednisone
Carcinoid Syndrome	Lanreotide Acetate (Somatuline Depot)
Cardiac Toxicity (Heart Side Effects)	Dexrazoxane Hydrochloride (Zinecard)
· · · · · · · · · · · · · · · · · · ·	Uridine Triacetate (Vistogard)
Condyloma Acuminata (Genital Warts)	Imiquimod (Aldara, Zyclara) Recombinant Human Papillomavirus (HPV) Nonavalent Vaccine
(Genital Waits)	(Gardasil 9)
	Recombinant Human Papillomavirus (HPV) Quadrivalent
	Vaccine (Gardasil)
	Recombinant Interferon Alfa-2b (Intron A)
Constipation	Methylnaltrexone Bromide (Relistor)
Cytokine Release	Tocilizumab (Actemra)
Syndrome	
Drug Extravasation (Drug	Dexrazoxane Hydrochloride (Totect)
Leakage in Tissues)	
Drug Toxicity (Severe Side	Amifostine (Ethyol)—for Cisplatin Toxicity
Effects)	Dexamethasone
	Dexrazoxane Hydrochloride (Zinecard)-for Doxorubicin
	Toxicity
	Glucarpidase (Voraxaze)—for Methotrexate Toxicity
	Prednisone
	Uridine Triacetate (Vistogard)—for Capecitabine or Fluorouracil
	Toxicity
Hemophagocytic	Emapalumab-lzsg (Gamifant)
Lymphohistiocytosis	
Hemorrhagic Cystitis	Mesna (Mesnex)
(Bleeding in the Bladder)	



Hepatic Veno – occlusive Disease (Blocked Liver Veins)	Defibrotide Sodium (Defitelio)
Hypercalcemia Malignancy (High Blood Calcium)	Denosumab (Xgeva) Dexamethasone Pamidronate Disodium (Aredia) Prednisone
Malignant Effusion	Zoledronic Acid (Zometa) Bleomycin Talc (Sterile Talc Powder, Sclerosol Intrapleural Aerosol, Steritalc) Thiotepa (Tepadina)
Mucositis (Inflamed Mucous Membranes)	Palifermin (Kepivance)
Nausea and Vomiting	Aprepitant (Cinvanti, Emend) Granisetron (Sancuso, Sustol) Granisetron Hydrochloride Netupitant and Palonosetron Hydrochloride (Akynzeo) Ondansetron Hydrochloride (Zofran) Palonosetron Hydrochloride (Aloxi) Rolapitant Hydrochloride (Varubi)
Neurotoxicity (Nervous System Side Effects)	Uridine Triacetate (Vistogard)
Neutropenia (Low Blood Neutrophils)	Filgrastim (Granix, Neupogen, Nivestym, Zarxio) Pegfilgrastim (Fulphila, Neulasta, Nyvepria, Udencyca, Ziextenzo)
Osteoporosis (Loss of Bone Density) Paroxysmal Nocturnal	Denosumab (Prolia) Raloxifene Hydrochloride (Evista) Ravulizumab-cwvz (Ultomiris)
Hemoglobinuria Renal Toxicity (Kidney Side Effects)	Amifostine (Ethyol)
Skin Changes Due to Cutaneous Metastases	Bexarotene (Targretin)
Thrombocytopenia (Low Blood Platelets)	Caplacizumab-yhdp (Cablivi) Dexamethasone Eltrombopag Olamine (Promacta) Fostamatinib Disodium (Tavalisse) Prednisone Romiplostim (Nplate)
Tumor Lysis Syndrome (Cell Breakdown and Organ Damage)	Rasburicase (Elitek)
Xerostomia (Dry Mouth)	Amifostine (Ethyol)

156 West Calle Guija, Suite 200, Sahuarita, AZ 85629 - 520-908-7246 - NovaRest.com Copyright © 2025 by NovaRest, Inc.



References

¹ We were unable to find an online link for 25.0547.02000. The Draft Bill was provided by NDLC. A similar bill is 25.0124.01000 (https://ndlegis.gov/assembly/68-2023/interim/25-0124-01000.pdf Accessed January 8, 2025), however, this bill includes reference to section 26.1-36.6-03. Regarding self-insurance which is not included in 25.0547.02000

² Canadian Cancer Society / Société canadienne du cancer. "What Is Metastatic Cancer?" *Canadian Cancer Society*, cancer.ca/en/cancer-information/cancer-types/metastatic/what-is-metastatic-

cancer#:~:text=Metastatic%20cancer%20is%20cancer%20that,cells%20as%20the%20primary%20cancer. Accessed 23 Dec. 2024.

³ "Metastasis: What To Expect When Cancer Spreads." *Cleveland Clinic*, 19 Dec. 2024,

my.clevelandclinic.org/health/diseases/22213-metastasis-metastatic-cancer.

⁴ Ibid.

⁵ Statistics and Graphs. (n.d.). Retrieved from

https://cancercontrol.cancer.gov/ocs/statistics#:~:text=There%20are%20623%2C405%20people%20living, 693%2C452%20by%20the%20year%202025.

⁶ United States Census Bureau. "Quick Facts United States". https://www.census.gov/quickfacts/. Accessed 31 Dec. 2024.

⁷ "What Are Advanced and Metastatic Cancers?" American Cancer Society,

www.cancer.org/cancer/managing-cancer/advanced-cancer/what-is.html. Accessed 23 Dec. 2024.

⁸ "Metastatic Cancer: When Cancer Spreads." *NCI*, www.cancer.gov/types/metastatic-cancer. Accessed 23 Dec. 2024.

⁹ "Metastasis: What To Expect When Cancer Spreads." Cleveland Clinic, 19 Dec. 2024,

my.clevelandclinic.org/health/diseases/22213-metastasis-metastatic-cancer.

¹⁰ Tuesday, J. 26. (2022). Metastatic and Metastasized Cancers: Answers to 7 Common Questions.

Retrieved from https://www.mskcc.org/news/what-are-metastatic-and-metastasized-cancers

¹¹ Treatment for metastatic cancer. (n.d.). Retrieved from https://www.cancer.ie/cancer-information-and-support/cancer-types/metastatic-cancer/metastatic-cancer-treatment

¹² Cancer Resources from OncoLink | Treatment, Research. "Bone Metastases Treatment." *OncoLink*, www.oncolink.org/cancers/bone/bone-metastases/bone-metastases-

treatment#:~:text=Bisphosphonates%20are%20more%20effective%20for,supplements%20while%20on%2 0this%20treatment. Accessed 24 Dec. 2024.

¹³ "Drugs Approved for Conditions Related to Cancer." NCI, www.cancer.gov/about-

cancer/treatment/drugs/related-conditions. Accessed 24 Dec. 2024.

¹⁴ www.sanfordhealthplan.com/-/media/files/documents/members/pharmacy-information/hp6912-north-dakota-public-employee-retirement-system-ndpers.pdf. Accessed 31 Dec. 2024.

¹⁵ https://www.ndpers.nd.gov/retired-members/insurance-plans-retired-members/health-insurance-plans-retired-members/medicare. Accessed 31 Dec. 2024.

¹⁶ www.sanfordhealthplan.com/-/media/files/documents/members/pharmacy-information/hp6911-4tier-simplicity-and-true-for-individual-and-small-groups.pdf. Accessed 31 Dec. 2024.

¹⁷ www.sanfordhealthplan.com/-/media/files/documents/members/pharmacy-information/hp8292-6tier-simplicity-and-true-for-individual-and-small-groups.pdf. Accessed 31 Dec. 2024.

¹⁸ www.sanfordhealthplan.com/-/media/files/documents/members/pharmacy-information/hp6909-3tiercommercial-large-group-selffunded.pdf. Accessed 31 Dec. 2024.

¹⁹ (N.d.). Retrieved from https://www.sanfordhealthplan.com/-/media/files/documents/members/pharmacy-information/hp6910-5tier-commercial-large-group-selffunded.pdf. Accessed 31 Dec. 2024.

²⁰ (N.d.). Retrieved from https://www.sanfordhealthplan.com/-/media/files/documents/members/pharmacy-information/hp8127-6tier-commercial-large-group-selffunded.pdf. Accessed 31 Dec. 2024.



21

www.bcbsnd.com/content/dam/bcbsnd/documents/pharmacy/HIM_4_Tier_Qualified_Health_Plan_Formul ary_2025.pdf. Accessed 31 Dec. 2024.

²² (N.d.). Retrieved from

https://www.bcbsnd.com/content/dam/bcbsnd/documents/pharmacy/HIM_6_Tier_Qualified_Health_Plan_Formulary_2025.pdf. Accessed 31 Dec. 2024.

²³ www.bcbsnd.com/content/dam/bcbsnd/documents/pharmacy/NetResults-Formulary-2024.pdf. Accessed 31 Dec. 2024.

²⁴ Search Pharmacy Benefits and Preferred Drug List for Group Plan Members. (n.d.). Retrieved from https://www.medica.com/find-care/select-employer-provided-plan/pharmacy-benefits#. Accessed 31 Dec. 2024.

²⁵ "Health Insurance State Laws: Step Therapy: Triage Cancer." *Triage Cancer*® / *Finances-Work-Insurance*, 16 Feb. 2024, triagecancer.org/state-laws/health-insurance-step-therapy#steptherapy-top. Accessed 31 Dec. 2024.

²⁶ Hawaii HB2194: 2024: Regular Session. (n.d.). Retrieved from

https://legiscan.com/HI/bill/HB2194/2024. Accessed 31 Dec. 2024.

²⁷ Bureau, US Census. "State Population by Characteristics: 2020-2024." *Census.Gov*, 25 Nov. 2024, www.census.gov/data/tables/time-series/demo/popest/2020s-state-detail.html.

²⁸ "Drugs Approved for Conditions Related to Cancer." NCI, www.cancer.gov/about-

cancer/treatment/drugs/related-conditions. Accessed 24 Dec. 2024.

²⁹ Wondm, S. A., Dagnew, S. B., Gubae, K., Tesfaye, T. C., & Tamene, F. B. (2024). Determinants of anemia among patients receiving cancer chemotherapy in Northwest Ethiopia. *Frontiers in Medicine*, *11*. https://doi.org/10.3389/fmed.2024.1415877. Accessed 31 Dec. 2024.

³⁰ Lee, E. M., Jiménez-Fonseca, P., Galán-Moral, R., Coca-Membribes, S., Fernández-Montes, A., Sorribes, E., ... Calderon, C. (2023). Toxicities and Quality of Life during Cancer Treatment in Advanced Solid Tumors. Retrieved from https://pmc.ncbi.nlm.nih.gov/articles/PM. Accessed 31 Dec. 2024.

³¹ Canadian Cancer Society / Société canadienne du cancer. (n.d.). High calcium levels (hypercalcemia). Retrieved from https://cancer.ca/en/treatments/side-effects/high-calcium-

levels#:~:text=Hypercalcemia%20means%. Accessed 31 Dec. 2024.

³² Wickham, R. J. (n.d.). Managing Constipation in Adults With Cancer. Retrieved from

https://pmc.ncbi.nlm.nih.gov/articles/P. Accessed 31 Dec. 2024.

³³ "Drugs Approved for Conditions Related to Cancer." *NCI*, www.cancer.gov/aboutcancer/treatment/drugs/related-conditions. Accessed 24 Dec. 2024.