

Performance Measures to Focus on Quality of Care

BY JANE ANDERSON
Contributing Writer

The National Committee for Quality Assurance is finalizing new performance measures that will look at quality of care all the way down to the physician group and even the individual physician level.

The measures, which will form the foundation of a new Health Employer Data and Information Set (HEDIS), could

require physicians to begin reporting some quality data to health plans directly—echoing other performance measurement efforts already underway nationwide.

The draft ambulatory care quality measures were released for public comment in October. Final measures are expected before the end of the year, according to an NCQA spokesman.

“This is a big change,” said Dr. Bruce Bagley, medical director for quality improvement at the American Academy of

Family Physicians (AAFP) and a member of the NCQA committee that approved the draft measures. “Physicians now will begin to report some data from their clinical records, such as ‘Why I didn’t give an indicated medication.’ ”

HEDIS, which measures quality of care, is the main tool that health plans use to track and report on their performance to payers. Until now, HEDIS has used administrative claims data “almost exclusively” to measure quality at the health

plan level, said Dr. Bagley. Now, “NCQA has rewritten these specifications so that it’s possible to drive the measures down to the physician level. The measures can be used at the plan level or at the physician group level or even at the individual physician level, if there are enough patients.”

The draft measures are designed to allow health plans to report on physician performance for their networks. They include six prevention measures, such as breast cancer screening and influenza vaccination rates, as well as measures that address care for coronary artery disease, depression, and asthma. Measures addressing overuse and misuse of health care services also are part of the proposed HEDIS addition.

The measures include detailed technical specifications and implementation methods, such as appropriate sample sizing, for use by health plans. The draft measures are not new, Dr. Bagley pointed out. They

“We see these [measures] as supplementing a number of national and regional physician-level measurement efforts that are already underway.”

These measures were included in the National Quality Forum-endorsed National Voluntary Consensus Standards for Physician-Focused Ambulatory Care, and the AQA (formerly the Ambulatory Care Quality Alliance) adopted these measures as part of its Recommended Starter Set of Clinical Performance Measures for Ambulatory Care. Therefore, physician organizations have had an opportunity to see them and comment on them prior to their release as part of HEDIS, Dr. Bagley said.

“We see these [measures] as supplementing a number of national and regional physician-level measurement efforts that are already underway,” said NCQA spokesman Jeff Van Ness. Because NCQA included detailed instructions for implementation, “this lowers the hurdle for plans to begin to move and implement these among physicians,” he said.

Nonetheless, Dr. Bagley said, once these measures are made part of HEDIS, physician groups and individual physicians will need to develop methods to collect the necessary information without resorting to retrospective chart audits. “We’re promoting prospective data collection,” such as checklists that can be filled out at the time of the patient visit, he said.

NCQA released the draft measures for public comment in October. Mr. Van Ness said that most of the comments NCQA has collected have come from large national health plans, although some comments have come from physicians and other stakeholders. He declined to provide information on the content of the comments, citing privacy concerns.

Dr. Lynne Kirk, president of the American College of Physicians, said that her organization’s main concern about the new quality measures was any additional paperwork and cost burden they might add to physicians’ workloads.

TRI-LUMA® Cream
(fluocinolone acetonide 0.01%, hydroquinone 4%, tretinoin 0.05%)
Brief Summary For External Use Only Not for Ophthalmic Use Rx only

INDICATIONS AND USAGE:

TRI-LUMA Cream is indicated for the short-term intermittent treatment of moderate to severe melasma of the face, in the presence of measures for sun avoidance, including the use of sunscreens.

The following are important statements relating to the indication and usage of TRI-LUMA Cream:

- TRI-LUMA Cream, a combination drug product containing corticosteroid, retinoid, and bleaching agent, was proven safe for the intermittent treatment of melasma, with cumulative treatment time of at least 180 days. Because melasma usually recurs upon discontinuation of TRI-LUMA Cream, patients can be retreated with TRI-LUMA until melasma is resolved. Patients need to avoid sunlight exposure, use sunscreen with appropriate SPF, wear protective clothing, and change to non-hormonal forms of birth control, if hormonal methods are used.
- In clinical trials used to support the use of TRI-LUMA Cream in the treatment of melasma, patients were instructed to avoid sunlight exposure to the face, wear protective clothing and use a sunscreen with SPF 30 each day. They were to apply the study medication each night after washing their face with a mild soapless cleanser.
- The safety and efficacy of TRI-LUMA Cream in patients of skin types V and VI have not been studied. Excessive bleaching resulting in undesirable cosmetic effect in patients with darker skin cannot be excluded.
- The safety and efficacy of TRI-LUMA Cream in the treatment of hyperpigmentation conditions other than melasma of the face have not been studied.
- Because pregnant and lactating women were excluded from, and women of child-bearing potential had to use birth control measures in the clinical trials, the safety and efficacy of TRI-LUMA Cream in pregnant women and nursing mothers have not been established (See PRECAUTIONS, Pregnancy).

CONTRAINDICATIONS: TRI-LUMA Cream is contraindicated in individuals with a history of hypersensitivity, allergy, or intolerance to this product or any of its components.

WARNINGS: TRI-LUMA Cream contains sodium metabisulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening asthmatic episodes in susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in non-asthmatic people.

TRI-LUMA Cream contains hydroquinone, which may produce exogenous ochronosis, a gradual blue-black darkening of the skin, whose occurrence should prompt discontinuation of therapy. The majority of patients developing this condition are Black, but it may also occur in Caucasians and Hispanics.

Cutaneous hypersensitivity to the active ingredients of TRI-LUMA Cream has been reported in the literature. In a patch test study to determine sensitization potential in 221 healthy volunteers, three volunteers developed sensitivity reactions to TRI-LUMA Cream or its components.

PRECAUTIONS: General: TRI-LUMA Cream contains hydroquinone and tretinoin that may cause mild to moderate irritation. Local irritation, such as skin redness, peeling, mild burning sensation, dryness, and pruritus may be expected at the site of application. Transient skin redness or mild burning sensation does not preclude treatment. If a reaction suggests hypersensitivity or chemical irritation, the use of the medication should be discontinued.

TRI-LUMA Cream also contains the corticosteroid fluocinolone acetonide. Systemic absorption of topical corticosteroids can produce reversible hypothalamic-pituitary-adrenal (HPA) axis suppression with the potential for glucocorticosteroid insufficiency after withdrawal of treatment. Manifestations of Cushing’s syndrome, hyperglycemia, and glucocele can also be produced by systemic absorption of topical corticosteroid while on treatment. If HPA axis suppression is noted, the use of TRI-LUMA Cream should be discontinued. Recovery of HPA axis function generally occurs upon discontinuation of topical corticosteroids.

Information for Patients: Exposure to sunlight, sunlamp, or ultraviolet light should be avoided. Patients who are consistently exposed to sunlight or skin irritants either through their work environment or habits should exercise particular caution. Sunscreen and protective covering (such as the use of a hat) over the treated areas should be used. Sunscreen use is an essential aspect of melasma therapy, as even minimal sunlight sustains melanocytic activity.

Weather extremes, such as heat or cold, may be irritating to patients treated with TRI-LUMA Cream. Because of the drying effect of this medication, a moisturizer may be applied to the face in the morning after washing.

Application of TRI-LUMA Cream should be kept away from the eyes, nose, or angles of the mouth, because the mucosa is much more sensitive than the skin to the irritant effect. If local irritation persists or becomes severe, application of the medication should be discontinued, and the health care provider consulted. Allergic contact dermatitis, blistering, crusting, and severe burning or swelling of the skin and irritation of the mucous membranes of the eyes, nose, and mouth require medical attention. If the medication is applied excessively, marked redness, peeling, or discomfort may occur.

This medication is to be used as directed by the health care provider and should not be used for any disorder other than that for which it is prescribed.

Laboratory Tests: The following tests may be helpful in evaluating patients for HPA axis suppression

- ACTH or cosyntropin stimulation test
- A.M. plasma cortisol test
- Urinary free cortisol test

Drug Interactions: Patients should avoid medicated or abrasive soaps and cleansers, soaps and cosmetics with drying effects, products with high concentration of alcohol and astringent, and other irritants or keratolytic drugs while on TRI-LUMA Cream treatment. Patients are cautioned on concomitant use of medications that are known to be photosensitizing.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term animal studies to determine the carcinogenic potential of TRI-LUMA Cream have not been conducted.

Studies of hydroquinone in animals have demonstrated some evidence of carcinogenicity. The carcinogenic potential of hydroquinone in humans is unknown.

Studies in hairless albino mice suggest that concurrent exposure to tretinoin may enhance the tumorigenic potential of carcinogenic doses of UVB and UVA light from a solar simulator. This effect has been confirmed in a later study in pigmented mice, and dark pigmentation did not overcome the enhancement of photocarcinogenesis by 0.05% tretinoin. Although the significance of these studies to humans is not clear, patients should minimize exposure to sunlight or artificial ultraviolet irradiation sources.

Mutagenicity studies were not conducted with this combination of active ingredients. Published studies have demonstrated that hydroquinone is a mutagen and a clastogen. Treatment with hydroquinone has resulted in positive findings for genetic toxicity in the Ames assay in bacterial strains sensitive to oxidizing mutagens, in *in vitro* studies in mammalian cells, and in the *in vivo* mouse micronucleus assay. Tretinoin has been shown to be negative for mutagenesis in the Ames assay. Additional information regarding the genetic toxicity potential of tretinoin and of fluocinolone acetonide is not available.

A dermal reproductive fertility study was conducted in SD rats using a 10-fold dilution of the clinical formulation. No effect was seen on the traditional parameters used to assess fertility, although prolongation of estrus was observed in some females, and there was a trend towards an increase in pre- and post-implantation loss that was not statistically significant. No adequate study of fertility and early embryonic toxicity of the full-strength drug product has been performed. In a six-month study in minipigs, small testes and severe hypospadias were found when males were treated topically with the full strength drug product.

Pregnancy: Teratogenic Effects: Pregnancy Category C: TRI-LUMA Cream contains the teratogen, tretinoin, which may cause embryo-fetal death, altered fetal growth, congenital malformations, and potential neurologic deficits. It is difficult to interpret the animal studies on teratogenicity with TRI-LUMA Cream, because the availability of the dermal applications in these studies cannot be assured, and comparison with clinical dosing is not possible. There are no adequate and well-controlled studies in pregnant women. TRI-LUMA Cream should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Summary Statement on Teratogenic Risk

TRI-LUMA Cream contains the teratogen, tretinoin, which may cause embryo-fetal death, altered fetal growth, congenital malformations, and potential neurologic deficits. However, human data have not confirmed an increased risk of these developmental abnormalities when tretinoin is administered by the topical route.

Clinical considerations relevant to actual or potential inadvertent exposure during pregnancy:

In clinical trials involving TRI-LUMA Cream in the treatment of facial melasma, women of child-bearing potential initiated treatment only after having had a negative pregnancy test and used effective birth control measures during therapy. Thus, safety and efficacy of TRI-LUMA Cream in pregnancy has not been established. In general, use of drugs should be reduced to a minimum in pregnancy. If a patient has been inadvertently exposed to TRI-LUMA Cream in pregnancy, she should be counseled on the risk of teratogenesis due to this exposure. The risk of teratogenesis due to topical exposure to TRI-LUMA Cream may be considered low. However, exposure during the period of organogenesis in the first trimester is theoretically more likely to produce adverse outcome than in later pregnancy.

The prescriber should have the following clinical considerations in making prescribing decisions:

- The potential developmental effects of tretinoin are serious but the risk from topical administration is small.
- Exposure during the period for organogenesis in the first trimester is theoretically more likely to produce adverse outcome than in later pregnancy.
- The risk to the mother for not treating melasma should be determined by the physician with the patient. Mild forms of melasma may not necessarily require drug treatment. TRI-LUMA Cream is indicated for the treatment of moderate to severe melasma. Melasma may also be managed with other forms of therapy such as topical hydroquinone in the presence of sunlight avoidance, or stopping the use of hormonal birth control methods. If possible, delaying treatment with TRI-LUMA Cream until after delivery should be considered.

• There are no adequate and well-controlled studies in pregnant women. TRI-LUMA Cream should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Data Discussion: Tretinoin is considered to be highly teratogenic upon systemic administration. Animal reproductive studies are not available with topical hydroquinone. Corticosteroids have been shown to be teratogenic in laboratory animals when administered systemically at relatively low dosage levels. Some corticosteroids have been shown to be teratogenic after dermal application in laboratory animals.

1. Human Data

• In clinical trials involving TRI-LUMA Cream in the treatment of facial melasma, women of child-bearing potential initiated treatment only after having had a negative pregnancy test, and used effective birth control measures during therapy. However, 15 women became pregnant during treatment with TRI-LUMA Cream. Of these pregnancies, 6 resulted in healthy babies, 6 outcomes still unknown, 2 were reported as miscarriages, and 1 case was lost to follow-up.

• Epidemiologic studies have not confirmed an increase in birth defects associated with the use of topical tretinoin. However, there may be limitations to the sensitivity of epidemiologic studies in the detection of certain forms of fetal injury, such as subtle neurologic or intelligence deficits.

2. Animal Data

• In a dermal application study using TRI-LUMA Cream in pregnant rabbits, there was an increase in the number of *in utero*

deaths and a decrease in fetal weights in litters from dams treated topically with the drug product.

• In a dermal application study in pregnant rats treated with TRI-LUMA Cream during organogenesis there was evidence of teratogenicity of the type expected with tretinoin. These morphological alterations included cleft palate, protruding tongue, open eyes, umbilical hernia, and retinal folding or dysplasia.

• In a dermal application study on the gestational and postnatal effects of a 10-fold dilution of TRI-LUMA Cream in rats, an increase in the number of stillborn pups, lower pup body weights, and delay in preputial separation were observed. An increase in overall activity was seen in some treated litters at postnatal day 22 and in all treated litters at five weeks, a pattern consistent with effects previously noted in animals exposed *in utero* with retinoic acids. No adequate study of the late gestational and postnatal effects of the full-strength TRI-LUMA Cream has been performed.

• It is difficult to interpret these animal studies on teratogenicity with TRI-LUMA Cream, because the availability of the dermal applications in these studies could not be assured and comparison with clinical dosing is not possible. All pregnancies have a risk of birth defect, loss, or other adverse event regardless of drug exposure. Typically, estimates of increased fetal risk from drug exposure rely heavily on animal data. However, animal studies do not always predict effects in humans. Even if human data are available, such data may not be sufficient to determine whether there is an increased risk to the fetus. Drug effects on behavior, cognitive function, and fertility in the offspring are particularly difficult to assess.

Nursing Mothers: Corticosteroids, when systemically administered, appear in human milk. It is not known whether topical application of TRI-LUMA Cream could result in sufficient systemic absorption to produce detectable quantities of fluocinolone acetonide, hydroquinone, or tretinoin in human milk. Because many drugs are secreted in human milk, caution should be exercised when TRI-LUMA Cream is administered to a nursing woman. Care should be taken to avoid contact between the infant being nursed and TRI-LUMA Cream.

Pediatric Use: Safety and effectiveness of TRI-LUMA Cream in pediatric patients have not been established.

Geriatric Use: Clinical studies of TRI-LUMA Cream did not include sufficient number of subjects aged 65 and over to determine whether they respond differently from younger subjects. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal or cardiac function, and of concomitant disease or other drug therapy.

ADVERSE REACTIONS: In the controlled clinical trials, adverse events were monitored in the 161 patients who used TRI-LUMA Cream once daily during an 8-week treatment period. There were 102 (63%) patients who experienced at least one treatment-related adverse event during these studies. In the long-term clinical study, from a total of 314 patients treated with TRI-LUMA Cream for at least 180 cumulative days, there were 202 (64%) patients who experienced at least one treatment-related adverse event. No significant increase in severity or incidence of the adverse events was observed from long term use of TRI-LUMA Cream compared with events reported during the 8-week controlled clinical studies. The most frequently reported adverse events that were observed from the controlled clinical trials and the long term safety were erythema, desquamation, and burning, at the site of application. The number and percentages of these events were markedly lower in the long-term study than in the controlled clinical studies. The majority of these events were mild to moderate in severity. Adverse events reported by at least 1% of patients and judged by the investigators to be reasonably related to treatment with TRI-LUMA Cream from the controlled clinical studies and the long-term study are summarized (in decreasing order of frequency).

Incidence and Frequency of Treatment-related Adverse Events with TRI-LUMA Cream in at least 1% or more of Patients (N=161)	
Adverse Event	Number (%) of Patients
Erythema	66 (41%)
Desquamation	61 (38%)
Burning	29 (18%)
Dryness	23 (14%)
Pruritus	18 (11%)
Acne	8 (5%)
Paresthesia	5 (3%)
Telangiectasia	5 (3%)
Hyperesthesia	3 (2%)
Pigmentary changes	3 (2%)
Irritation	3 (2%)
Papules	2 (1%)
Acne-like rash	1 (1%)
Rosacea	1 (1%)
Dry mouth	1 (1%)
Rash	1 (1%)
Vesicles	1 (1%)

In an open-label long-term safety study, patients who have had cumulative treatment of melasma with TRI-LUMA Cream for 6 months showed a similar pattern of adverse events as in the 8-week studies.

Summary of Most Common Treatment-related Adverse Events (TRAE) Study 29		
Preferred Term	All Patients (N=569)	Number (%) of Patients
		Treatment Group
		TRI-LUMA
		Patients with at least 180 Cumulative Days of TRI-LUMA Treatment (N=314)
Total number of TRAE*	326 (57.29)	202 (64.33)
Application site erythema	166 (29.17)	105 (33.44)
Application site desquamation	145 (25.48)	91 (28.98)
Application site dryness	46 (8.08)	27 (8.60)
Application site burning	38 (6.68)	25 (7.96)
Application site inflammation	31 (5.45)	24 (7.64)
Application site reaction nos	31 (5.45)	17 (5.41)
Application site rash	30 (5.27)	18 (5.73)
Application site pruritus	24 (4.22)	18 (5.73)
Application site pigmentation changes	23 (4.04)	18 (5.73)

* Defined as “probably” or “possibly” related to study medication

Data source: Section 14.3, Tables 8.1.1, 8.1.2, and 8.1.3

The severity, incidence and type of adverse events experienced from 6 months cumulative use were not significantly different from the events reported for all patients.

The incidence of application site pigmentation changes that occurred in both the controlled and long-term safety studies included 11 occurrences of hyperpigmentation and 18 occurrences of hyperpigmentation in 27 patients.

The following local adverse reactions have been reported infrequently with topical corticosteroids. They may occur more frequently with the use of occlusive dressings, especially with higher potency corticosteroids. These reactions are listed in an approximate decreasing order of occurrence: burning, itching, irritation, dryness, folliculitis, acneiform eruptions, hyperpigmentation, perioral dermatitis, allergic contact dermatitis, secondary infection, skin atrophy, striae, and milaria.

TRI-LUMA Cream contains hydroquinone, which may produce exogenous ochronosis, a gradual blue-black darkening of the skin, whose occurrence should prompt discontinuation of therapy.

Cutaneous hypersensitivity to the active ingredients of TRI-LUMA Cream has been reported in the literature. In a patch test study to determine sensitization potential in 221 healthy volunteers, three volunteers developed sensitivity reactions to TRI-LUMA Cream or its components.

Marketed by: Galderma Laboratories, L.P., Fort Worth, TX 76177 USA
GALDERMA is a registered trademark.

Manufactured by: Hill Laboratories, Inc., Sanford, FL 32773 USA
20024-1203 Revised: December 2003

References: 1. Balkrishnan R, Kelly AP, McMichael A, Torok H. Improved quality of life with effective therapy of facial melasma. *J Drugs Dermatol.* 2004;3:247-249. 2. Taylor SC, Torok H, Jones T, et al. Efficacy and safety of a new triple-combination agent for the treatment of facial melasma. *Cutis.* 2003;72:67-72. 3. Torok H, Taylor S, Baumann L, et al. A large 12-month extension study of an 8-week trial to evaluate the safety and efficacy of triple combination (TC) cream in melasma patients previously treated with TC cream or one of its dyads. *J Drugs Dermatol.* 2005;4:592-597.

Tri-Luma and Galderma are registered trademarks.
©2006 Galderma Laboratories, L.P.
TRI-336 Printed in USA 01/06

GALDERMA