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PATIENT GUIDE

Prescription skin creams *for pigment, acne and skin ageing*

These creams put several prescription and cosmetic ingredients in one base for melasma, acne or ageing skin. Each ingredient has its own evidence, and the mixtures have never been tested as written.

FORM	USED FOR	ACTIVES	STATUS	SOURCES
Compounded cream	Pigment, acne, ageing	16 ingredients	Not FDA approved	33 · PMID linked

§ 01

Overview

A compounded prescription cream puts two or more active ingredients into one base, so that a single application at night works on more than one part of a skin problem. Several of the ingredients in ours carry their own FDA approval: tretinoin for acne and, as a 0.02 percent cream, for fine facial wrinkles,[1] azelaic acid 20 percent for mild to moderate inflammatory acne,[2] clindamycin and erythromycin for acne vulgaris,[3] ketoconazole 2 percent for seborrheic dermatitis and fungal infections, and hydrocortisone for dermatoses that respond to a corticosteroid.[4] One prescription cream combining fluocinolone acetonide, hydroquinone and tretinoin is approved for the short term treatment of moderate to severe melasma of the face.[5]

The multi ingredient creams themselves are a different matter. They are compounded, which means a licensed pharmacy prepares them for one named patient against a prescription, and a compounded preparation is not FDA approved: the agency does not verify its safety, effectiveness or quality before it is sold.[6] No published study has tested the particular mixtures, so what follows is the evidence for each ingredient at the strengths used on skin. Copper peptide has a guide of its own (OCW WP 019).

38%	**Melasma cleared at 8 weeks on the approved triple cream.** In the first trial behind the label, 32 of 85 subjects had lesions cleared of hyperpigmentation, against 12 of 83 given hydroquinone with tretinoin in the same base.[5]
1.58	**What the third ingredient adds.** A Cochrane review of 20 randomized trials in 2,125 participants found the triple cream better at lightening melasma than hydroquinone alone, a risk ratio of 1.58 (1.26 to 1.97).[7]
15%	**Gain from blocking visible light.** Among 68 patients using 4 percent hydroquinone for 8 weeks, those given a sunscreen containing iron oxide improved 15 percent more on the severity index.[8]
Six	**Ingredients here with an approved topical product.** Tretinoin, azelaic acid, clindamycin, erythromycin, ketoconazole and hydrocortisone. Hydroquinone is approved only inside the triple cream, and the rest are not approved drugs.[9]

§ 02

What these creams are

Each cream is mixed by a pharmacy to the strengths on your prescription, so two patients with melasma may leave with different bottles. The ingredients fall into four groups, and most formulas draw from more than one.

The pigment ingredients. Hydroquinone is the oldest and the most studied, and the approved triple cream describes it as a melanin synthesis inhibitor.[5] Kojic acid, from a fungus, and azelaic acid, first identified in grain, act on the same pigment enzyme.[10] [2] Tranexamic acid is approved in the United States only as a tablet and an injection for bleeding, and is used here on the skin.[9] Niacinamide, a form of vitamin B3, reduces the handover of pigment packets to skin cells,[11] and vitamin C is an antioxidant that also feeds collagen synthesis.[12]

The acne ingredients. Tretinoin is a vitamin A derivative, and its label describes increased turnover of the cells lining the follicle, which pushes out the plug that starts a spot.[1] Clindamycin 1 percent and erythromycin 2 percent are antibiotics applied to the skin,[3] azelaic acid appears here too since the approved 20 percent cream is an acne product,[2] and ketoconazole, an antifungal, belongs in a cream when the eruption is seborrheic dermatitis or a yeast folliculitis rather than ordinary acne.[4]

The repair and comfort ingredients. Hyaluronic acid holds water in the upper skin,[13] dexpanthenol is a moisturizer and barrier repair ingredient,[14] vitamin E is a fat soluble antioxidant,[15] GHK copper is a tripeptide bound to copper that supports collagen production in cells and animals,[16] and caffeine is included for its effect on small blood vessels.[17]

The steroid. Hydrocortisone is a mild corticosteroid, and in a pigment cream its job is to settle the redness and stinging the other ingredients cause. That is also why the approved triple cream contains a corticosteroid, fluocinolone acetonide, and that cream is licensed for short term use and is not indicated for maintenance treatment.[5] A steroid left in a face cream for months brings problems of its own, which section 7 sets out.[18]

WHAT IS IN THE CREAM The last column refers to an approved topical product containing that ingredient.

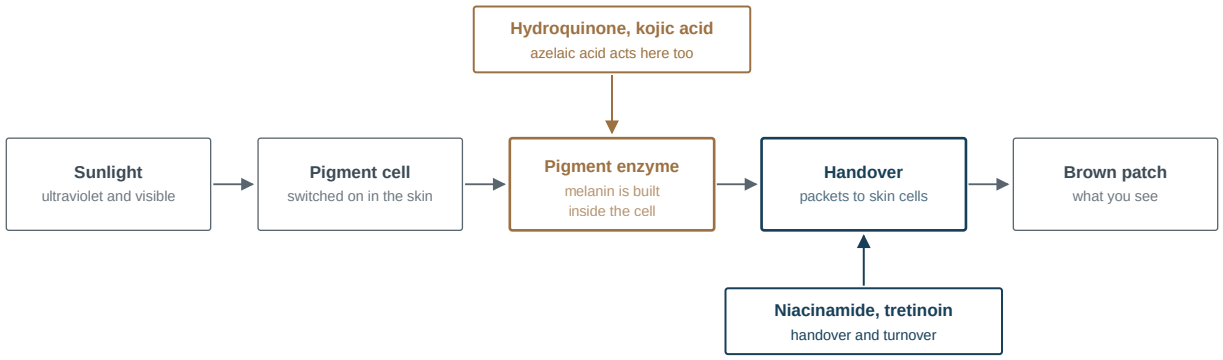
INGREDIENT	WHY IT IS IN THE CREAM	APPROVED TOPICAL PRODUCT OF ITS OWN
Hydroquinone	Melasma and uneven pigment	ONLY inside the triple cream[19]
Tretinoin	Acne, pigment, fine wrinkles	YES acne and fine wrinkles[1]
Hydrocortisone	Settles the irritation	YES steroid responsive rashes[4]
Kojic acid	Added lightening	NO under evaluation for compounding[20]
Azelaic acid	Acne, pigment, redness	YES acne at 20 percent[2]
Niacinamide	Pigment transfer, oiliness	NO[9]
Tranexamic acid	Melasma	NO tablet and injection only[9]
Vitamin C	Pigment and photoageing	NO[9]
Vitamin E	Antioxidant	NO[9]
Hyaluronic acid	Hydration	NO[9]
Dexpanthenol	Barrier repair	NO[9]
Clindamycin	Inflammatory acne	YES acne vulgaris[3]

INGREDIENT	WHY IT IS IN THE CREAM	APPROVED TOPICAL PRODUCT OF ITS OWN
Erythromycin	Inflammatory acne	YES acne vulgaris[3]
Ketoconazole	Seborrheic dermatitis	YES not for acne[4]
Caffeine	Redness and puffiness	NO[9]
GHK copper	Collagen support	NO sold as a cosmetic[9]

§ 03

How they work

Brown patches come from pigment cells pushed into overproduction. Ultraviolet and visible light both drive that, which is why a sunscreen absorbing visible light outperformed an ultraviolet only sunscreen alongside hydroquinone.[8] Inside the pigment cell an enzyme turns an amino acid into melanin, which is packaged and handed to the surrounding skin cells, where it becomes the colour you see. Hydroquinone slows the making of melanin,[5] kojic acid and azelaic acid act on the same enzyme,[10 2] niacinamide reduces the handover,[11] and tretinoin speeds the turnover of the epidermis. In the melasma trial of 0.1 percent tretinoin, epidermal pigment fell by 36 percent after 40 weeks while it rose by 50 percent under the vehicle cream.[21]



The lightening ingredients act at two different points on one chain. Hydroquinone slows the building of melanin, and kojic acid and azelaic acid act on the same enzyme.[5 10] Niacinamide reduces the handover of pigment packets to skin cells, and tretinoin speeds the turnover that carries pigment out of the epidermis, where it lowered epidermal pigment by 36 percent over 40 weeks.[11 21] Sun protection sits at the start of the chain, and sunscreen covering visible light as well as ultraviolet improved the response to hydroquinone by 15 percent on the severity index.[8]

Acne follows a different chain. Dead cells and oil block the follicle, bacteria multiply behind the block, and inflammation follows. Tretinoin works at the block, and its label warns of an apparent flare in the early weeks as plugs are pushed out.[1] Clindamycin and erythromycin work on the bacteria, azelaic acid works on both, and ketoconazole helps only where a yeast is driving the eruption.[3 2 4] For the signs of ageing the target is the dermis: tretinoin thickened the epidermis and altered the sun damaged dermis in the original randomized trial,[22] vitamin C feeds collagen synthesis,[12] GHK copper raises collagen and glycosaminoglycan production in cells and in animal wounds,[16] and hyaluronic acid and dexpanthenol hold water and repair the barrier.[13 14]

KEY POINT

Slowing pigment production, moving pigment out of the epidermis and calming the inflammation that follows sun exposure are three separate jobs, which is the argument for combining ingredients in one cream. The approved triple combination cream is the worked example, and the Cochrane review found it better at lightening melasma than any pair of its own three ingredients.[7] What has not been shown is that a fourth, fifth or sixth ingredient adds anything further.

§ 04

What the research shows

The evidence is grouped by what the cream is being asked to do. Every trial named here tested one ingredient, or a fixed combination of two or three, against a placebo or another treatment.

What the evidence supports

Pigment and melasma. Two randomized trials in 641 adults aged 21 to 75 with moderate to severe facial melasma and Fitzpatrick skin types I to IV compared fluocinolone acetonide 0.01 percent with hydroquinone 4 percent and tretinoin 0.05 percent against each pair of those ingredients in the same base, nightly for 8 weeks. Complete clearing reached 38 percent against 15 percent for hydroquinone with tretinoin in the first trial, and 13 against 4 percent in the second.[5] The Cochrane review put that comparison at a risk ratio of 1.58 (95 percent confidence interval 1.26 to 1.97) against hydroquinone alone.[7]

Hydroquinone, azelaic acid, vitamin C and niacinamide. Hydroquinone 4 percent is the yardstick in melasma research. Azelaic acid 20 percent beat hydroquinone 2 percent in the pooled Cochrane analysis (risk ratio 1.25, 95 percent confidence interval 1.06 to 1.48) and matched hydroquinone 4 percent (1.11, 0.94 to 1.32).[7] In 16 women who applied 5 percent ascorbic acid to one side of the face and 4 percent hydroquinone to the other for 16 weeks, the patients rated hydroquinone better, 93 against 62.5 percent good or excellent, while colour measurement found no difference and side effects affected 11 of 16 on hydroquinone against 1 of 16 on vitamin C.[23] In 27 patients treated the same way for 8 weeks, good to excellent improvement was recorded in 44 percent on 4 percent niacinamide and 55 percent on 4 percent hydroquinone.[11]

Kojic acid, tretinoin and tranexamic acid. Forty Chinese women applied a gel of 10 percent glycolic acid with 2 percent hydroquinone to both sides of the face for 12 weeks, with 2 percent kojic acid added to one randomized side; more than half the melasma cleared in 24 of 40 on that side against 19 of 40 on the other.[10] Tretinoin alone was tested in 38 women using 0.1 percent cream or vehicle for 40 weeks: 13 of 19 were rated improved or much improved against 1 of 19, although the first significant improvement appeared at 24 weeks and 88 percent had redness and peeling.[21] Twenty three women applied 5 percent tranexamic acid gel to one cheek and its base to the other for 12 weeks; pigment fell on both sides and the treated side was no better than the base.[24]

Acne. The American Academy of Dermatology guideline of 2024 makes strong recommendations for topical retinoids and topical antibiotics, and gives as good practice that topical treatments with different mechanisms be combined and that topical antibiotics be used with benzoyl peroxide.[25] A meta analysis of 23 studies in 7,309 patients reported a weighted mean reduction in inflammatory lesions at 10 to 12 weeks of 45.9 percent for clindamycin and 55.6 percent for clindamycin with benzoyl peroxide, against 26.8 percent for placebo.[26] Erythromycin has the harder record: in 208 patients given 2 percent gel or its base for 12 weeks, erythromycin resistant staphylococci on the face rose from 87 to 98 percent and no anti acne efficacy was seen.[27] The Cochrane review of 49 trials in 3,880 participants found azelaic acid probably less effective than benzoyl peroxide on patient rated improvement (risk ratio 0.82, 0.72 to 0.95) and probably no different from tretinoin (0.94, 0.78 to 1.14), and found that the four nicotinamide trials never measured patient rated improvement.[28] Where the diagnosis is seborrheic dermatitis rather than acne, a meta analysis of nine randomized trials found ketoconazole more effective than an inactive base, a pooled relative risk of 5.78 (2.17 to 15.40).[29]

Skin ageing. In the original 16 week randomized double blind trial, 30 patients applied tretinoin to one forearm and the base to the other, half of them also treating the face: every patient improved on the treated forearm and none on the vehicle forearm, and 14 of 15 improved on the treated face against none of the vehicle faces.[22] The approved 0.02 percent cream was tested for 24 weeks in 279 patients against 280 on the base, with moderate improvement in fine wrinkling in 10 percent against 3 percent. [1] A 6 month double blind trial of a 5 percent vitamin C cream found a better global score and shallower deep furrows, [12] 50 women using 5 percent niacinamide on half the face for 12 weeks had fewer fine lines, spots and red blotches and better elasticity, [30] and 76 women using 0.1 percent hyaluronic acid creams around one eye for 60 days improved in hydration and elasticity. [13] Dexpanthenol has a long record as a moisturizer and barrier repair ingredient, [14] and copper peptide creams have small controlled cosmetic studies behind them, including a 12 week facial cream study in 71 women, known mainly through review articles. [16]

What is not yet known

The mixtures themselves. No trial has tested a cream combining four, five or six of these ingredients, so the effect and the safety of the mixture in your bottle are not known from research. What is known is the behaviour of the ingredients separately and, for the three in the approved cream, of that combination over 8 weeks.[5] The Cochrane authors judged the overall quality of melasma studies poor and the available treatments inadequate. [7]

Longer use, and skin of colour. The approved triple cream was studied for 8 weeks, is not indicated for maintenance, and has not been studied in Fitzpatrick skin types V and VI, where the label states that excessive lightening cannot be excluded.[5] The 0.02 percent tretinoin cream was studied for 24 weeks, and in its single trial in 107 darkly pigmented subjects fewer improved on tretinoin than on the base, 29 against 43 percent. [1] Neither label reports what happens after a year of continuous use on the face.

Several ingredients rest on very little. Kojic acid has the one split face study described above, as an addition to a gel that already contained hydroquinone, [10] and topical tranexamic acid did not separate from its base in the trial that tested it alone. [24] For vitamin E and caffeine on facial skin the published work is reviews and laboratory studies rather than randomized trials of a prescription cream, and neither has an approved topical drug product. [15] [17] [9] Copper peptide by injection has no published human trial at all, which our copper peptide guide (OCW WP 019) sets out in full. [16]

THE MAIN HUMAN STUDIES Randomized trials unless the design says otherwise.

STUDY	N	WHO AND HOW	MAIN FINDING
The two label trials[5]	641	Moderate to severe melasma, triple cream against each pair, 8 weeks	Clearing 38 against 15 percent, and 13 against 4 percent
Rajaratnam 2010[7]	2,125	Cochrane review of 20 melasma trials	Triple cream above hydroquinone alone, risk ratio 1.58
Lim 1999[10]	40	Split face, 2 percent kojic acid added to a hydroquinone gel, 12 weeks	More than half cleared in 24 against 19 of 40
Griffiths 1993[21]	38	Tretinoin 0.1 percent or vehicle, melasma, 40 weeks	Improved in 13 of 19 against 1 of 19; first effect at 24 weeks
Castanedo Cazares 2014[8]	68	Hydroquinone with visible light or ultraviolet only sunscreen, 8 weeks	15 percent greater improvement in severity index
Seidler 2010[26]	7,309	Meta analysis of 23 acne studies	Inflammatory lesions down 45.9 percent on clindamycin, 26.8 on placebo
Mills 2002[27]	208	Erythromycin 2 percent gel or base, acne, 12 weeks	Resistant staphylococci 87 to 98 percent; no efficacy seen
Weiss 1988[22]	30	Tretinoin against vehicle, photoaged skin, 16 weeks	Improvement in 14 of 15 treated faces, none on vehicle

SUMMARY

Hydroquinone, tretinoin and the approved three ingredient combination have the strongest melasma evidence, measured over 8 to 40 weeks. Azelaic acid holds its own against hydroquinone, and vitamin C and niacinamide come close with less irritation. Clindamycin helps inflammatory acne while erythromycin mostly breeds resistance. For ageing skin, tretinoin has the deepest record, with smaller trials behind vitamin C, niacinamide and hyaluronic acid. Kojic acid, topical tranexamic acid, vitamin E, caffeine and copper peptide have the thinnest evidence here, and no study has tested the combinations we prescribe.

§ 05

How these creams are used

Where an approved product exists, its label sets the strength and the schedule. For a compounded cream no regulator has set either, so your physician writes them and the pharmacy follows the prescription.[6]

The approved products, for scale. The triple combination cream goes on as a thin film once daily, at least 30 minutes before bedtime, extending about half an inch onto normal skin, with treatment stopped once control is achieved and a sunscreen of SPF 30 used during the day.[5] Tretinoin cream and gel for acne go on once a day before retiring, and the 0.02 percent cream for fine wrinkles in the evening as a pearl sized amount, with a sunscreen of SPF 15 or greater in the morning.[1] Azelaic acid 20 percent cream is massaged in twice daily, clindamycin goes on twice daily, and erythromycin gel sparingly once or twice a day with treatment stopped if there is no improvement after 6 to 8 weeks.[2 3] Ketoconazole cream is applied once daily, or twice daily for 4 weeks for seborrheic dermatitis, and hydrocortisone cream two to four times daily.[4]

The compounded creams. These are mixed for you, so the only honest guide to strength is what has been studied in people: hydroquinone at 2 to 4 percent,[7 23] kojic acid at 2 percent added to a hydroquinone gel,[10] azelaic acid at 20 percent,[2] niacinamide at 4 to 5 percent,[11 30] vitamin C at 5 percent,[12] tranexamic acid at 5 percent,[24] tretinoin at 0.02 to 0.1 percent,[1 21] hyaluronic acid at 0.1 percent,[13] clindamycin at 1 percent, erythromycin at 2 percent[3] and ketoconazole at 2 percent.[4] Most formulas go on at night to clean dry skin, because tretinoin and the lightening agents make skin more sensitive to light. Ask what is in your bottle and at what strength, and in particular whether it contains a steroid and for how long.

Sun protection is part of the treatment. The approved melasma cream is indicated only in the presence of measures for sun avoidance, and its label asks for SPF 30 and protective clothing every day.[5] Visible light matters as well as ultraviolet: adding iron oxide to a sunscreen of SPF 50 or above improved the response to hydroquinone by 15 percent on the severity index and 28 percent on colour measurement over 8 weeks.[8] Treatment without daily sun protection wastes the cream.

§ 06

What to expect

The first two weeks are the rough ones. In the trials of the approved triple cream, 63 percent of 161 subjects had at least one treatment related reaction, most often redness in 41 percent and peeling in 38 percent.[5] With the 0.02 percent tretinoin cream, almost every patient reported peeling, dryness, burning, stinging, redness or itching, and 32 percent had irritation severe enough to interrupt treatment or to need a mild steroid.[1] Starting every other night is a common way through this.

Pigment moves slowly. Some subjects improved on the triple cream as early as 4 weeks, although of 7 who cleared at 4 weeks, 4 did not hold that remission through another 4 weeks of treatment.[5] Tretinoin alone took 24 of 40 weeks to show a significant change in melasma, and photographs taken in the same light at the start are more reliable than memory.[21]

Acne follows its own clock. The tretinoin label describes an apparent worsening of inflamed spots in the early weeks as deeper plugs are brought to the surface.[1] Azelaic acid improved inflammatory lesions in most patients within 4 weeks, and the erythromycin label sets a decision point at 6 to 8 weeks.[2] [3]

Stopping. Melasma usually recurs when the triple cream is stopped, and the label describes short courses rather than continuous use.[5] The lightening ingredients hold pigment down only while they are being used, and sun exposure can undo months of work in a summer. If the blue black darkening of ochronosis appears on skin treated with hydroquinone, treatment should stop and you should be seen.[5] [19]

§ 07

Safety

The approved three ingredient cream is the only one of these formulas with real numbers from a controlled trial, and it is a fair guide to what a pigment cream feels like.

TREATMENT RELATED REACTIONS IN THE TRIALS OF THE APPROVED TRIPLE CREAM 161 subjects, once daily for 8 weeks.[5]

REACTION	SUBJECTS	PERCENT
Any treatment related event	102	63%
Erythema, or redness	66	41%
Desquamation, or peeling	61	38%
Burning	29	18%
Dryness	23	14%
Pruritus, or itching	18	11%

The steroid, used for a long time. Cutaneous side effects of topical corticosteroids occur regularly with prolonged treatment: thinning of the skin, stretch marks, rosacea, dermatitis around the mouth, acne and bruising are the most frequent, with increased hair growth, pigment changes and slower wound healing less often, and allergy to the corticosteroid itself is commoner than is generally believed.[18] Enough corticosteroid can be absorbed through the skin to suppress the adrenal axis, which is why the approved melasma cream carries that warning and why the hydrocortisone label asks for periodic evaluation when a large area is treated.[5] [4] The face is thin skinned and the usual site for these problems, so the strength of the steroid and how long it stays in the formula are worth settling deliberately rather than by repeat refill.

Hydroquinone. Hydroquinone can produce exogenous ochronosis, a gradual blue black darkening of the skin, and the label says its appearance should prompt stopping treatment; most patients who develop it are Black, although it also occurs in white and Hispanic patients.[5] The FDA has also received reports of skin rashes, facial swelling and ochronosis from unapproved over the counter lightening products, and describes the discolouration as possibly permanent.[19] Irritation, redness and stinging are the ordinary effects.[5]

Tretinoin, pregnancy and sunlight. The 0.02 percent tretinoin cream should not be used during pregnancy, and the label tells patients not to use it if they are pregnant or trying to conceive.[1] The approved melasma cream states that it contains the teratogen tretinoin, which may cause embryo fetal death, and should be used in pregnancy only if the potential benefit justifies the potential risk.[5] Over two decades of use of another topical tretinoin product, 30 cases of congenital malformation were reported in time association with it, 5 of them a rare midline brain defect, with no pattern and no causal link established.[1] Tretinoin also raises sensitivity to sunlight.[1]

The antibiotics and the antifungal. Clindamycin applied to the skin is absorbed in small amounts, and its label carries the warning that clindamycin given by mouth or by injection has been associated with severe colitis that can be fatal; it is contraindicated in anyone with a history of regional enteritis, ulcerative colitis or antibiotic associated colitis, and diarrhoea during treatment should be reported.[3] Topical erythromycin raised resistant bacteria from 87 to 98 percent over 12 weeks, and the guideline advice is to pair a topical antibiotic with benzoyl peroxide rather than use one alone.[27] [25] Ketoconazole cream contains sodium sulfite and the approved melasma cream sodium metabisulfite, either of which can cause allergic reactions including severe asthma in susceptible people.[4] [5] Azelaic acid has been followed by isolated reports of lightening of normal skin, which matters more in a dark complexion.[2]

TELL YOUR PHYSICIAN BEFORE STARTING IF ANY OF THESE APPLY

- You are pregnant, breastfeeding or trying to conceive
- You have had a reaction to a sulfite, to hydroquinone, to a retinoid or to clindamycin or erythromycin
- You have asthma, inflammatory bowel disease or a history of colitis after an antibiotic
- You have been using a steroid cream on your face, or any lightening cream bought without a prescription
- You have eczema or sunburned skin, or you are having a peel, laser or waxing treatment soon
- You take a medicine that increases sensitivity to sunlight, or you cannot avoid daily sun exposure
- You have noticed any grey, blue or blue black change in the colour of treated skin

What the research does not provide is a safety record for these mixtures over years. The approved cream was studied for 8 weeks,[5] the 0.02 percent tretinoin cream for 24 weeks, with a label stating that the results of continued irritation beyond 52 weeks are not known,[1] and no controlled trial has followed a four or five ingredient compounded cream at all.[6]

§ 08

Is this right for you

These creams suit pigment that sits in the epidermis, acne that has not needed oral treatment, and the early signs of sun damage. The first job of a consultation is to be sure of what we are treating, because several conditions look alike and respond differently.

Before we begin

- [ ] A review of your medical history, any pregnancy plans, and every medication, supplement and skin product you use, including anything bought online
- [ ] An examination of the affected skin in good light, noting where the pigment or the spots sit and how deep the colour looks
- [ ] Baseline bloodwork where your history calls for it, so that anything found later can be compared with where you began
- [ ] A written note of your goals and standardized photographs, taken in the same light and at the same angles each visit

Melasma, pigment left behind by old acne or a rash, freckling from sun exposure and the darkening of ochronosis are all brown or grey brown patches, and only the first two respond well to a lightening cream. Pigment treated for a long time with a lightening product bought without a prescription deserves a careful look before more is prescribed, since the ochronosis the FDA describes follows exactly that history.[19] Hormonal contributors and medicines that raise sensitivity to light belong in the same conversation, as does an eruption that turns out to be rosacea or a yeast folliculitis rather than acne, where an antifungal is the ingredient that helps.[4]

Reviewing your progress

We compare your photographs against the baseline at agreed intervals, under the same lighting, because skin colour changes too slowly for memory to judge. The approved products set useful checkpoints: melasma within 4 to 8 weeks,[5] inflammatory acne lesions within 4 weeks on azelaic acid and a decision on erythromycin by 6 to 8 weeks, [2] [3] and fine wrinkles over 24 weeks. [1] If a steroid is in your cream, the review also covers whether it is still needed. You are welcome to stop at any time, and we will tell you what to expect as pigment returns.

> QUESTIONS TO ASK YOUR PHYSICIAN
>
> What exactly are we treating, and what else did you consider? What is in my cream, at what strength, and which ingredient is doing the work? Does it contain a steroid, and when will we take that out? Which ingredients have evidence behind them at these strengths and which do not? How long should I use it before we judge it? What sunscreen do you want me to use? What happens to my pigment if I stop? Is any part of this a problem if I become pregnant? We are glad to answer all of these.

§ 09

Regulatory status

The combination creams. A compounded cream containing several of these ingredients is not an FDA approved product. Compounded drugs are not FDA approved, and the agency does not verify their safety, effectiveness or quality before they are marketed; a pharmacy or physician licensed by the state prepares them for one patient against that patient's prescription under section 503A of the federal Food, Drug, and Cosmetic Act.[6] Under that section the bulk ingredients must comply with a United States Pharmacopeia or National Formulary monograph where one exists, or be components of FDA approved drug products, or appear on the FDA's 503A bulks list. [20]

Tretinoin. Tretinoin cream and gel are approved for the topical treatment of acne vulgaris. RENOVA, a 0.02 percent cream, is approved as an adjunct for the mitigation of fine facial wrinkles in patients who use a comprehensive skin care and sun avoidance programme, and that label states plainly that the product does not eliminate wrinkles or repair sun damaged skin and has not shown an effect on coarse wrinkling, mottled hyperpigmentation, tactile roughness or laxity. The 0.05 percent emollient cream that once carried the broader indication is no longer marketed.[1] [9] Using tretinoin for melasma therefore falls outside the labelled uses, which a physician may lawfully do and which the published trials support. [21]

The triple combination cream. The fixed combination of fluocinolone acetonide 0.01 percent, hydroquinone 4 percent and tretinoin 0.05 percent is approved for the short term treatment of moderate to severe melasma of the face in the presence of measures for sun avoidance including sunscreens. The label sets no fixed number of weeks: it says to stop when control is achieved, states that the cream is not indicated for maintenance, and notes that melasma usually recurs after it is stopped. The controlled trials ran 8 weeks, after which treatment continued only as needed.[5]

Hydroquinone. Over the counter hydroquinone is no longer legally sold in the United States. Reforms in the Coronavirus Aid, Relief, and Economic Security Act of 2020 settled the status of these products, so over the counter skin lightening products containing hydroquinone are deemed new drugs and are misbranded, and products without an approved application had to come off the market as of 23 September 2020. The FDA states that the triple combination cream is currently the only approved drug containing hydroquinone.[19] [9] Hydroquinone at other strengths therefore reaches patients only as a compounded preparation on a prescription, which is not FDA approved. [6]

Azelaic acid, the antibiotics and the antifungal. Azelaic acid 20 percent cream is approved for mild to moderate inflammatory acne vulgaris, and the 15 percent gel and foam for the papules and pustules of mild to moderate rosacea; neither carries a melasma indication, so that use is off label.[2] [9] Clindamycin phosphate and erythromycin 2 percent are

approved for acne vulgaris. [3] Ketoconazole 2 percent cream is approved for tinea, tinea versicolor, cutaneous candidiasis and seborrheic dermatitis, and hydrocortisone cream for the inflammatory and itching manifestations of corticosteroid responsive dermatoses. [4]

The ingredients with no drug approval. Kojic acid, tranexamic acid applied to the skin, niacinamide, caffeine and GHK copper are not FDA approved drugs for pigment, acne or ageing. A search of approved products finds no topical drug containing kojic acid, niacinamide, ascorbic acid, vitamin E, hyaluronic acid, dexpanthenol, caffeine or a copper tripeptide, and tranexamic acid approved only as a tablet and an injection for bleeding.[9] Kojic acid sits in Category 1 of the FDA's nominated bulk substances, which means its possible place on the 503A list is still under evaluation, as does GHK copper for routes other than injection. [20] Copper peptide creams are sold as cosmetics, which are not reviewed by the FDA as drugs. [16]

For athletes. On the World Anti Doping Agency list in force for 2026, all glucocorticoids are prohibited in competition when given by injection, by mouth or rectally, while application to the skin is not prohibited within the licensed doses and indications. Caffeine is in the monitoring programme and is not prohibited, and tranexamic acid, hydroquinone, tretinoin, clindamycin and ketoconazole do not appear on the list.[31] The list is reissued each year, so athletes in tested sport should check the current one every season.

If you would like details about the preparation used in your treatment, please ask.

§ 10

Common questions

Is my cream FDA approved?

A compounded cream is not, and neither is any multi ingredient lightening cream mixed by a pharmacy.[6] Several of the ingredients inside it are approved on their own: tretinoin for acne and for fine facial wrinkles, azelaic acid for acne, clindamycin and erythromycin for acne, ketoconazole for seborrheic dermatitis and fungal infections, and hydrocortisone for rashes that respond to a steroid. [1] [2] [3] [4] The one approved prescription cream for melasma combines fluocinolone acetonide, hydroquinone and tretinoin. [5]

Which ingredient is actually doing the work?

For melasma, hydroquinone and tretinoin carry the evidence, and the approved combination of the two with a corticosteroid outperformed every pair of its own ingredients.[5] [7] For acne it is the retinoid and, for inflamed spots, clindamycin. [25] [26] Niacinamide, vitamin C and azelaic acid have genuine if smaller trials behind them, [11] [23] [28] while kojic acid, topical tranexamic acid, caffeine, vitamin E and copper peptide have little or nothing behind them at these strengths. [10] [24] [17] [15] [16]

Is it safe to keep a steroid cream on my face for months?

Prolonged use of a topical corticosteroid regularly produces thinning of the skin, visible small vessels, stretch marks, rosacea and dermatitis around the mouth, and the face is the usual site.[18] The approved melasma cream contains a corticosteroid and is licensed for short term use only, with instructions to stop when the pigment is controlled. [5] If a steroid is in your compounded cream, ask at every review whether it is still needed.

Can I use this if I am pregnant or breastfeeding?

Any cream containing tretinoin is a problem in pregnancy. The 0.02 percent cream should not be used during pregnancy, and the approved melasma cream notes that it contains the teratogen tretinoin and should be used only if the benefit justifies the risk.[1] [5] Melasma often appears during or after pregnancy, so tell us if you are pregnant, breastfeeding or trying to conceive and we will take the retinoid out of the plan.

Do I really need sunscreen every single day?

Yes, and it is the part of the treatment patients most often skip. The approved cream is indicated only alongside sun avoidance, and its label asks for SPF 30 and protective clothing daily.[5] Visible light drives pigment too: adding iron oxide to a high factor sunscreen improved the response to hydroquinone by 15 percent on the severity index over 8 weeks.[8] A tinted mineral sunscreen is the practical way to cover both.

Where is a compounded medicine made, and who oversees it?

Federal law sets out two kinds of compounding. Under section 503A, a state licensed pharmacy or physician prepares a medicine for one patient against that patient's own prescription, and the state board of pharmacy carries the day to day oversight while the FDA inspects for cause and on surveillance.[6] Under section 503B, an outsourcing facility registers with the FDA, works to federal manufacturing quality standards, reports adverse events and the products it makes to the agency, and is inspected by the FDA on a risk based schedule; it may also supply a clinic directly rather than for one named patient.[32] We use both kinds, and which one prepares your medicine depends on the preparation.

Is a compounded medicine the same as an FDA approved one?

No, and the difference matters. A compounded preparation is not FDA approved, and the agency does not check its safety, effectiveness or quality before it is sold, which is why an approved product is the first choice whenever one fits your situation.[6] What a prescription from a licensed pharmacy or a registered outsourcing facility does give you is a named prescriber, a facility answerable to a state board or to the FDA, ingredients that meet federal requirements, and a route for reporting a problem. A jar bought online and labelled for research use only has none of that: the FDA treats those products as unapproved new drugs when they are meant for people, and has written to the companies selling them.[33] Please do not use one.

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