

# Active Ingredient Summary Table

## Alopecia

Active Pharmaceutical Ingredient	Mechanism of Action (MoA)	Type of Alopecia Treated/Treatment Group	Dosing	Studies
<b>Adapalene</b>	Recent studies propose that retinoids have an impact on the enzyme that converts minoxidil to its active form, follicular sulfotransferase, and may increase response to minoxidil via increased expression of this enzyme <sup>76</sup> Retinoids also impact generation and differentiation of hair follicles. <sup>82</sup>	Alopecia areata in male and female patients, though, the mechanism could apply to androgenetic alopecia as well	Adapalene 0.1% in combination with mometasone 0.1% once daily	One small study compared adapalene 0.1% gel in combination with mometasone furoate 0.1% cream applied once daily vs twice daily mometasone alone for patients with alopecia areata. The study found mean hair growth to be statistically significantly greater with combination treatment at the 4, 8, and 12 week timepoints. <sup>82</sup>
<b>Anthralin</b>	The mechanism for anthralin in alopecia areata has not been fully elucidated, it is primarily used topically for psoriasis as it has anti-proliferative effects, it may also have anti-inflammatory effects	Alopecia areata, tested in men and women <sup>31,33</sup>	0.5-1% cream applied topically daily	Results concerning anthralin are mixed, one study evaluating 0.5%-1% cream found response in 25% of patients, but another in combination with minoxidil found only 11% acceptable hair regrowth <sup>33,34</sup>
<b>Azelaic Acid</b>	Inhibits 5-alpha-reductase, involved in inhibiting conversion of testosterone to DHT <sup>50</sup>	Alopecia areata, tested in men and women <sup>48</sup>	20% cream for alopecia areata <sup>48</sup> , 1.5% in combo with minoxidil 5%, caffeine 1% also tested <sup>49</sup>	Study evaluating azelaic acid 20% vs anthralin over 12 weeks. Treatments were found to be equally effective for both treatment groups <sup>48</sup> Azelaic acid 1.5% with minoxidil 5%, caffeine 1% demonstrated superior to minoxidil alone in placebo controlled 32 week trial.

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<p><b>Betamethasone</b></p>	<p>Immune suppression, as an autoimmune disorder, alopecia areata can be treated by immunosuppressant drugs</p>	<p>Alopecia areata, less effective for alopecia totalis and alopecia universalis, can be for men or women</p>	<p>0.1% betamethasone valerate foam preferred over 0.05% lotion<sup>31,32</sup></p>	<p>Study evaluating betamethasone valerate foam vs betamethasone dipropionate lotion found 61% of those on betamethasone valerate achieved more than 75% hair regrowth compared to only 27% in the lotion group.<sup>31</sup></p>
<p><b>Bexarotene</b></p>	<p>Vitamin A related compound that binds to retinoid X receptors. Mechanism not entirely clear, but may be similar to tretinoin (i.e. causing contact dermatitis)</p>	<p>Alopecia areata, tested in men and women</p>	<p>1% gel</p>	<p>Study found that 12% of patients had 50% or more partial hair regrowth on the treated side, 14% on both sides, however, many of the patients experienced irritation in response to treatment<sup>38</sup></p>
<p><b>Bimatoprost</b></p>	<p>Prostaglandin mediated anagen induction. Latanoprost and bimatoprost are prostaglandin analogues<sup>20</sup></p>	<p>Alopecia areata and androgenetic alopecia</p>	<p>0.03% topical solution</p>	<p>Study evaluating bimatoprost 0.03% topical solution twice daily for three months vs mometasone furoate for alopecia areata found the bimatoprost to be significantly more effective.<sup>54</sup> Another study comparing it to 5% minoxidil also found no statistically significant difference between the two groups regarding hair growth.<sup>55</sup></p>
<p><b>Biotin</b></p>	<p>Biotin, Vitamin B7, is a common oral supplement for hair loss however despite biotin deficiency being a common finding in women experiencing hair loss<sup>42</sup> mechanism of action is not totally clear. Could be related to mitochondrial function in hair root cells as a cofactor<sup>43</sup></p>	<p>Most studies evaluate oral biotin between 1-10mg and find benefit in patients with genetic or iatrogenic reasons for hair loss<sup>44</sup></p>	<p>Though no studies currently exist that I could find, if biotin is used it is often between 0.1-0.5%</p>	<p>Though studies on the benefit of oral supplementation have demonstrated benefit in specific populations, studies on topical use are not yet available. Evidence for use is mainly anecdotal.</p>

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<b>Caffeine</b>	A possible mechanism is increased cAMP via phosphodiesterase inhibition resulting in increased cell proliferation of follicles (combating DHT induced miniaturization of the follicle) <sup>23</sup>	Androgenetic alopecia tested, though possible use in other non-cicatricial alopecia types. Tested in men	0.2% topical liquid	One open-label non-inferiority trial testing caffeine 0.2% topical liquid as compared to minoxidil 5% solution found caffeine to be as effective as minoxidil at increasing the amount of anagen hairs over a 6-month period. <sup>23</sup>
<b>Cetirizine</b>	Cetirizine has some anti-PGD2 activity, prostaglandin D2 has been implicated as a causative factor in some alopecias <sup>46</sup>	Studied in androgenetic alopecia	1% topical cream or liquid	Study evaluating cetirizine 1% vs placebo noted significant improvement in total hair density and decrease in vellus hair density. No adverse effects reported <sup>46</sup>
<b>Clascoterone</b>	Clascoterone is an androgen receptor inhibitor, though trials are still underway, it may help by decreasing the impact of androgens on hair follicle miniaturization on the scalp. <sup>59</sup>	Studies underway for treatment of androgenetic alopecia	5-7.5% solution applied twice daily	One phase II trial of clascoterone vs placebo found significant improvement with clascoterone compared to vehicle. <sup>60</sup>
<b>Clobetasol propionate</b>	Clobetasol as a steroid may have immunosuppressive benefits in the management of alopecia areata	Alopecia areata <sup>25</sup> Studied in men and women as well as children	0.05% topical cream or ointment	Study of 28 patients with alopecia areata who applied 2.5g of 0.05% ointment for 6 months to one side of scalp resulted in some regrowth for 28.5% of patients <sup>26</sup>
<b>2-Deoxy-D-ribose (note, this does not qualify for compounding)</b>	Stimulation of revascularization to promote hair growth <sup>78</sup>	Androgenetic alopecia in male and female patients <sup>78</sup>	0.394% studied in vitro	Currently limited to animal trials
<b>Diclofenac Sodium</b>	May cause regrowth of hair via mitigation of perifollicular micro-inflammation and correcting prostaglandin imbalance. <sup>85</sup>	Limited case studies in male patients with androgenetic alopecia and alopecia areata	Diclofenac 3% gel once nightly in androgenetic alopecia study, diclofenac 1% applied twice daily in alopecia areata study	Three male patients applied diclofenac 3% gel to the scalp nightly for management of actinic keratosis, significant hair regrowth was noted at the 4 and 6 month follow up appointments. <sup>85</sup> Another study of diclofenac 1% gel applied twice daily for 2 months found significant hair regrowth. <sup>86</sup>

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<p><b>Diphencyclopropenone</b></p>	<p>Acts as a contact allergen. The mechanism has not been fully elucidated, but it is hypothesized that the inflammatory response that is causing the hair loss is redirected</p>	<p>Alopecia areata<sup>31</sup>, Tested in men and women</p>	<p>Generally, an initial treatment of 2% is applied followed by a much lower concentration (perhaps 0.001%) after 2 weeks and gradually increased (on a weekly basis)</p>	<p>Response rate (considered to be 75% or greater terminal hair regrowth) in one study was 77% cumulatively and 17.4% for those suffering from alopecia totalis/universalis<sup>31,35</sup></p>
<p><b>Dutasteride</b></p>	<p>Only known medication which blocks both type I and II 5-alpha reductase, more potent inhibition than finasteride, which shares a similar mechanism of action, resulting in inhibition of conversion of testosterone to DHT resulting in decreased DHT in serum and scalp<sup>51</sup></p>	<p>Androgenetic alopecia, studied in men<sup>51</sup> and women<sup>53</sup></p>	<p>Orally 2.5mg in men<sup>52</sup> and 0.15mg orally in women<sup>53</sup> Topical dutasteride strengths not reported in literature at this time, but 0.25% is common</p>	<p>Limited data is available on topical use. Dutasteride 2.5mg orally daily was observed to be more effective than finasteride 5mg or placebo over a 24 week study in men.<sup>52</sup> 0.15mg daily orally in women also demonstrated benefit for androgenetic alopecia<sup>53</sup></p>
<p><b>EGCG (Green Tea Extract)</b></p>	<p>EGCG acts as an antioxidant and is thought to perhaps have some inhibitory effect on 5-alpha reductase therefore preventing formation of DHT. It may also stimulate growth of human dermal papilla cells via upregulation of phosphorylated Erk and Akt</p>	<p>Androgenetic alopecia<sup>41</sup> and possibly general hair loss as well</p>	<p>10% solution</p>	<p>An Ex vivo study found 10% EGCG solution to result in significant follicle elongation<sup>41</sup></p>
<p><b>Estradiol</b></p>	<p>A possible mechanism is estrogen induced increase in glycoprotein sex hormone-binding globulin leading to decreased free testosterone.<sup>19</sup></p>	<p>Androgenetic alopecia. Studied in women</p>	<p>0.025% topical lotion</p>	<p>One 6-month long study evaluating estradiol 0.025% topical lotion in patients with androgenetic alopecia found a decrease in hair loss, however, regrowth of new hairs was not demonstrated<sup>19</sup></p>

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<b>Finasteride</b>	Inhibition of type II 5-alpha reductase inhibiting conversion of testosterone to DHT resulting in decreased DHT in serum and scalp. <sup>8,9</sup>	Androgenetic alopecia. Studied in men and women	0.005% solution to 1% gel (wide variability)	Finasteride 0.005% has been tested in men and women and statistically significant benefit was observed. <sup>7</sup> 1% finasteride gel formulation vs finasteride oral tablets in men and found efficacy with the topical gel. <sup>8</sup> 0.25% finasteride in combination with 3% minoxidil vs 3% minoxidil alone the combination therapy with significantly superior to minoxidil alone. <sup>9,10</sup>
<b>Fluocinolone Acetonide</b>	Immune suppression, as an autoimmune disorder, alopecia areata can be treated by immunosuppressant drugs	Alopecia areata <sup>47</sup>	0.2% Fluocinolone acetonide cream twice daily <sup>47</sup>	Fluocinolone ac 0.2% cream twice daily (under occlusion at night) found regrowth of hair in 54% of treatment group compared with 0% of vehicle group <sup>47</sup>
<b>Flutamide</b>	Proposed mechanism of action is inhibition of alpha reductase <sup>60</sup>	Androgenetic alopecia	2% gel	One randomized, double-blinded study evaluated flutamide 2% with minoxidil 5% vs minoxidil alone and found combination treatment significantly more effective. <sup>77</sup>
<b>GHK-Cu (Copper Peptide or glycy-L-histidyl-L-lysine copper complex)</b>	GHK-Cu may promote fibroblast proliferation resulting in collagen synthesis which may in turn promote increased scalp health and blood flow to hair follicles. GHK-Cu also suppresses TGF-beta1 leading to hair shaft thickening and elongation <sup>69,70</sup>	Androgenetic alopecia	Data is mainly in vitro, some compounders use 0.05-0.5%	Human use studies not yet available.
<b>Ketoconazole</b>	Unclear mechanism of action, possibly due to anti-inflammatory effects <sup>18</sup>	Androgenetic alopecia. Studied in men	2% lotion or shampoo	Some limited studies in humans of ketoconazole 2% lotion or shampoo have shown benefit for some patients, and other studies in mice have noted hair regrowth as well, though the improvement was not as significant as

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				minoxidil compared to the placebo group. <sup>13,14,15,16</sup>
<b>Latanoprost</b>	Prostaglandin mediated anagen induction. Latanoprost and bimatoprost are prostaglandin analogues <sup>20</sup>	Androgenetic alopecia. Studied in men	0.1% solution	Increased hair density observed with latanoprost 0.1% solution at 24 weeks as compared to placebo
<b>Levocetirizine</b>	Proposed mechanism of action consistent with cetirizine, reduction of prostaglandin D2, a mediator of inflammation. Levocetirizine is the R enantiomer of racemic cetirizine. <sup>73-75</sup>	Androgenetic alopecia	Not currently studied, but given its increased potency compared to cetirizine 0.5% could be considered.	No human studies currently, theoretical benefit based off of studies with racemic form (cetirizine).
<b>Melatonin</b>	Though the mechanism of action isn't totally clear, melatonin appears to induce anagen phase. <sup>21</sup> Some have postulated this is due to its antioxidant properties and anti-apoptotic effects <sup>22</sup>	Androgenetic alopecia and general (non-cicatricial) hair loss. Benefits for both men and women	1ml of 0.1%	Melatonin 0.1% solution was applied to the scalps of these women resulting in increased hair growth as compared to the placebo group. <sup>21,22</sup>
<b>Metformin</b>	Thought to improve fibrosis through mediation of adenosine monophosphate-activated protein kinase (AMPK). <sup>79</sup> AMPK activation is thought to be the mechanism behind improving insulin sensitivity as well. <sup>80</sup>	Central centrifugal cicatricial alopecia	10% cream applied once daily	One case report of two patients with central centrifugal cicatricial alopecia refractory to treatments such as steroids, minoxidil, and ketoconazole found success after 4 months of treatment with metformin 10% cream. <sup>79</sup> Another case involved topical metformin 10% in combination with minoxidil 5% lotion, significant hair regrowth was noted after 8 months. <sup>80</sup>
<b>Minoxidil</b>	Topical vasodilator that prolongs anagen phase and increases the size of smaller hair follicles. Proposed mechanism involves	Androgenetic alopecia and general (non-cicatricial) hair loss. Benefits for both men and women	2-5% topical solution	Topical minoxidil has been well studied in both men and women at both 2 and 5%. Studies have demonstrated the superior efficacy of 5% minoxidil over

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	modulation of prostaglandin levels.			2% minoxidil twice daily with one study reporting 45% more hair growth in the 5% minoxidil group. <sup>4,6</sup>
<b>Progesterone</b>	Progesterone can inhibit conversion of testosterone to DHT. <sup>81</sup>	Androgenetic Alopecia. Studied in female patients	Progesterone 2% 2mL applied once daily	One small study of female patients compared progesterone 2% (2mL applied daily) to minoxidil 2% and found that while benefit was greater in the minoxidil group, significant hair regrowth was noted in the progesterone group as well. <sup>81</sup>
<b>Rosemary Oil</b>	May increase hair count via enhancement of microcapillary perfusion. <sup>65</sup> Some data suggests anti-inflammatory and even some anti-androgenic effects as well <sup>66</sup>	Androgenetic alopecia in both males and females	Concentration to use is not well established, some studies have looked at formulas with up to 10% rosemary oil <sup>67</sup> another study looked at 1% rosemary oil, 1mL applied twice daily. <sup>68</sup>	One study of rosemary oil vs minoxidil 2% noted increases in hair count at the 6-month time point with no significant differences between groups. <sup>65</sup>
<b>Sirolimus</b>	Proposed mechanism of action is induction of anagen phase. <sup>71,72</sup>	Androgenetic alopecia	Up to 0.25%	Data is mainly in mice or vitro currently, but thus far has shown increased hair growth rate and hair follicle density with use of topical sirolimus. Studied concentrations have been quite low, on the mcg level, anecdotally, concentrations currently being used for human use are higher up to 0.25%. <sup>71,72</sup>
<b>Spirolactone</b>	Competitive inhibition of androgen receptors, systemically inhibits ovarian androgen production. <sup>24</sup>	Androgenetic alopecia. Studied in women	1% topical solution and oral use	One study of 60 female patients found a spironolactone 1% topical to be effective at promoting hair growth, however, the study has not been repeated and benefit has not been studied in men. <sup>17,18</sup>
<b>Squaric Acid Dibutylester</b>	Acts as a contact allergen. The mechanism has not been fully elucidated, but it is hypothesized that the inflammatory response	Alopecia areata <sup>27</sup> Studied in men and women as well as children <sup>29</sup>	Generally, an initial treatment of 2% is applied followed by a much lower concentration (perhaps 0.001%) after 1-2	A prospective, double-sides patient-controlled trial found that sensitization with 2% SADBE followed by weekly application resulted in “excellent

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	that is causing the hair loss is redirected		weeks and gradually increased (on a weekly basis) until the pt has a reaction usually resulting in 0.01-1% final concentration for therapy <sup>29,30</sup>	response” in 60% of those treated on the treated sites. <sup>28</sup> Another comprehensive review determined that 44.05% of patients using this therapy experienced at least 50% of terminal hair regrowth. <sup>29</sup> Fun fact: A retrospective study found that topical irritants in combination with oral fexofenadine resulted in statistically significant greater hair regrowth <sup>37</sup>
<b>Tacrolimus</b>	Tacrolimus is a calcineurin inhibitor that suppresses the immune system	Alopecia areata and frontal fibrosing alopecia in male and female patients	Tacrolimus 0.1% applied twice daily	One study of tacrolimus 0.1% ointment applied twice daily for 24 weeks did not find benefit with this treatment, they noted it may be due in part to the ointment formulation. <sup>83</sup> Another study that looked at tacrolimus 0.1% solution applied twice daily for one month, then once daily for one month, then every other day for four months found benefit for frontal fibrosing alopecia. <sup>84</sup>
<b>Tea Tree Oil</b>	Thought to treat alopecia via a combination of effects including anti-inflammatory antimicrobial,, and potentially impacting follicle sensitivity to androgens. <sup>66</sup>	Androgenetic alopecia. Applications in both male and female patients	5% tea tree oil applied 1mL twice daily	One study of combination minoxidil 5%, diclofenac 0.5%, tea tree oil 5%, 1mL applied twice daily for 32 weeks found greater improvement in hair count than the minoxidil alone group. <sup>66</sup>
<b>Tofacitinib (Xeljanz)</b>	Attenuation of inflammatory cascade via JAK inhibition may play a role <sup>39</sup>	Alopecia areata. Studied in both men and women	Has been used orally for alopecia areata, or topically at 1 to 2% solution for eyelashes <sup>39</sup> or 2% ointment to the scalp (authors theorized oint may be bad vehicle choice) <sup>40</sup>	Case study of patient with alopecia areata of the eyelashes found that after 7mo of treatment with tofacitinib 2% solution eyelashes regrew completely. <sup>39</sup> Another small study of 10 patients found improvement in 3 with the application of 2% ointment <sup>40</sup>

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<b>Tretinoin</b>	Known to increase percutaneous absorption of minoxidil therefore could assist in getting minoxidil to site of action <sup>12</sup> Additionally, may have own benefit by causing contact dermatitis <sup>31</sup>	Androgenetic alopecia, studied in men (though mechanism could also apply to women). Also alopecia areata, studied in men and women	Tretinoin 0.01% topical solution in combo with minoxidil <sup>12</sup> or up to 0.05% as a solo agent <sup>31</sup>	One study of once daily tretinoin 0.01% with minoxidil 5% vs twice daily minoxidil 5% found that once daily combination therapy was as effective as twice daily minoxidil treatment. <sup>12</sup> In one study 0.05% tretinoin resulted in response from 55% of patients <sup>31,36</sup>
<b>Valproic Acid</b>	Inhibits glycogen synthase kinase 3-beta and activates other pathways (Wnt/beta-catenin), that are associated with hair growth cycle and the induction of anagen (growth) phase <sup>45</sup>	Studied in men with androgenetic alopecia, though could conceivably apply to other populations <sup>45</sup>	Sodium valproate 8.3% topical spray <sup>45</sup>	Study of 8.3% sodium valproate vs placebo spray for 24 weeks found mean increase in total hair count in VPA group as compared to placebo. No significant adverse events reported <sup>45</sup>

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