København, den 29. oktober 2024

AFGØRELSE

Afgørelse vedr. KO-2024-3608 - reklamemateriale

Granskningsmandspanelet har dags dato truffet følgende afgørelse i klagesagen imellem parterne:

Klager: ALK-Abelló Nordic A/S
Sauntesvej 13
2820 Gentofte

og

Indklagede: Stallergenes Greer Danmark ApS
C/O Business Center
Rådhuspladsen 16
1550 København V
Danmark

Vedrørende: Reklamemateriale udarbejdet af indklagede.

Resumé:
Stallergenes Greer Danmark ApS findes at have overtrådt Reklamekodeksets §§ 8, stk. 1 og 2, jf. § 4, stk. 2 og § 7, stk. 1.

Baggrund:
ALK-Abelló Nordic A/S [ALK-Abelló Nordic] indsendte den 3. oktober 2024 en klage over reklamemateriale udarbejdet af Stallergenes Greer Danmark ApS [Stallergenes Greer], med henblik på en vurdering af, hvorvidt reklamen er i strid med Reklamekodekset.

ALK-Abelló Nordic har den 3. oktober 2024, fremsendt følgende bemærkninger til sagen:

> *'Vedhæftede detail-aid er blevet udleveret til personer som deltog på årsmødet for Dansk Selskab for Allergologi (DSA) August 2024. Denne klage drejer sig primært om indholdet på s. 3, hvor der efter vores skøn fremvises sammenlignende reklame med utilstrækkeligt indhold. Vi mener, dette strider mod ENLI's regelgrundlag, jf. Lægemiddelindustriens kodeks vedrørende reklame mv. for lægemidler rettet mod sundhedspersoner (Reklamekodekset) Reklamekodeksets § 8, stk. 1, jf. § 4, stk. 2. og § 7 stk. 1.*

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Paragraf 8 stykke 1
Af vejledningen til Reklamekodeksets § 8, stk. 1, fremgår:
"Stk. 1 er formuleret som reklamebekendtgørelsens § 16, stk. 1.

Sammenlignende reklame er lovlig, når reklamen i sin helhed er korrekt, relevant og loyal.

Sammenligningen skal være objektiv og relatere sig til dokumenterbare oplysninger. I enhver sammenlignende reklame skal det nøje angives, hvilke lægemidler, der sammenlignes med. Dette gælder også, hvor virksomheden sammenligner lægemidler, som kun forhandles af virksomheden selv. Det vil også være en sammenlignende reklame at angive at lægemidlet "gør det bedre" eller lægemidlet "virker hurtigst". I så fald skal der foreligge fuld dokumentation i forhold til alle relevante lægemidler på markedet, jf. reglerne for dokumentation i § 7. Mere ubestemte angivelser som "andre" eller "konkurrerende produkter" er ikke acceptable. Sammenligning med en gruppe af lægemidler, hvor denne er af mere udefinerbar karakter, kan således ikke accepteres.

"Aitgrys er den mest potente SLIT-behandling" Vi mener ikke, at det er sagligt korrekt at fremstille Aitgrys som "den mest potente SLIT-behandling".

For det første er det uklart hvad betydning der ligger i ordet "potent" som kan opfattes på flere forskellige måder jævnfør dansk retskrivningsordbog. I forbindelse med et lægemiddel bør man fraholde sig fra dette ord, da det henfører til en subjektiv vurdering af lægemidlet. For det andet er vi uenige i at Aitgrys er den "mest potente SLIT-behandling" hvis man vurderer ordets betydning som "mest effekt", (hvilket vi antager har været intentionen), da effekt ikke blot afhænger af "styrken af græspollen". Det skal kunne demonstreres med kliniske data at effekten er bedre. Herudover ses det fra reference publikation, at hvis man kun vurderer udfra BAU, så er der flere SLIT-behandlinger som er mere potente end Aitgrys hvorfor Aitgrys ikke kan være "mest potente SLIT-behandling" Vi henleder ENLIs opmærksomhed på tabel 1 i Passalaqua referencen.

ALKs holdning er jf. vejledning til reklamekodekset side 48 at Aitgrys markedsføres på parametre, der er irrelevante, når sundhedspersonen skal vurdere lægemidlets terapeutiske effekt i forhold til patienten. ALK vil gerne tilkendegive, at der i denne sammenlignende reklame er inkluderet alle de på markedet relevante og tilgængelige produkter. Sammenligningen er dog hverken loyal eller objektiv.

Paragraf 4 stykke 2 "Reklame for et lægemiddel skal være fyldestgørende og saglig, og den må ikke være vildledende eller overdrive lægemidlets egenskaber. Oplysninger i reklamen skal være i overensstemmelse med lægemidlets godkendte produktresumé." "GRAZAX® 2800 BAU" Referencer: GRAZAX® produkt-resume og Passalaqua publikation. Vi protesterer kraftigt mod at vores produkt bliver nævnt med et indhold i BAU med store bogstaver, uden at denne måleenhed er nævnt i GRAZAX® produktresume.

Vi mener, det er svært misledende i forhold til vores produkt. Det bemærkes at indholdet af BAU ej heller fremgår af produktresuméet for Aitgrys, og at begge produktresumeer endvidere

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er refereret uden dato eller versions-styring. Det bør også nævnes at måling af styrken af allergen indholdet i forskellige produkter kan ændre sig meget afhængigt af metoden. Den nævnte Passalaqua reference nævner allerede i abstractet, at der ikke er en godkendt europæisk fælles måleenhed "..with European regulatory authorities yet to adopt a common unit" og som tilføjelse kan nævnes at EU ser ud til at komme med en fælles anbefaling af metode, og det bliver ikke BAU metoden. ALK ser dette, som at der her er udvalgt ét enkelt studie, der angiver positive resultater for Aitgrys, som er misvisende og usaglig i forhold til den samlede viden på området.

Vi vil endvidere gøre ENLI opmærksomme på at de primære endepunkter og definitionen af klinisk relevant forbedring ved allergenindhold mangler i reklamematerialet. ALK betragter således informationsniveauet i den sammenlignende anprisning i strid med kravet om fyldestgørende (sammenlignende) reklame, jf. Reklamekodeksets § 8, stk. 1, jf. § 4, stk. 2 samt vejledningerne hertil. Reklamekodekset § 7, stk. 1: "Lægemiddelreklamer skal tilskynde rationel brug af lægemidler ved at præsentere lægemidler objektivt og uden overdrivelse af deres egenskaber. Påstande må ikke antyde, at et lægemiddel eller en aktiv bestanddel har særlige fordele, kvaliteter eller egenskaber, medmindre dette kan dokumenteres. En sådan dokumentation skal ved rimelige forespørgsler fra sundhedspersonale kunne tilvejebringes hurtigt."

Vi mener ikke at der foreligger tilstrækkelig dokumentation til at påvise at lige præcis BAU måling har indflydelse på effekten af behandlingen. Der er ingen dokumentation for at det er mængden af BAU som er årsagen til at "man kun behøver behandle i 7 mdr". Herunder kan præciseres at STG produktet ikke har hverken bedre effekt data end GRAZAX®, ej heller har STG produktet sygdomsmodifikation i deres indikation (selvom det kraftigt antydes på side 8) i modsætning til GRAZAX® label (baseret på et positivt studie med bevist langtidseffekt 2 år efter endt behandling), hvorfor der ikke er andet som understøtter, at det er en fordel med en højere BAU.'

Sagen blev sendt i høring til Stallergenes Greer den 3. oktober 2024, jf. ENLI's Sagsbehandlingsregler § 9. I høringssvar af 16. oktober 2024 havde Stallergenes Greer følgende bemærkninger;

Our company Stallergenes Greer Danmark ApS has been informed about the complaint from ALK Abelló Nordic A/S related to one of our advertising activities, under the reference KO-2024-3608.

This complaint takes place in a context where our Stallergenes Greer's sublingual immunotherapy (SLIT) tablet AITGRYS®, indicated to treat grass pollen-induced allergic rhinitis, has been marketed in Denmark in August 2024, now providing an alternative treatment option to the SLIT tablet GRAZAX®, having the same indication and marketed by the company ALK-Abelló. Both tablets are made of a small quantity of grass pollen[1,2].

Because these products are derived from natural sources, they are heterogeneous and variable. In order to ensure batch-to-batch consistency, each company has developed its own standardized unit based on in-house methods[3]: one tablet of AITGRYS® contains "300 RI" of grass pollen[1], while one tablet of GRAZAX® contains "75,000 SQ-T" of grass pollen[2]. Despite both

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companies providing a grass pollen-based tablet, authorities and prescribers were therefore unable to compare these units.

As explained by the World Allergy Organization last year and in order to facilitate cross-product comparability, the Food and Drug Administration in the US has been the first to require uniform potency-related labelling and to use its Center for Biologics Evaluation and Research (CBER) to define and manage such standardized unit[4]. For grass pollen, this process has led to the BAU (bioequivalent allergy unit) that now provides labelling in a common potency unit. Since both AITGRYS® (under the name ORALAIR®) and GRAZAX® (under the name GRASTEK®) are available in the US, strictly identical to their European form, they both had their potency in BAU measured by FDA and published in a peer-reviewed article[5] in an independent scientific journal, also captured in the US version of their Summary of Product Characteristics (SPC)[6,7]:

- *AITGRYS® (under the name ORALAIR®) 300 RI tablet: 9,000 BAU*
- *GRAZAX® (under the name GRASTEK®) 75,000 SQ-T tablet: 2,800 BAU*

In a comparative advertisement, one may only compare products that are relevant to compare (cf. ENLI's guidelines for the advertising code, version 4.2, p. 47, lines 5-6), which in this case are SLIT tablets for the treatment of grass pollen allergy, i.e. AITGRYS® and GRAZAX®. BAU is the only allergen unit approved by a regulatory agency (FDA): in the absence of similar cross-product comparability initiated so far at European level, BAU is therefore the only way to compare the potency of AITGRYS® and GRAZAX® in an accurate, relevant and loyal way and is perceived as being "highly indicative for clinicians"[5]. The complaint states that "the EU seems to come up with a common recommendation of method, and it will not be the BAU method": this assessment is not backed by any sources, there is no decision taken at today by European Authorities. Obviously, if a uniform potency-related standardized unit were adopted in Europe and differed from the BAU, our company would provide the most relevant unit according to the local market.

The use of word "potency" relates to the wording used in all scientific publications and by all allergy related Medical Associations at global (World Allergy Organization), American and European levels[3,4]. In the Global Atlas of Allergy published by the European Academy of Allergy & Clinical Immunology (EAACI), the word "potency" is mentioned 17 times[8], without any room for subjectivity. The targeted audience of the AITGRYS® promotional material challenged by ALK-Abelló are Danish healthcare professionals actively prescribing allergy immunotherapy products and therefore educated and aware of the principle of potency in the context of allergy. At Stallergenes Greer's level, we have not received queries from any Danish prescribers regarding the principle of potency at today, but in case such request would be received, Stallergenes Greer's Medical Affairs department will address such requests in accordance with the Danish rules for written responses to unsolicited inquiries from healthcare professionals.

Both AITGRYS® (under the name ORALAIR®) and GRAZAX® have been available for several years in many European countries and their respective potencies have been compared using this FDA unit in multiple occasions. Based on the above, our company Stallergenes Greer considers that:

- *Healthcare professionals operating in Denmark should not be limited in their access to*

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useful, indicative information.
- The comparison of the potency and of the treatment regimen of AITGRYS® and GRAZAX® based on their SPC and on publicly available information is of medical relevance to those healthcare professionals.

The comparative advertisement is done according to ENLI's guidelines for the Advertising Code v. 4.2, p. 48, section documentation, 1 st. line: "Full documentation about the comparative medicinal products can be done by reference to their SPCs". When compared in terms of potency, both AITGRYS® and GRAZAX® are clearly specified in the brochure, both with their respective trade name and the reference to their respective SPC. It is clear and transparent that AITGRYS® potency is compared to GRAZAX®. The BAU values are not in the Danish version of AITGRYS® and GRAZAX® SPCs, but it is not a requirement that all information in advertising materials must be included in the SPC. This is clarified in the European Court of Justice's decision C-249/09, the following (reproduced from the ENLI Guide on Information Material and Documentation, v1.2, p.7): "If advertising material includes information about the medicinal product in question that does not appear in the summary of product characteristics, scientific studies that meet the above criteria may be used. Such information must therefore confirm or clarify the content of the summary of product characteristics and thus be compatible with it, cf. the above on the European Court of Justice's decision in C-249/09". It is the opinion of Stallergenes Greer that the Passalacqua publication[5] provides this 'supplementary information'.

The complaint also states that the reference to respective products' SPC "are also referenced without date or version control". This is not a requirement, cf. ENLI Guide regarding Information Material and Documentation, version 1.2, p. 28, Q&A #279.

As acknowledged by ALK-Abelló in their complaint, "this comparative advertisement includes all the products relevant and available on the market", meaning that AITGRYS® having a potency more than 3 times higher than GRAZAX® automatically means that AITGRYS® has the highest potency of all the grass pollen products that are relevant and available on the Danish market at today. This conclusion is fully aligned with the content of our promotional material.

Apart from the potency comparison, the tablets' treatment regimen is mentioned: as stated in their respective Danish SPC, AITGRYS®'s treatment regimen involves fewer treatment days than GRAZAX®. AITGRYS® has a discontinuous, pre- and coseasonal regimen[1,5] (starting 4 months before the pollen season, pausing at the end of a season, and resuming the next year with the same protocol, which represents approx. 6 to 7 months of treatment per year for patients), while GRAZAX® has a continuous, year-round regimen[2,5] (starting at least 4 months before the pollen season and continuing without any pause). The GRAZAX® documentation provided by ALK-Abelló during the same annual meeting of the Danish Society of Allergology (DSA) in August 2024 clearly confirm on its cover that GRAZAX® must be taken "one tablet daily during 3 years" [10].

In terms of efficacy, both products, with their respective potency and regimen described above and in their respective studies, have demonstrated a prolonged efficacy of 2 years after a

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treatment course of 3 years (i.e. 5 years in total)[11,12]. This prolonged efficacy has been obtained for AITGRYS® with the discontinuous regimen[11], and for GRAZAX® with the continuous regimen[12], with both studies published in a peer-reviewed article in an independent scientific journal. It is clearly indicated in GRAZAX® Danish SPC that the prolonged efficacy cannot be obtained with a shorter regimen that the continuous, year-round one discussed above (see chapter 4.2, section "Administration")[2]. Guidelines from the Danish Association for Allergology (DSA) do not say otherwise[13], while the Danish Medicine Agency clearly states the following in the AITGRYS® reimbursement decision[14]:

"We assess that the therapeutic value of AITGRYS is at the same level as Grazax, which has general conditional reimbursement for the same clause. In this assessment, we emphasize that the indirect comparison analysis indicates that there is no statistically significant difference between AITGRYS and Grazax in the short and long term, and we do not find that there are any other factors about the medicines that give reason to believe that there should be a difference in the short-term and longterm effect of the two medicines". AITGRYS® efficacy data displayed in the material are provided with clear endpoints and definitions (RTSS) on page 4 and 5 of the material. As a conclusion, Danish healthcare professionals are presented in this comparative advertisement with the only 2 options to treat their patients with a grass pollen SLIT tablet: AITGRYS®, with a potency of 9,000 BAU and a discontinuous, pre- and coseasonal regimen, or GRAZAX®, with a potency of 2,800 BAU and a continuous, year-round regimen, with the level of details and references that comply with ENLI guidelines. For reference, this promotional material has also been uploaded on ENLI's web portal prior to being used in Denmark under the number R-2024-2834. We thank you in advance for the time and effort you will put into reviewing our response to this complaint and remain at your all disposal, should you need further information from our side.

Appendix – Summary table

#	*Position from ALK-Abelló Nordic A/S (original complaint translated into English)*	*Position from Stallergenes Greer Danmark ApS*
a)	[...] We do not believe that it is objectively correct to present Aitgrys as "the most potent SLIT treatment". [...] It can be seen from the reference publication that if you only assess based on BAU, then there are several SLIT treatments that are more potent than Aitgrys, which is why Aitgrys cannot be the "most potent SLIT treatment". [...]	This position a) is in conflict with the other ALK position captured in d) where it is acknowledged that "this comparative advertisement includes all the products relevant and available on the market". In a comparative advertisement, one may only compare products that are relevant to compare (cf. ENLI's guidelines for the advertising code, version 4.2, p. 47, lines 5-6), which in this case are SLIT tablets for the treatment of grass pollen allergy, i.e. AITGRYS® and GRAZAX®. There is only one unit approved by a regulatory authority in the world to compare potency of Grass SLIT tablets and it is the BAU. Both tablets had their potency in BAU measured by FDA and published in a peer-reviewed article in an independent scientific journal, also captured in the US version of their Summary of Product Characteristics (SPC): - AITGRYS® (under the name ORALAIR®) 300 RI tablet: 9,000 BAU - GRAZAX® (under the name GRASTEK®) 75,000 SQ-T tablet: 2,800 BAU. AITGRYS® has a potency more than 3 times higher than GRAZAX®, which automatically means that AITGRYS® has the highest potency of all the grass pollen products relevant and available on the Danish market at today. This is fully aligned with the content of our promotional material.
b)	[...] It is unclear what meaning lies in the word "potent", which can be understood in several different ways according to the Danish spelling dictionary. In the case of a medicinal product, this word should be avoided as it refers to a subjective assessment of the medicinal product. [...]	The use of word "potency" relates to the wording used in all scientific publications and by all allergy-related Medical Associations at global (World Allergy Organization), American and European levels. In the Global Atlas of Allergy published by the European Academy of Allergy & Clinical Immunology (EAACI), the word "potency" is mentioned 17 times, without any room for subjectivity. The targeted audience of the AITGRYS® promotional material challenged by ALK-Abelló are Danish healthcare professionals actively prescribing allergy immunotherapy products and therefore educated and aware of the principle of potency in the context of allergy.

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		At Stallergenes Greer's level, we have not received queries from any Danish prescribers regarding the principle of potency at today, but in case such request would be received, Stallergenes Greer's Medical Affairs department will address such requests in accordance with the Danish rules for written responses to unsolicited inquiries from healthcare professionals.
c)	[...] We disagree that Aitgrys is the "most potent SLIT treatment" if you consider the meaning of the word as "most effect", (which we assume has been the intention), as the effect does not depend solely on "the strength of grass pollen". [...]	As explained in b), the potency is well defined in the field of allergy immunotherapy. We have not claimed having the "most effect".
d)	[...] Aitgrys is marketed on parameters that are irrelevant when the healthcare professional is to assess the therapeutic effect of the medicinal product in relation to the patient. [...] This comparative advertisement includes all the products relevant and available on the market. However, the comparison is neither fair nor objective. [...]	See a).
e)	[...] We strongly object to our product being mentioned with a content in BAU in capital letters, without this unit of measurement being mentioned in the GRAZAX® summary of product characteristics. We believe it is very misleading in relation to our product. It should be noted that the content of BAU is not included in the summary of product characteristics for Aitgrys. [...]	Both AITGRYS® (under the name ORALAIR®) and GRAZAX® have been available for several years in many European countries and their respective potencies have been compared using this FDA unit in multiple occasions. Based on the above, our company Stallergenes Greer considers that: - Healthcare professionals operating in Denmark should not be limited in their access to useful, indicative information. - The comparison of the potency and of the treatment regimen of AITGRYS® and GRAZAX® based on their SPC and on publicly available information is of medical relevance to those healthcare professionals. The BAU values are not in the Danish version of AITGRYS® and GRAZAX® SPCs, but it is not a requirement that all information in advertising materials must be included in the SPC. This is clarified in the European Court of Justice's decision C-249/09, the following (reproduced from the ENLI Guide on Information Material and Documentation, v1.2, p.7): "*If advertising material includes information about the medicinal product in question that does not appear in the summary of product characteristics, scientific studies that meet the above criteria may be used. Such information must therefore confirm or clarify the content of the summary of product characteristics and thus be compatible with it, cf. the above on the European Court of Justice's decision in C-249/09*". It is the opinion of Stallergenes Greer that the Passalacqua publication provides this 'supplementary information'.
f)	[...] Both summaries of product characteristics are also referenced without date or version control. [...]	This is not a requirement, cf. ENLI Guide regarding Information Material and Documentation, version 1.2, p. 28, Q&A #27.
g)	[...] It should also be mentioned that the measurement of the strength of the allergen content in different products can change greatly depending on the method. The mentioned Passalaqua reference already mentions in the abstract that there is no approved European common unit of measurement "..with European regulatory authorities yet to adopt a common unit". [...] ALK sees this as a single study that indicates positive results for Aitgrys, which are misleading and unobjective in relation to the overall knowledge in the field. [...]	As explained by the World Allergy Organization last year and in order to facilitate cross-product comparability, the Food and Drug Administration in the US has been the first to require uniform potency-related labelling and to use its Center for Biologics Evaluation and Research (CBER) to define and manage such standardized unit. For grass pollen, this process has led to the BAU (bioequivalent allergy unit) that now provides labelling in a common potency unit. Both the unit and the method to measure it have been developed by the FDA, this not an experimental unit that could change depending on the method. The BAU does not originate from the Passalacqua study which only shows the BAU amount per product as measured by FDA and captured in their US SPC, and the Passalacqua study is a peer-reviewed article published in an independent scientific journal.
h)	[...] It can be mentioned that the EU seems to come up with a common recommendation of method, and it will not be the BAU method. [...]	This assessment is not backed by any sources, there is no potency unit selected at today by European Authorities. Obviously, if a uniform potency-related standardized unit were adopted in Europe and differed from the BAU, our company would provide the most relevant unit according to the local market.
i)	[...] The primary endpoints and the definition of clinically relevant improvement in allergen content are missing from the promotional material. [...]	AITGRYS® efficacy data displayed in the material are provided with clear endpoints and definitions (RTSS) on page 4 and 5 of the material.
j)	[...] We do not believe that there is sufficient documentation to demonstrate that exactly BAU measurement has an impact on the effect of the treatment. There is no documentation that it is the amount of BAU that is the reason why "you only need to treat for 7 months". It can be clarified below that the STG product does not have either better efficacy data than GRAZAX®, nor does the STG product have disease modification in their indication (although it is strongly suggested on page 8) unlike the GRAZAX® label (based on a positive study with proven long-term effect 2 years after the end of treatment), which is why there is nothing else to support that it is an advantage with a higher BAU. [...]	In parallel of the BAU comparison, the comparative advertisement mentions the tablets' treatment regimen. As stated in their respective Danish SPC, AITGRYS®'s treatment regimen involves fewer treatment days than GRAZAX®. AITGRYS® has a discontinuous, pre- and coseasonal regimen (starting 4 months before the pollen season, pausing at the end of a season, and resuming the next year with the same protocol, which represents approx. 6 to 7 months of treatment per year for patients), while GRAZAX® has a continuous, year-round regimen (starting at least 4 months before the pollen season and continuing without any pause). The GRAZAX® documentation provided by ALK-Abelló during the same annual meeting of the Danish Society of Allergology (DSA) in August 2024 clearly confirm on its cover that GRAZAX® must be taken "*one tablet daily during 3 years*". As mentioned in c), we have not claimed having "better efficacy data" and did not use the wording "disease modification" in our material.

Granskningsmandspanelet tog herefter sagen op til afgørelse.

Regelgrundlag

Det fremgår af Reklamekodeksets § 4, stk. 2, at reklame for et lægemiddel skal være fyldestgørende og saglig, og den må ikke være vildledende eller overdrive lægemidlets egenskaber. Oplysninger i reklamen skal være i overensstemmelse med lægemidlets godkendte produktresumé.

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Af Reklamekodeksets § 7, stk. 1, fremgår det, at lægemiddelreklamer skal tilskynde rationel brug af lægemidler ved at præsentere lægemidler objektivt og uden overdrivelse af deres egenskaber. Påstande må ikke antyde, at et lægemiddel eller en aktiv bestanddel har særlige fordele, kvaliteter eller egenskaber, medmindre dette kan dokumenteres. En sådan dokumentation skal ved rimelige forespørgsler fra sundhedspersonale kunne tilvejebringes hurtigt.

Af Reklamekodeksets § 8, stk. 1, fremgår det, at hvis en reklame indeholder en sammenligning mellem flere lægemidler, skal det tydeligt fremgå, hvilke lægemidler sammenligningen omfatter. Sammenligningen må kun omfatte lægemidler, som det objektivt set er relevant at sammenligne, dvs. lægemidler med sammenfaldende anvendelsesområde.

Af Reklamekodeksets § 8, stk. 2, fremgår det, at sammenlignende reklame skal udarbejdes på grundlag af oplysningerne i produktresuméerne for de lægemidler, som indgår i sammenligningen.

Granskningsmandspanelets vurdering og afgørelse
Nærværende klage vedrører indklagedes reklamemateriale - en 12-siders e-detailer, primært omhandlende Aitgrys. Klager påpeger, at der på side 3 fremføres sammenlignende reklame med Grazax, som klager finder i strid med Reklamekodeksets § 8, stk. 1, jf. § 4, stk. 2 samt § 7, stk. 1.

Reklamens indhold på denne side indbefatter overskriften *"Periodisk pollenbehandling med pause under lavsæson[ref.]"*, og en efterfølgende brødtekst, der bl.a. indeholder sammenlignende udsagn:

"Aitgrys er den mest potente SLIT-behandling, hvor hver 300 RI tablet indeholder 9000 BAU sammenlignet med en tablet Grazax, der indeholder 2800 BAU[ref.]. Aitgrys høj potens muliggør derfor en periodisk pollenbehandling med pause i lavsæsonen. Dette behandlingsregime betyder færre behandlingsdage for dine patienter sammenlignet med Grazax[ref.]"

Siden indeholder i øvrigt, med stor, iøjnefaldende og fremhævet skrift svarende til et omfang på ca. en halv side *"Aitgrys 300 RI* ***9000 BAU***[ref.]*"* og *"Grazax 75,000 SQ-T* ***2800 BAU***[ref.]*"*. Der henvises nederst på siden som en fodnote til, at *"SLIT = sublingual immunterapi"* og *"BAU = Bioequivalent Allergy Unit, udviklet af FDA til at måle styrken af græspollen"*, hvor der for sidstnævnte henvises til *Passalacqua et al. Comparison of allergenic extracts from different origins: the value of the FDA's bioequivalent allergy unit (BAU). Exp Clin Rev Immunol. 2015.*

Klager påpeger overordnet, at det sammenlignende reklameelement er illoyalt, da lægemidlernes "potens" sammenlignes på baggrund af BAU (Bioequivalent Allergy Unit), der ikke er anvendt i lægemidlernes gældende danske produktresuméer. Der knyttes en række andre understøttende punkter for denne pointe.

Indklagede argumenterer overordnet for, at sammenligning er foretaget med udgangspunkt i anvendelig komparativt dokumentationsgrundlag bl.a. i form af SmPC'er for lægemidlerne ved FDA og en fagfællebedømt publikation.

Granskningsmandspanelet bemærker, at sammenlignende reklame for lægemidler skal tage udgangspunkt

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i lægemidlernes produktresuméer, jf. Reklamekodeksets § 8, stk. 2. Det betyder implicit, at man tager udgangspunkt i de produktresuméer, der er gældende for lægemidler godkendt til det danske marked. Hverken produktresuméet for hhv. Aitgrys eller Grazax indeholder oplysninger om styrken målt i BAU. Derimod indeholder de fabrikant-specifikke ekstrakt-potenser. For Grazax er styrken opgjort til 75.000 SQ-T [standardized quality tablet unit], og for Aitgrys er styrken opgjort til 300 IR [index of reactivity].

Granskningsmandspanelet kan samlet set ud fra den forelagte litteratur fra både klager og indklagede konstatere, at der ikke foreligger en standardiseret international harmonisering eller vedtagelse af en målbar enhed for allergeniciteten og/eller potensen mellem diverse græspollen-ekstrakter og dermed afledte immunterapier baseret herpå.

Det kan endvidere konstateres, at der i forhold til diverse regulatoriske myndigheder internationalt, herunder i EU, er en opmærksomhed på dette, om end der ikke endnu foreligger en klart defineret standard herfor. Dog foreligger der ved FDA et krav om estimering af BAU ved ansøgning om markedsføringsgodkendelse – en måleenhed, som ultimativt fremgår af lægemidlernes respektive amerikanske produktresuméer mhp. understøttelse af en "standardiseret" estimering af ekstrakt-potensen på tværs af ellers fabrikant-specifikke ekstrakter med forskelligartede enheder for disses allergeniske aktivitet. Center for Biologics Evaluation and Research (CBER) vedligeholder og distribuerer reference ekstrakter og serum-pools til brug for denne kvantificering.

Det er derfor Granskningsmandspanelets vurdering, at sagen i dansk kontekst først og fremmest omhandler, hvorvidt enheden BAU i nærværende konkrete situation vurderes at være forenelig med, herunder præcisere eller bekræfte, oplysninger i de dansk-gældende produktresuméer. Derudover skal sammenligningens beskaffenhed vurderes i kontekst af reglerne for både sammenlignende og saglig reklame.

Det er Granskningsmandspanelets vurdering, at selvom en regulatorisk myndighed som FDA anser BAU målemetoden og enheden som nødvendig, har andre anerkendte regulatoriske myndigheder internationalt, herunder særligt Danmark, på nuværende tidspunkt ikke tiltrådt denne. Kravet om anvendelse af metoden og enheden ved FDA (og dermed forankring samt inklusion i amerikanske SmPC'er) er ikke ensbetydende med, at metoden eller enheden nødvendigvis kan anses som værende af supplerende eller præciserende karakter til det dansk gældende produktresumé, ligesom det ikke nødvendigvis muliggør sammenlignende anvendelse eller promovering heraf i markedsføringsmateriale i Danmark.

Granskningsmandspanelet er opmærksom på, at der henvises til en fagfællebedømt publikation, der bl.a. diskuterer metoden, enheden og anfører denne for en række lægemidler i produktklassen i relation til deres producent-specifikke allergenicitets-enheder. At en oplysning fremgår af en peer-reviewed artikel er dog ikke ensbetydende med, at den frit kan anvendes i en lægemiddelreklame, jf. vejledning til Reklamekodeksets § 7, stk. 1 hvoraf følgende bl.a. fremgår: *"At et studie er peer-reviewed og publiceret i et tidsskrift, der formelt set opfylder § 7, stk. 5, er ikke ensbetydende med, at referencen kan anvendes helt ukritisk. Hvis referencen fx indeholder oplysninger om forhold, der strider mod SPC'et, vil referencen ikke kunne anvendes, selvom den opfylder § 7, stk. 5, da den samtidig strider mod andre bestemmelser i reklamereglerne. Se endvidere Ankenævnets afgørelse i AN-2017-1490".*

Det er således Granskningsmandspanelets vurdering, at BAU enheden *ikke kan* anses som en supplerende

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og præciserende information til lægemidlernes (danske) produktresuméer, idet enheden (på nuværende tidspunkt) relaterer sig til anvendelse for udenlandsk regulatorisk praksis.

Derfor vurderes materialet i strid med Reklamekodeksets § 8, stk. 2, hvoraf det fremgår, at *"Sammenlignende reklame skal udarbejdes på grundlag af oplysningerne i produktresuméerne for de lægemidler, som indgår i sammenligningen"*.

Granskningsmandspanelet finder derudover, at sammenligningen er usaglig og i strid med Reklamekodeksets § 8, stk. 1, jf. § 4, stk. 2 og § 7, stk. 1.

I det konkrete materiale anvendes BAU-enheden primært som et differentierende og sammenlignende element og på en særdeles iøjnefaldende og fremhævet facon. Enheden præsenteres ikke på en saglig, objektiv, informativ og supplerende facon analogt med en "faktuel" oplysning, hvilket er i strid med kriterierne for saglig (sammenlignende) reklame, da helhedsindtrykket af anvendelsen fremstår særligt pågående i lyset af de samlede omstændigheder, jf. Reklamekodeksets § 8, stk. 1, og særligt vejledningen til bestemmelsen, hvor det konkret vedrørende andre forhold end lægemidlets effekt og sikkerhedsprofil fremgår, at *"[…] Saglighedskriteriet i Reklamekodeksets § 4, stk. 2, skal sikre, at en reklame altid som primært formål indeholder faglige, fyldestgørende og relevante oplysninger om lægemidler, hvilket ENLI finder væsentligt, især for sammenlignende reklamer. Dette særligt for at undgå reklamer, hvor lægemidler med evt. dårligere/lavere effekt end det lægemiddel, der sammenlignes med, markedsføres på parametre, der er irrelevante, når sundhedspersonen skal vurdere lægemidlets terapeutiske effekt i forhold til patienten"*.

Dette vurderes uagtet, at reklamen specificerer "potens", selvom det anføres, at potens-begrebet i allergologisk kontekst kan fortolkes synonymt med allergenicitets-begrebet, idet den iøjnefaldende og markante fremhævelse i reklamematerialet indirekte synes at antyde en afledt betydende bedre klinisk (effekt)profil, selvom der ikke i materialet direkte fremhæves komparative effekt-udsagn. På trods af, at målgruppen for reklamen (deltagende ved Dansk Selskab for Allergologi) vurderes at være allergologiske eksperter, kan det ikke forudsættes, at deltagere har ekspertise vedr. BAU, som er forankret i udenlandsk regulatorisk praksis. Dette vurderes uagtet, at det som fodnote fremgår, at metodikken er *"… udviklet af FDA til at måle styrken af grænspollen"*.

Granskningsmandspanelet bemærker derfor, at selv hvis enheden BAU kunne anvendes til at præcisere eller bekræfte oplysninger i de danske produktresuméer, findes måden, hvorpå indklagede har opsat sammenligningen til klagers lægemiddel i strid med saglighedskravet under de givne omstændigheder og vurderes som en illoyal sammenlignende reklame, jf. ovenstående.

Granskningsmandspanelet giver således klager medhold i den samlede klage, idet reklamen giver et usagligt og illoyalt indtryk af, at Aitgrys har bedre effekt end Grazax baseret på en enhed, der for nuværende alene finder anvendelse i udenlandsk regulatorisk praksis, og som der ikke anses som præciserende eller supplerende til de danske produktresuméer.

Afgørelse:
Stallergenes Greer Danmark ApS findes således at have overtrådt Reklamekodeksets §§ 8, stk. 1 og 2, jf. § 4, stk. 2 og § 7, stk. 1, og pålægges som følge heraf følgende sanktioner:

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Sanktion:

- Stallergenes Greer Danmark ApS pålægges at ophøre med at anvende reklamen i dens foreliggende form.
- Stallergenes Greer Danmark ApS pålægges endvidere en bøde på 60.000 kr. + moms i henhold til ENLI's Sanktions- og gebyrregulativ § 4, stk. 1, litra h).

Kopi af nærværende skrivelse sendes til klager hhv. indklagede og til Lægemiddelstyrelsen til orientering, når sagen er endelig.

Med venlig hilsen

Kasper Hasseriis Andersen
Lægefaglig granskningsmand

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