

Adverse reactions after switch from compounded dexamfetamine to Amfexa®

Introduction

Dexamfetamine (Amfexa®) is indicated as *part of a comprehensive treatment program for attention deficit / hyperactivity disorder (attention deficit hyperactivity disorder or ADHD) in children and adolescents from 6 to 17 years when the response to previous treatment with methylphenidate is not clinically satisfactory*. An extensive treatment program usually consists of psychological, pedagogical and social measures. Amfexa® was granted a Marketing Authorization on 20 October 2014 (1).

In the Netherlands, many patients were started on pharmacy compounded dexamfetamine, before Amfexa® became available.

In 2019 the Inspectorate for Healthcare and Youth (IGJ) reported that they had investigated whether pharmacists who prepare dexamfetamine themselves and deliver it to other pharmacists adhere to all conditions for delivery of compounded dexamfetamine.

An important principle of the Circular on Compounded products (Circulaire 'handhavend optreden bij collegiaal doorleveren van eigen bereidingen door apothekers' 2019-01-IGZ) is that collegial resale is only permitted if there is clear added value of the resupplied preparation. This added value must be described by the preparatory pharmacy in a product file and depends on two factors; 1. absence of registered adequate alternatives and 2. a clear pharmacotherapeutic rationale. Both factors must be laid down in a structured way by the preparatory pharmacy, ending with a clear conclusion. From this conclusion it must be apparent for which therapeutic objective(s) and in which patient population(s) the preparation provided has added value (indication(s)). The added value must be based on a special need of a medical nature. In addition, the added value of the supplied preparation must be clearly stated in the accompanying product information for healthcare provider and / or patient. The investigation showed that for dexamfetamine the above mentioned conditions are not (always) adhered to (2).

The IGJ noted that dexamfetamine is available in the Netherlands as the registered product Amfexa®. This medicine is only available in 5 milligram tablets. Pharmacies can only deliver the compounded product to patients if there is no suitable registered alternative. This means that most patients can use the registered Amfexa®. For a small group of patients, namely children from 3 to 6 years with ADHD, a lower dose is regularly prescribed. Because there is a special need of a medical nature, compounded preparations for this patient group may be supplied. In some other cases too, there may be a medical necessity for a compounded drug, such as in patients with an allergy to an excipient (2).

The IGJ investigation led to many additional patients being switched from the compounded dexamfetamine to Amfexa® in 2019.

Reports

From 2016 until 23 November 2019 the Netherlands Pharmacovigilance centre Lareb received 65 reports of ADRs after drug substitution from compounded dexamfetamine to Amfexa®, see Appendix 1. 10 reports originated from 2016, 1 from 2018 and 54 from 2019. The reporter was a consumer in 50 cases, a pharmacist in 8 cases, a medical doctor in 5 cases and an 'other' healthcare professional in 2 cases.

Five reports concern the age group (6-17 years) for which the medicine is registered, other reports concern "off-label" use in adults. Ages of the children using Amfexa® in the reports range from 9 to 17 years.

In the reports of ADRs after drug substitution from compounded dexamfetamine to Amfexa®, a total of 255 ADRs were reported. Most commonly reported ADRs were Headache (n=19), Depressed mood (n=16), Palpitations (n=11), Restlessness (n=10), Insomnia (n=9), Dizziness (n=8), Disturbance in attention (n=8), Dry mouth (n=8).

In 23 cases the manufacturer of the previous compounded product was known; De Magistrale Bereider (DMB) (n =19), Fagron (n=1), Pharmaline (n=2), Centrale Bereidingsapotheek (n=1).

In 26 cases patients (previously) used a dosage that could not be obtained with 5 mg tablets, for example 2.5 or 7.5 mg. That means that Amfexa® tablets either had to be broken, Amfexa® 5 mg was used in combination with a compounded tablet (for instance of 2.5 mg) or the patient was switched to a higher dosage when starting with Amfexa® (from 2.5 mg to 5 mg).

Other sources of information

SmPC

The SmPC states that 'Amfexa® 5 mg is not approved for use in adults. The safety and efficacy of dexamfetamine in adults has not been established (1).'

The most reported reactions after substitution to Amfexa® such as headache, depression, palpitations, restlessness are mentioned in the SmPC for Amfexa®.

Literature

Although Amfexa® is only registered for the age for 6 to 17 years, this does not mean that adults cannot be switched to this product. The Healthcare Institute states: '*When drawing up the further conditions, we did not use the option to limit the reimbursement to the age category for which registration was granted (6 to 17 years), because the pharmacy preparation of dexamfetamine has been going on for years applied to adults*' (3).

The Dutch Pharmacists' association KNMP explains in their questions and answers about Amfexa® that the product cannot be divided into equal parts for dosing (3). According to the Dutch summary of product characteristics (SmPC), Amfexa® is not registered to dose in 2 or 4 equal parts. The tablet is only registered to break into 2 or 4 equal parts, if this is convenient for intake (1). The KNMP states that Amfexa® should be delivered as much as possible to meet the prescribed dosage. In short, 7.5 mg means: 1 tablet of Amfexa® and 1 tablet of 2.5 mg of compounded dexamphetamine.

In addition, if Amfexa® 5 mg tablets are sufficient to reach the prescribed dosage, there is no longer a special need of a medical nature and a compounded product should not be delivered (3).

Prescription data

No data are available yet for Amfexa® use in 2019 and the number of switches between compounded dexamfetamine to Amfexa® through the GIP website (4).

Discussion and conclusion

The Netherlands Pharmacovigilance Centre Lareb sees a sharp increase in the reports on Amfexa®, related to ADRs after drug substitution, since the IGJ reported on the terms of delivery for compounded dexamfetamine in July 2019 (2). Until October 31 2019, 36 spontaneous reports of ADRs after drug substitution from compounded dexamfetamine to Amfexa® were received, with 25 reports from 2019. Five reports concern the age group (6-17 years) for which the medicine is registered, other reports concern "off-label" use in adults. The KNMP has mentioned that the age mentioned in the SmPC (6-17 years) is no reason to deliver compounded dexamfetamine to adults (3). In 16 cases patients (previously) a dosage was used that could not have been obtained with 5 mg tablets, for example 2.5 or 7.5 mg. That means that Amfexa® tablets either had to be broken, Amfexa® 5 mg was used in combination with a compounded tablet (for instance of 2.5 mg) or the patient was switched to a higher dosage when starting with amfexa® (from 2.5 mg to 5 mg).

Dutch Pharmacists recently studied whether it is possible to manually split tablets in half using a reliable and validated method. All six tablet types tested met the requirements of the test for loss of mass (< 3%). Two of the six tablets met the requirements of the European Pharmacopoeia test for loss of uniformity. Type of scoring and the thickness of the tablet seem to be factors influencing the process of tablet splitting. They concluded that tablet splitting by hand in the pharmacy is not feasible because for most tablets it will not be possible to develop a reliable and validated method (5).

The pattern of most reported drug reactions for Amfexa® is similar to that of compounded dexamfetamine, with the exception of Restlessness (n=5), Rebound effect (n=4), Hyperhidrosis (n=3) and Lack of drug effect (n=3). In the reports after switching patients often mentioned that the symptoms of their ADHD had returned/worsened since they started using Amfexa®.

The total number of reports on compounded dexamfetamine is 194 with a total of 392 ADRs reported. Most commonly reported ADRs are depressed mood (n=10), headache (n=9), palpitations (n=8). Also, some reports (n = 9) describe ADRs related to switches between different compounded dexamfetamine products.

There are a number of factors that can underlie these reports. Apart from actual ADRs as a result of the use of Amfexa®, other factors may also play a role, such as the fact that this is an involuntary switch for many patients, which sometimes entails additional costs for the patient. A clear pattern in the reports after substitution is still missing. The extent to which there are differences in pharmacokinetics and

stability in between Amfexa® and compounded dexamfetamine products, that could be responsible for the reported reactions, is as yet unclear. For instance, differences in dissolution could cause differences in bioavailability. Attention is warranted for possible negative effects in patients switching from compounded dexamfetamine to Amfexa®, including have to break tablets to obtain the right dosage or being switched to a higher dosage.

Literature

1. College ter Beoordeling van Geneesmiddelen. Dutch SmPC Amfexa(R) 2019 [updated 20-07-2018; 31-10-2019]. Available from: https://www.geneesmiddeleninformatiebank.nl/smpc/h110336_smpc.pdf.
2. Inspectie voor Gezondheidszorg en Jeugd. Bereidende apotheken voldoen niet aan voorwaarden bij doorlevering dexamfetamine 2019 [updated 01-07-2019; 31-10-2019]. Available from: <https://www.igi.nl/actueel/nieuws/2019/07/01/bereidende-apotheken-voldoen-niet-aan-voorwaarden-bij-doorlevering-dexamfetamine>.
3. KNMP. Vragen en antwoorden over Amfexa en dexamfetamine 2019 [updated 27-09-2019]. Available from: https://www.knmp.nl/patientenzorg/geneesmiddelen/apotheekbereidingen/copy_of_veelgestelde-vragen-dexamfetamine.
4. College voor Zorgverzekeringen. GIPdatabase - Drug Information System of the Dutch Health Care Insurance Board 2019 [updated 2019]. Available from: <http://www.gipdatabank.nl>
5. van Gosliga F, Burgler, L., Heijnen, M., Last, T., van Zante, E., Yska, J.P. Kunnen tabletten op een betrouwbare manier handmatig worden gehalveerd? Nederlands Platform voor Farmaceutisch Onderzoek. 2019;2019;4:a1712.

This signal has been raised on December 19, 2019. It is possible that in the meantime other information became available. For the latest information, including the official SmPC's, please refer to website of the MEB www.cbq-meb.nl

Appendix 1

Colour codes

Previous brand unknown

Previous brand known

Dosages that cannot be obtained with 5 mg tablets (without breaking them)

Reports of ADRs after drug substitution from compounded dexamfetamine to Amfexa® in the Lareb database

Nr	ID (NL-LRB) Sex, Age Primary Source	Suspec IA drug Indication Dosage/unit	Concomitant medication	Reported LLTs	Latency Action taken Outcome	Year	Info on dosage change (meldtekst)
1	217145 male, 30-40 Years Consumer	AMFEXA TABLET 5MG Attention deficit hyperactivity disorder 30 milligram / 1 Days		Therapeutic response unexpected with drug substitution Previous brand unknown Drowsiness Concentration impairment Irritable Sweating Hyperactivity	1 Hour Unknown Not Recovered	2016	
2	219050 female, 10-20 Years Other health professional	AMFEXA TABLET 5MG Attention deficit/hyperactivity disorder 5 milligram / 1 Days		Therapeutic response unexpected with drug substitution Previous brand unknown Listless Feeling sad Withdrawn Apathy	1 Hour Drug Withdrawn Recovered	2016	

3	219719 female, 30-40 Years Consumer	AMFEXA TABLET 5MG DEXAMFETAMINE TABLET 2,5MG Attention deficit disorder Attention deficit disorder 4 dosage form / 1 Days 4 dosage form / 1 Days	fluoxetine	Therapeutic response unexpected with drug substitution Previous brand unknown Palpitations Insomnia Tremor Rebound effect	1 Hour 1 Day 8 Hours Dose Not Changed Not Recovered	-- -	slikte dexamfetamine in de dosering: 7,5 + 7,5 mg + 5 mg en 's avonds 5 of 2,5 mg. Aangezien de dex 2,5 niet leverbaar is en ik daarvan nog een paar pilletjes had, stelt Apotheek voor om amfexa 5mg te combineren met dex 2,5 mg, zodat ik deze dosering kan blijven gebruiken. Volgens apothek gaat het om exacte hetzelfde middel, dus combineren kan geen kwaad.
4	219888 female, 60-70 Years Consumer	AMFEXA TABLET 5MG Attention deficit disorder 3x2,5mg		Therapeutic response unexpected with drug substitution Previous Brand De Magistrale Bereider (DMB) Derealisation Aggression Depressed mood Lack of drug effect	5 Days Not Applicable Not Recovered Unknown	2016	
5	221735 male, 10-20 Years Pharmacist	AMFEXA TABLET 5MG Attention deficit hyperactivity disorder dosage form / 1 Days		Therapeutic response unexpected with drug substitution Previous brand unknown Nausea	30 Minutes Drug Withdrawn Recovered	2016	

6	221877 male, 30-40 Years Other health professional	AMFEXA TABLET 5MG Attention deficit hyperactivity disorder 30 milligram / 1 Days	quetiapine	Therapeutic response unexpected with drug substitution Previous brand unknown Aggression Agitation Rebound effect Depressed mood	4 Months Drug Withdrawn Recovered, patient was switched to atomoxetine	2016	
7	224884 male, 50-60 Years Pharmacist	AMFEXA TABLET 5MG Restlessness 15 milligram / 1 Days	levothyroxine citalopram salbutamol colecalfiferol cromoglicinezuur	Therapeutic response unexpected with drug substitution Previous brand Fagron Arrhythmia Blood pressure increased	- Drug Withdrawn Recovered	2016	De dosering was en is 2x daags 7,5mg. De patiënt gebruikt nu de 2,5mg tabletten van Fagron
8	225025 male, 7-10 Years Physician	AMFEXA TABLET 5MG Attention deficit/hyperactivity disorder 2 dosage form / 1 Days		Therapeutic response unexpected with drug substitution Previous brand Pharmaline Abnormal behaviour	- Drug Withdrawn Recovered	2016	Voor de het starten van de Amfexa® gebruikte de patient Dexamfetamine tablet a 5mg van Pharmaline. Nu gebruikt deze client Dexamfetamine Pharmaline tabletten a 2,5mg. (alleen deze dosis wordt nog vergoed) op dezelfde tijdstippen en dosering als de twee andere Dexamfetamine preparaten

9	228773 male, 20-30 Years Consumer	AMFEXA TABLET 5MG Attention deficit/hyperactivity disorder 45 milligram / 1 Days		Therapeutic response unexpected with drug substitution Previous brand unknown Headache Restlessness Hyperhidrosis Seizure	2 Hours Drug Withdrawn Recovering (1 month later)	2016	
10	241276 male, 40-50 Years Consumer	AMFEXA TABLET 5MG Attention deficit disorder 45 milligram / 1		Therapeutic response unexpected with drug substitution Previous brand unknown Fatigue Poor sleep Unrest	2 Days Drug Withdrawn Recovering	2016	
11	00323108 female, 30-40 years Consumer	AMFEXA TABLET 5MG ADHD 10 milligram / 12 Hours		Therapeutic effect unexpected Previous brand unknown Common cold (3 times since the start of Amfexa in a period of 6 weeks, unusual for the reporter)	25 Minutes Dose Not Changed Not Recovered Not Recovered	2018	
12	00333322 male, 40-50 Years Physician	AMFEXA TABLET 5MG Drug use for unknown indication 5 milligram / 8 Hours	flupentixol olanzapine quetiapine	Therapeutic response unexpected with drug substitution Previous brand unknown Drug craving Alcohol craving Concentration impairment	- Dose Not Changed Not Recovered	2019 05-10	

13	00346459 female, 40-50 Years Consumer	AMFEXA TABLET 5MG ADD 1 dosage form		Therapeutic response unexpected with drug substitution Previous brand unknown Headache Palpitations Restlessness Tic Anger Pruritus Sleep disorder Bad mood	1 Hour Drug Withdrawn Recovered	2019 08-01	
14	00347611 female, 20-30 Years Consumer	AMFEXA TABLET 5MG ADHD 5 milligram / 12 Hours		Therapeutic response unexpected with drug substitution Previous brand unknown Agitation Restlessness Insomnia Nervousness Mood change	4 Hours Drug Withdrawn Recovered	2019 08-09	1x7,5 mg en 1x 2,5mg dexamfetamine naar 2x 5mg Amfexa , na staken Amfexan hersteld; Amfexa niet gebroken, eerder geen ontregeling
15	00349287 male, 40-50 Years Consumer	AMFEXA TABLET 5MG ADHD 5 milligram		Therapeutic response unexpected with drug substitution Previous Brand De Magistrale Bereider (DMB) Headache Restlessness Hyperhidrosis Rebound effect	- Dose Not Changed Not Recovered	2019 08-22	Verplicht over moeten stappen van de 2,5 mg van de Magistrale Bereider naar Amfexa
16	00349439 female, 30-40 Years Physician	AMFEXA TABLET 5MG ADHD 10 milligram / 6 Hours		Therapeutic response unexpected with drug substitution Previous Brand De Magistrale Bereider (DMB) Lack of drug effect Depressed mood Listlessness	1 Day Dose Not Changed Not Recovered	2019 08-23	

17	00349633 female, 50-60 Years Pharmacist	AMFEXA TABLET 5MG ADHD 15 milligram / 8 Hours	omeprazol macrogol diclofenac- sumatriptan	Therapeutic response unexpected with drug substitution Previous brand unknown Rebound effect	4 Hours Drug Withdrawn Recovering	2019 08-26	
18	00349635 female, 50-60 Years Consumer	AMFEXA TABLET 5MG ADHD 2x per dag 10 mg gevolgd door 2x per dag 7,5 mg		Therapeutic response unexpected with drug substitution Previous Brand De Magistrale Bereider (DMB) Lack of drug effec Dry mouth Dizziness Oral discomfort Bruxism Compulsive cheek biting Dyspnoea	1 Day Drug Withdrawn Recovered, back to brand DMB	2019 08-26	
19	00349951 female, 40-50 Years Pharmacist	AMFEXA TABLET 5MG ADHD 3x per dag 1,5 tablet	levonorgestrel iud	Therapeutic response unexpected with drug substitution Previous brand unknown Headache Restlessness Drug effect decreased	1 Day Dose Not Changed Unknown	2019 08-28	
20	00351163 male, 60-70 years Consumer or other non health professional	AMFEXA TABLET 5MG ADHD 40 milligram / 1 Days 4maal daags 2 tabletten a 5mg Naar halve tablet. Een enkele keer kruimels	atorvastatine lisinopril	Therapeutic response unexpected with drug substitution Previous Brand De Magistrale Bereider (DMB) Dry mouth Condition aggravated Oral pain Oromandibular dystonia	1 Day Dose Reduced from 40 mg to 30 mg Recovering from ADRs (Oromandibular dystonia has markedly improved, however not the dry mouth), but lack of effect	2019 09-08	Was 4maal daags 4 tabletten 2,5mg dexamfetamine van Magistrale Bereider

21	00351225 female, 40-50 Years Consumer	AMFEXA TABLET 5MG ADHD 1 dosage form / 8 Hours	colecalfierol omeprazol estradiol/dydrogesteron tabletten (femoston 1/10)	Therapeutic response unexpected with drug substitution Previous Brand De Magistrale Bereider (DMB) Lack of drug effect Apathy Pyrosis Abdominal cramps Raynaud's phenomenon Muscle tension Headache Dizziness Diarrhoea	22 Hours 45 Minutes 15 Hours 22 Hours 1 Hour 45 Minutes 12 Hours 45 Minutes Drug Withdrawn Recovered Not Recovered Recovering	2019 09-09	Eerder gebruik van dexamfetamine 2.5 mg 4x dgs. Magistrale Bereider Weer herstart van Amfexa, maar lagere doseringen; met Amfexa gestart met 3x2 tabletten, volgende dag 2x 1,5 tabletten en dag daarna 2x1 tablet. Tablet was gehalveerd Bw werden minder maar gingen niet weg. Geen doseering Amfexa zorgde voor beoogd effect, wel bijwerkingen Nu op Elvanse 1x 110mg per dag, geen bw wel goed effect Eerder (nog voor dexamfetamine) methylfenidaat met depressieve klachten.
22	00352028 male, 10-20 Years Consumer	AMFEXA TABLET 5MG Drug use for unknown indication	sertraline hydrochloride	Therapeutic response unexpected with drug substitution Previous Brand De Magistrale Bereider (DMB) Palpitations Neck pain Disturbance in attention Nervousness Headache	- Unknown Not Recovered	2019 09-05 IVM	Gebruikte eerder de Magistrale Bereider (DMB) 2.5 mg tabletten, switch naar 5 mg Amfexa

23	00353362 female, 40-50 Years Consumer	AMFEXA TABLET 5MG ADD 2x daags een halve tablet van 5mg	venlafaxine	Therapeutic response unexpected with drug substitution Previous Brand De Magistrale Bereider (DMB) Confused Emotional poverty Hearing decreased Pruritus Headache Insomnia	1 Hour Dose Not Changed Recovered, switched back to Brand De Magistrale Bereider (DMB)	2019 09-24	
24	00354377 male, 40-50 Years Consumer	AMFEXA TABLET 5MG ADD 5,5 stuks per dag (27.5 mg)		Therapeutic response unexpected with drug substitution Previous brand unknown Headache Behavior abnormal Spasm oculomotor Drowsiness	30 Minutes Dose Not Changed Not Recovered	2019 10-01	Eerder 2.5 mg pillen
25	00354572 female, 10-20 years Physician	AMFEXA TABLET 5MG ADHD 7,5mg per dag		Therapeutic response unexpected with drug substitution Previous brand unknown Behavior abnormal Mood swings	5 Days Drug Withdrawn Recovered, switch back to old brand	2019 10-02	Moeder moest bij Amfeaxa 1 tablet breken om 7.5 mg te bereiken
26	00354602 female, 20-30 Years Consumer	AMFEXA TABLET 5MG ADHD 5 mg 3x dag		Therapeutic response unexpected with drug substitution Previous brand Pharmaline Unrest Palpitations Hyperhidrosis Sleeplessness Appetite lost	1 Hours Drug withdrawn Outcome unknown	2019 10-03	Voor mij werkte pharaline het beste en met de 2.5 mg kon ik goed dosseren. Dosering was 2,5mg 3maal daags. Met Amfeaxa dosering 3maal daags 5mg Geen halvering, bij afbreken brokkelt het en dosering t klopt niet

							Eerst nog methylfenidaat als bw depressieve klachten
27	00354756 male, 40-50 Years Consumer	AMFEXA TABLET 5MG ADHD 5 milligram /		Therapeutic response unexpected with drug substitution Previous brand unknown Concentration loss Listless Headache Dizziness	- Drug Withdrawn Unknown	2019 10-03	Gebruikte dexamfetamine 2,5
28	00355040 male, 60-70 Years Consumer	AMFEXA TABLET 5MG ADHD 7,5 mg 2x dag		Therapeutic response unexpected with drug substitution Previous brand unknown Blurred vision Dizziness Dry mouth Listless	1 Day Unknown Not Recovered	2019 10-06	Gebruikte 2 maal daags 3x 2.5 dexamfetamine magistrale bereiding Geen aanpassing dosering; gestopt met Amfexa, geen halve tablet Amfexa, dosering was aangevuld met dexamfetamine 2,5mg, bereider dex onbekend
29	00355252 male, 40-50 Years Consumer	AMFEXA TABLET 5MG Attention deficit hyperactivity disorder 1 dosage form /		Therapeutic response unexpected with drug substitution Therapeutic response decreased Previous brand unknown Impatience Anger Behaviour abnormal Sleep difficult Depressed mood	2 Hours Not Applicable Not Recovered	2019 10-07	

30	00355268 female, 30-40 Years Consumer or other non health professional	AMFEXA TABLET 5MG ADHD 3x daags 12,5 mg		Therapeutic response unexpected with drug substitution Previous brand Centrale Bereidingsapotheek Nederland Breda Palpitations Heart rate increased Migraine type headaches	1 Days 1 Hours Drug Withdrawn Not Recovered	2019 10-08	Voorheen dexamfetamine magistrale bereiding, Centrale Bereidingsapotheek Nederland Breda 3x daags 12,5 mg, toen geen bijwerkingen. dexamphetamine moest sneller opeenvolgend ingenomen worden dan gangbaar is Bij Amfexa tablet gehalveerd; daarna io arts dosis verminderd naar 3maal daags 10mg; minder bijwerkingen maar ook minder effect daarna weer terug naar dexamfetamine 3dd 12,5mg, klachten hersteld
31	00355578 female, 30-40 years Physician	AMFEXA TABLET 5MG ADHD 10 milligram /		Therapeutic response unexpected with drug substitution Previous brand unknown Attention impaired Mood disorder Condition aggravated Malaise Emotional lability	- Drug Withdrawn Recovering	2019 10-10	

32	0035579 male, 40-50 Years Pharmacist	AMFEXA TABLET 5MG ADHD 5 milligram / 8 Hours	bupropion quetiapine	Therapeutic response unexpected with drug substitution Previous Brand De Magistrale Bereider (DMB) Anxiety Depressed mood Nausea	3 Days Drug Withdrawn Unknown	2019 10-10	
33	00355753 male, 40-50 Years Consumer	AMFEXA TABLET 5MG Attention deficit hyperactivity disorder 5 milligram /	paroxetine	Therapeutic response unexpected with drug substitution Previous brand unknown Tension Fear Nausea Depressed mood	2 Hours Drug Withdrawn Recovered	2019 10-11	Amfexa gestopt en hersteld, nu 2x daags 2,5mg dexamfetamine, bij opbouw Amfexa was tablet gehalveerd, eerder geen klachten/switch
34	NL-LRB-00356179 Female, 20-30 years Consumer	AMFEXA TABLET 5MG 10 milligram		Therapeutic response unexpected with drug substitution Previous Brand De Magistrale Bereider (DMB) Depressed mood Suicidal thoughts Insomnia Jaw stiffness	8 hours for jaw stiffness, 1 day for other reaction, drug withdrawn, recovered, positive rechallenge	2019 10-14	
35	NL-LRB-00356213 Female, 20-30 years Pharmacist	AMFEXA TABLET 5MG Attention deficit hyperactivity disorder 5 milligram / 6 hours 2-1,5-1,5-1 tablet per dag= 10mg;7,5mg;7,5mg;5mg Tablet gehlaveerd voor 7,5mg	Levonorgestrel IUD	Therapeutic response unexpected with drug substitution Previous Brand De Magistrale Bereider (DMB) Cramps in the calves Palpitations Decreased appetite	Palpitations 30 minutes, decreased appetite 1 day, cramp in calves 2 days, not withdrawn, not recovered	2019 10-15	
36	NL-LRB-00356725 Female, 30-40 years Pharmacist	AMFEXA TABLET 5MG Attention deficit hyperactivity disorder 5 milligram / 6 hours	Cyproterone/estradiole, fexofenadine, fusidinic acid, ketoconazole	Therapeutic response unexpected with drug substitution Previous brand unknown	4 months, switched back to compounded 2.5 mg dexamfetamine	2019 10-18	Patient gebruikte voor amfexa , de dexamfetamine 2,5mg zonder klachten

				Alopecia			
37	NL-LRB-00359039 female, 30-40 Years Consumer or other non health professional	AMFEXA TABLET 5MG Attention deficit hyperactivity disorder		Abdominal discomfort, Migraine, Fatigue, Mood swings, Therapeutic response unexpected with drug substitutio Previous brand unknown	2 days, action taken unknown, not recovered	2019-10-26	
38	NL-LRB-00359267, Consumer or other non health professional, male, 50-60 Years	AMFEXA TABLET 5MG ADHD Obsessive compulsive disorder	Oxazepam	Slow response to stimuli, Depressed mood, Lack of drug effect, Therapeutic response unexpected with drug substitution Previous brand unknown	48 Days, Dose not changed, Not Recovered	2019-10-29	
39	NL-LRB-00359389, Consumer or other non health professional, female, 30-40 Years	AMFEXA TABLET 5MG 55 milligram / day ADHD		Therapeutic response unexpected with drug substitution, Depressed mood, Aggression, Heartburn Previous brand unknown	1 Days Drug Withdrawn Recovered	2019-10-30	Dexamfetamine magistraal om de 3.5 uur innemen. Nu over .op lisdexamferamine
40	NL-LRB-00359551, Consumer or other non health professional, female, 20-30 Years	AMFEXA TABLET 5MG 15 milligram / 8 Hours ADHD		Decreased appetite, Sleep problem, Nervousness, Headache, Rash erythematous, Therapeutic response unexpected with drug substitution Previous brand unknown	Unknown, Dose Not Changed, Not Recovered	2019-10-30	Voorheen dexamfetamine magistraal 2.5 mg
41	NL-LRB-00359921, Consumer or other non health professional, female, 20-30 Years	AMFEXA TABLET 5MG 20 milligram / day ADHD		Pyrosis, Mental distress, Depressed mood, Therapeutic response unexpected with drug substitution, Lack of drug effect Previous brand unknown	1 Hours, Drug Withdrawn, Recovered after switch back to compounded product	2019-11-02	
42	NL-LRB-00360175, Consumer or other non health professional, female, 30-40 Years	AMFEXA TABLET 5MG 10 milligram / 8 Hours Attention deficit hyperactivity disorder		Drug effect incomplete, Headache, Therapeutic response unexpected with drug	60 Minutes, Dose Not Changed, Not Recovered	2019-11-04	

				substitution, Abdominal discomfort Previous brand unknown			
43	NL-LRB-00360866, Consumer or other non health professional, female, 40-50 years	AMFEXA TABLET 5MG 5 milligram / 8 Hours ADHD	Levothyroxine	Concentration impaired, Accommodation difficulty, Agitation, Memory impairment, Therapeutic response unexpected with drug substitution Previous brand unknown	3 Days for the memory impairment, 2 days for the other ADRs, Dose Reduced, Not Recovered	2019-11-07	,
44	NL-LRB-00360903, Consumer or other non health professional, female, 30-40 Years	AMFEXA TABLET 5MG 5 milligram / ADHD	Escitalopram	Hyperexcitability, Palpitations, Panic attacks, Depressed mood, Diplopia, Fatigue, Sleep problem, Therapeutic response unexpected with drug substitution, Drug effect decreased Previous brand unknown	2 Days, Drug Withdrawn, Recovered	2019-11-07	
45	NL-LRB-00360936, Consumer or other non health professional, male, 20-30 years	AMFEXA TABLET 5MG 5 milligram / 8 Hours ADHD		Tic, Therapeutic response unexpected with drug substitution Previous brand unknown	2 Days, Drug Withdrawn, Recovering	2019-11-07	
46	NL-LRB-00361131, Consumer or other non health professional, female, 20-30 Years	AMFEXA TABLET 5MG 10 milligram / ADHD		Headache, Dizziness, Listless, Drug effect incomplete, Therapeutic response unexpected with drug substitution Previous brand unknown	12 Minutes, Drug Withdrawn, Recovered	2019-11-08	
47	NL-LRB-00361217, Consumer or other non health professional, female, 20-30 Years	AMFEXA TABLET 5MG 5 milligram / 6 Hours ADHD		Feeling detached, Tic, Therapeutic response unexpected with drug substitution, Palpitations, Social disinhibition, Dry mouth, Dry skin, Rebound effect	2 Days for feeling detached, 3 Hours for tics and days for the other ADRs, Not Applicable, Not Recovered	2019-11-10	

48	NL-LRB-00361237, Consumer or other non health professional, female, 20-30 Years	AMFEXA TABLET 5MG 1 dosage form / 3 Hours ADD	Bisoprolol	Sleep difficult, Palpitations, Unrest, Therapeutic response unexpected with drug substitution Previous Brand De Magistrale Bereider (DMB) , Drug effect incomplete	1 Hour, Dose Not Changed, Not Recovered	2019-11-10	Van dexamfetamine DMB naar lisdexamfetamine (Elvanse®) en daarna naar Amfexa® geswitched
49	NL-LRB-00361268, Consumer or other non health professional, female, 30-40 Years	AMFEXA TABLET 5MG 1 dosage form / 8 Hours ADD		Feeling abnormal, Palpitations, Therapeutic response unexpected with drug substitution Previous brand unknown	Unknown, Dose Not Changed, Unknown	2019-11-10	Voorheen dexamfetamine magistraal 2.5 mg
50	NL-LRB-00361368, Consumer or other non health professional, female, 30-40 Years	AMFEXA TABLET 5MG 3 milligram / 8 Hours Attention deficit hyperactivity disorder		Headache, Muscle hypertonia, Decreased appetite, Chest pain cardiac, Mydriasis, Unrest, Depressed mood, Therapeutic response unexpected with drug substitution Previous Brand De Magistrale Bereider (DMB) ,	2 Days for headache, 3 days for chest pain cardiac, 1 day for other ADRs Drug Withdrawn, not recovered from chest pain cardiac, other ADRs recovered	2019-11-11	Voorheen dexamfetamine magistraal (DMB) 2.5 mg
51	NL-LRB-00361385, Consumer or other non health professional, female, 40-50 Years	AMFEXA TABLET 5MG 1 dosage form Attention deficit hyperactivity disorder	Levonorgestrel IUD	Nausea, Aggression, Impulsive behavior, Therapeutic response unexpected with drug substitution Previous brand unknown	10 Minutes for nausea, 2 weeks for other ADRs Drug Withdrawn, Unknown	2019-11-11	
52	NL-LRB-00361427, Consumer or other non health professional, male, 30-40 Years	AMFEXA TABLET 5MG ADD		Blurred vision, Dizziness, Cold extremities, Sleep difficult, Mucus discharge, Therapeutic response unexpected with drug substitution Previous Brand De Magistrale Bereider (DMB) ,	1 Days, Dose Not Changed, Not Recovered	2019-11-12	
53	NL-LRB-00361641, Consumer or other non health professional, male, 30-40 Years	AMFEXA TABLET 5MG 8 milligram / 8 Hours Attention deficit hyperactivity disorder		Palpitations, Vision decreased, Concentration impaired, Irritability, Therapeutic response	60 Minutes for palpitations, 2 Hours for vision decreased and concentration impaired, 3 hours for irritability	2019-11-12	Voorheen dexamfetamine magistraal (DMB) 2.5 mg

				unexpected with drug substitution Previous Brand De Magistrale Bereider (DMB)	Not Applicable, Not Recovered		Op advies van de apotheek slik ik per keer 5mg Amfexa en 2.5 mg dexamfetamine van, de magistrale bereider
54	NL-LRB-00361661, Consumer or other non health professional, male, 20-30 years	AMFEXA TABLET 5MG ADHD	Dexamfetamine 2.5 mg, Fluticason, Omeprazol	Headache, Aggression, Depressed mood, Restless, Therapeutic response unexpected with drug substitution Previous brand unknown	2 days for aggression, 4 days for headache, 5 days for depressed mood, 7 days for restlessness, Drug Withdrawn, Recovering	2019-11-12	
55	NL-LRB-00361688, Consumer or other non health professional, female, 20-30 years	AMFEXA TABLET 5MG 1 dosage form / ADHD		Depressed mood, Hyperresponsive to stimuli, Fatigue, Therapeutic response unexpected with drug substitution Previous brand unknown	3 Weeks, Dose Not Changed, Not Recovered	2019-11-13	
56	NL-LRB-00362447, Consumer or other non health professional, female, 40-50 years	AMFEXA TABLET 5MG 10 milligram / 8 Hours unknown		Dry mouth, concentration impaired, insomnia, Therapeutic response unexpected with drug substitution Previous brand unknown	1 Hours Not Applicable, Not Recovered	2019-11-14	
57	NL-LRB-00362456, Consumer or other non health professional, female, 20-30 years	AMFEXA TABLET 5MG 8 milligram unknown		Nausea, Headache, Therapeutic response unexpected with drug substitution Previous brand unknown	30 Minutes, Drug Withdrawn, Recovered	2019-11-15	
58	NL-LRB-00362739, Consumer or other non health professional, male, 30-40 years	AMFEXA TABLET 5MG 8 milligram / 8 Hours ADHD		Cold extremities, headache, neck ache, forgetfulness, agitation, Therapeutic response unexpected with drug substitution Previous brand unknown	2 Days, Unknown, Recovered with squelae,	2019-11-18	
59	NL-LRB-00360057, Pharmacist, female, 20-30 Years	AMFEXA TABLET 5MG 3 milligram / 8 Hours ADHD		Feeling strange, Anxiety, Panic attack, Headache,	2 Hours, Drug Withdrawn, Recovered	2019-11-01	Voorheen dexamfetamine magistraal 2.5 mg

				Concentration loss, Hyperventilation, Crying, Therapeutic response unexpected with drug substitution			
60	NL-LRB-00355762, Consumer or other non health professional, female, 20-30 years	AMFEXA TABLET 5MG 7,5mg 2x per dag attention deficit hyperactivity disorder		Dry mouth, Neck cramps, Blurred vision, Therapeutic response unexpected with drug substitution Previous Brand De Magistrale Bereider (DMB)	1 hour, dose not changed, outcome unknown	2019-10-11	Voorheen dexamfetamine magistraal 2.5 mg
61	NL-LRB-00364145, Consumer or other non health professional, male, 20-30 years	Amfexa Tablet 5Mg 10 milligram / 12 Hours Attention deficit disorder		Dry mouth, Neck cramps, Depressed mood, Headache, Therapeutic response unexpected with drug substitution Previous Brand De Magistrale Bereider (DMB)	30 Minutes, Dose Reduced, Not Recovered	2019-11-20	
62	NL-LRB-00364523, Consumer or other non health professional, female, 40-50 years	Amfexa Tablet 5Mg 1 dosage form / 4 Hours Sertraline Hydrochloride		Headache, Lack of drug effect, Fatigue, Dry mouth, Dry eyes, Therapeutic response unexpected with drug substitution Previous Brand De Magistrale Bereider (DMB)	1 day for headache and lack of drug effect, 2 days for dry mouth, dry eyes, Dose Not Changed, Not Recovered	2019-11-21	3 X daags dexamfetamine (de magistrale bereider) dit was eerst 4+4+3+3+1 x 2,5 dexamfetamine maar daarvoor moest de Amfexa in de plaats komen
63	NL-LRB-00364526, Consumer or other non health professional, male, 40-50 years	Amfexa Tablet 5Mg 10 milligram / 8 Hours		Hot flushes, Libido decreased, Bruxism, Flat affect, Therapeutic response unexpected with drug substitution Previous Brand De Magistrale Bereider (DMB)	2 days, Dose Not Changed, Not Recovered	2019-11-21	
64	NL-LRB-00364760, Consumer or other non health professional, female, 30-40 years	Amfexa Tablet 5Mg 1 dosage form / 5 Hours ADHD		Dizziness, Mood swings, Therapeutic response unexpected with drug substitution	2 hours, Not Applicable, Not Recovered	2019-11-23	
65	NL-LRB-00364861, Consumer or other non health	Amfexa Tablet 5Mg ADHD		Headache, Depression, Nervous, Therapeutic response	1 day for headache, 2 days for nervousness and depression, Drug	2019-11-23	

	professional, female, 20-30 years			unexpected with drug substitution	Withdrawn, Not Recovered		
--	--------------------------------------	--	--	--------------------------------------	-----------------------------	--	--