

Overview of reports on adverse drug reactions of melatonin

Introduction

Melatonin is a hormone produced by the pineal gland and plays a role in the regulation of the day/night rhythm and sleep. Melatonin is therefore used to treat disorders or situations in which the sleep rhythm is disturbed (1). A number of melatonin-containing products are formally approved as a medicine: Circadin® 2mg since 2007, Melatonine Slenyto® (1mg /5mg), Melatonine Thiofarma® (3mg/ 5mg) and Melatonine Pharma Nord® (3mg) since 2018 and Clinigen® (3mg), Davitamon®, DMB® and Nytol® (all 1mg/3mg /5mg) since 2019. The indication that is mentioned in the Summary of Product Characteristics (SmPC) varies per manufacturer. Circadin® is registered for *the short-term treatment of primary insomnia (any identified cause, including any medical, mental or environmental cause) in patients aged 55 years or over* (1). Melatonin from the manufacturer Slenyto® is indicated for *insomnia in the elderly, the treatment of insomnia in children and adolescents with autism spectrum disorder and / or Smith-Magenis syndrome, or for short-term treatment of jet lag in adults* (2). Melatonine Davitamon®, Clinigen®, PharmaNord®, Thiofarma®, DMB® and Nytol® are indicated for *short-term treatment of jet-lag in adults* (3-8).

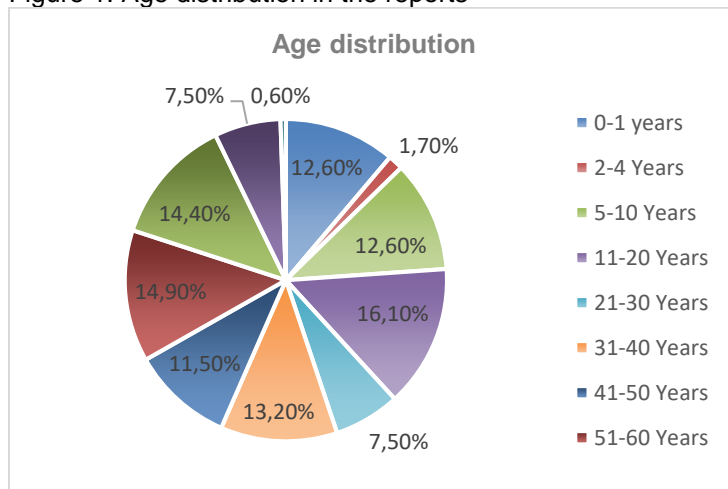
In addition to the registered melatonin products that are supplied by the pharmacy on prescription, unregistered melatonin supplements are available in drugstores, web-shops, pharmacies and also supermarkets.

The Inspectorate for Healthcare and Youth (IGJ) has recently intensified the supervision of products containing melatonin in collaboration with the Dutch Food and Consumer Product Safety Authority (NVWA). The traders and / or producers of melatonin-containing products that are known to IGJ have been informed by letter (9). This letter states that the IGJ and NVWA consider products with dosing advice that leads to an intake of less than 0.3 mg of melatonin per day as a product covered by the Commodities Act. This, of course, on condition that the products are not provided of a medical claim, which falls under the application criterion for medicines. The IGJ takes the position that products with a daily dose of 0.3 mg melatonin pharmacologically performs several physiological functions of the human body. Products with dosing advice that leads to intake of an amount of melatonin of 0.3 mg or more per day should be used up considered as a medicinal product on the basis of the application criterion and as a consequence as covered by the Medicines Act, provided that the provisions are met laid down in the case law of the European Court of Justice (inter alia HechtPharma judgment). This means that the latter products, before they are put on the market must be registered as a medicinal product for the purposes of marketing of the product requires a permit (10).

Reports

From September 1997 until 29 November 2019, the Netherlands Pharmacovigilance Centre Lareb received 181 reports of Adverse Drug Reactions (ADRs) associated with the use of melatonin (Table 1 Appendix). Seven reports were reported by the pharmaceutical industry. From the 174 reports reported directly to Lareb 66 (38%) concern men, 107 (61%) concern women and in one report the gender is not reported. 46 % of the reports were sent by consumers, 28% by pharmacists and 25% by medical doctors and 1% by other health care professionals. The age distribution in the reports is shown in Figure 1.

Figure 1. Age distribution in the reports

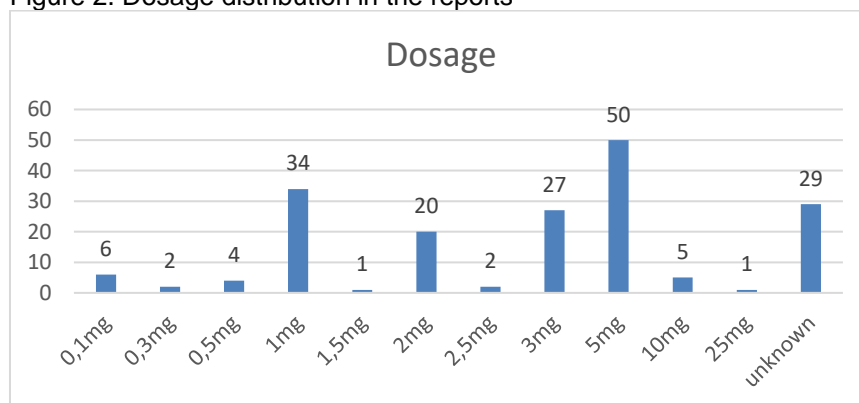


From the 181 reports 17 reports concern the registered drug Circadin® which contains 2mg melatonin per tablet. In addition, in six other reports the name of a melatonin supplement was reported: Schiff Sleep Support melatonin® (3mg), Sleepzz Melatonin® 1,5mg and Sleepzz Melatonin Time released® (0,1mg per tablet, advised 10 tablets per night and maximum 5mg), Melatonin 3mg Pharma Nord®, Melatonin Kruidvat® (5mg), and Arkorelax® (1mg). In the other reports, the melatonin product is reported under the generic name.

In 101 reports no co-medication is reported. In nine reports also a medication registered for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) is reported as co-medication; eight times this was methylphenidate and once dexamphetamine. Combination with melatonin in patients with ADHD suffering from insomnia is common and melatonin is usually prescribed by their treating physician. In those cases often the desired dosage of melatonin is compounded by the pharmacist or a registered melatonin preparation is delivered.

All reports of melatonin are included in this overview. From the 181 reported melatonin preparations 50 reports (27.6%) concern a product with 5mg melatonin, 34 reports (18.8%) with 1mg, 27 reports (14.9%) with 3mg and 20 reports (11%) with 2mg and 5 reports (92.8%) 10mg. The highest reported dosage was 25mg, reported once. In 29 reports the dosage is not unknown. The complete dosage distribution is shown in the Figure 2.

Figure 2. Dosage distribution in the reports



In 181 reports 370 ADRs were reported. More than one ADR can be reported in a single report. The most reported ADR was diarrhoea, followed by headache and dizziness, see Table 1. All of the ADRs in the Top-10 are labelled in de SmPC of Circadin® (1).

Table1: Top- 10 reported ADRs

Reported PT	Number
Diarrhoea	17
Headache	15
Dizziness	15
Palpitations	12
Nausea	11
Insomnia	9
Hyperhidrosis	9
Abdominal pain	7
Abnormal dreams	7
Nightmare	6
Constipation	6
Anxiety	6
Feeling abnormal	6
Total	126

Beside the well-known and labelled ADRs, also ADRs were reported which are not common in all SmPCs (1-8). In 3 reports an influence on the female hormonal balance was reported. In one case, reported by the specialist doctor, galactorrhea with hyperprolactinaemia has been reported in a 10-20 years old girl. She was treated for sleep disorder with 5mg melatonin. After 2 years she experienced galactorrhea with hyperprolactinaemia. Her serum prolactin was 900mU/l (ref. <500mU/l). One week after withdrawal the prolactin level decreased to 680mU/l, the galactorrhea was still ongoing at the time of reporting. A 20-30-years old women reported delay of her menstruation after administration of supplement Melatomatine Pure * for difficulty with falling asleep. The dosage of melatonin was tapered down by 0,1mg during 3 days. The menstrual bleeding occurred the first day after withdrawal. In one report a 10-20 years old girl experienced breast tenderness among other complains, such as palpitations, headache, dizziness, agitation, polyuria, mood swings, blurred vision, nightmares and flatulence with a latency of 7 weeks. The dose of melatonin was reduced but at the reporting time the patient was still not recovered.

In 5 reports a possible relationship between the use of melatonin and the occurrence of epileptic seizures or convulsions is reported. In 3 cases the patient had already a history of epilepsy. In one case the patient recovered after withdrawal of melatonin and increasing the dose of antiepileptic drug. For the patients in 2 cases no history of epilepsy or use of antiepileptic drugs has been reported. In one case the patient recovered after withdrawal of melatonin.

Other sources

SmPCs

The information about the ADRs in the SMPC's of registered melatonin products varies per manufacturer.

Both, Melatonin Slenyto® and Circadin®, are approved as a medicine via the centralised authorisation procedure. The SmpC of Slenyto® mentions as ADRs: mood swings, aggression, irritability, somnolence, headache, sudden onset of sleep, sinusitis, fatigue, hangover and adverse reactions which were reported with an with off-label use: epilepsy, visual impairment, dyspnoea, epistaxis, constipation, decreased appetite, swelling face, skin lesion, feeling abnormal, abnormal behaviour and neutropenia (1, 2).

The SmPC of Circadin® mentions: headache, somnolence, irritability, nervousness, restlessness, insomnia, abnormal dreams, anxiety, migraine, lethargy, psychomotor hyperactivity (restlessness with increased activity), dizziness, hypertension, abdominal pain dyspepsia, mouth ulcers, dry mouth, hyperbilirubinaemia, dermatitis, night sweats, pruritus, rash, dry skin, pain in the extremities, symptoms of the menopause, galactorrhea, asthenia, chest pain, glycosuria, proteinuria, abnormal liver function tests and increased weight (1).

The SmPC of Melatonin Cliningen® and Pharma Nord® are identical. Galactorrhoea is mentioned as an ADR, but symptoms of the menopause and epilepsy not (7, 8).

The SmPCs of Melatonin DMB®, Davitamon®, Thiopharma® and Nytol® are also identical. Some ADRs are not mentioned in those SmPCs. For example galactorrhoe and symptoms of the menopause are not mentioned. On the other hand the epilepsy is mentioned, in contrast with the SmPC of Circadin® where epilepsy is not included (3-6).

The information about the possible ADRs in the consumer leaflets of the melatonin supplements is scarce or is often even missing (11, 12).

Literature

An effect of melatonin on the prolactin level has been described: Large melatonin doses (80 mg) can substantially increase prolactin secretion. Doses of 100 mg daily in the evening potentiate the suppression of luteinizing hormone by testosterone in men. Also an effect on other reproductive hormones has been seen. Chronic ingestion of 1 g/day in humans resulted in depression of serum luteinizing hormone (LH). A combination of 75mg melatonin with contraceptive norethindrone 0.5 mg daily for months to years, lead to abnormal bleeding and breast complaints (13).

A case report describes a 56-year-old man with amyotrophic lateral sclerosis (ALS). He had been taking over-the-counter preparations of melatonin for 1.5 years. During the first year he took 1 mg per day and then gradually increased the daily dose to 2 mg. He developed painful, asymmetric gynecomastia. Physical examination confirmed bilateral gynecomastia and homogeneously enlarged breasts that were painful when palpated. There was no galactorrhea. No signs or symptoms of other endocrine dysfunction were noted. Discontinuation of the melatonin without any changes in other drug regimens resulted in complete regression of the gynecomastia within a few weeks(14).

Many studies have examined the effect of melatonin on sleep induction and sleep quality in patients with epilepsy. In the literature the supplementation of exogenous melatonin is described as a

promising treatment for epilepsy. On the other hand, also a relationship between sleep deprivation and epilepsy has been described. Sleep disturbances ranging from insomnia and hypersomnia are commonly reported by patients with epilepsy. Moreover, whether epilepsy is controlled with medication or not and regardless of the type of epilepsy syndrome, sleep deprivation is frequently reported as a trigger for “breakthrough” seizures (15, 16). There is no clear explanation of the relationship between some types of epilepsy and its presentation during drowsiness, sleep, or awakening. Both sleep and some generalized seizure types share common neuroanatomical elements. The most accepted thesis suggests that the relationship is reciprocal and that overall both conditions (sleep and sleep deprivation) have an excitatory effect on certain types of epilepsy (17).

Discussion and conclusion

We do not know the origin of different melatonin products if they are reported under the generic name. The reports may concern the pharmacy compounded melatonin preparations, melatonin purchased as a freely available supplement in the drugstore or in the web shops or as medicine registered melatonin reported under the generic name. When the used product was specified by name or distribution channel this was registered (Table 1 in Appendix). Unfortunately this was not the case for all reports. Reports received by Lareb show that many melatonin products are used in practice with dosages higher than 0,3mg. A (large) part of these products is likely sold as supplements.

In 181 reports 371 ADRs were reported. Most of the ADRs are mentioned in the various SmPCs for registered products on the market, but not in all of them. The SmPCs do not completely overlap in the information on ADRs they provide. The information about the possible ADRs in the consumer leaflets of the melatonin supplements is scarce. Most of them only have label information where no side effects are mentioned at all (11, 12, 18).

The cases reported to Lareb show no clear relation between the reported ADRs and melatonin dosage. Most ADRs are reported with the use of 5mg melatonin preparations. Although the strength of the melatonin preparation is mentioned in most cases, a dosing schedule is often not reported.

Therefore the total daily dosage remains uncertain. For example, the advised dosage of the Melatonin 1mg Kruidvat® is 10 tablets at once half an hour before bedtime (11).

The reports show ADRs can occur regardless the status of the melatonin product and the strength of the melatonin preparation.

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This signal has been raised on February 17, 2020. It is possible that in the meantime other information became available.

Appendix: Table1

No	ID sex age primary source	Drug	Dosage	Indication	Concomitant medication	Reported ADRs	Latency after start	Action taken	Outcome
1	NL-LRB-18762 male, 60-70 Years Physician Pharmacist	Melatonine 2.5Mg	1 / 1 Days	Sleep disorder NOS	Alginzuur/Natriumwaterstofcarbon susp Timolol Oogdruppels 1 Budesonide Neusspray	Diarrhoea	3 Weeks	Drug Withdrawn	
2	NL-LRB-19571 Unknown, 10-20 Years Physician Pharmacist	Melatonine 2,5Mg	1 / 1 Days			Rash maculopapular	3 Months	Drug Withdrawn	
3	NL-LRB-22310 male, 70 years and older Physician Pharmacist	Melatonine 5Mg	1 dosage form / 1 Days	Sleep disorder NOS	Prednison Calciumcarbonaat Lactogluconaat Alendroninezuur	Polymyalgia rheumatica	3 Months	Drug Withdrawn	
4	NL-LRB-22441 female, 50-60 Years Physician Pharmacist	Melatonine 5Mg	5 dosage form / 1 Days		Amlodipine Fludrocortison Hydrocortison	Hypoglycaemia	-	Unknown	
5	NL-LRB-22883 male, 70 Years and older Pharmacist	Melatonine 0,2Mg	1 / 1 Days	Sleep disorder NOS	Triamteren/Hydrochlorothiazide Valproïnezuur Fenprocoumon Alfuzosine - Oxazepam	Prothrombin time prolonged	-	Drug Withdrawn	
6	NL-LRB-28659 male, 40-50 Years Physician	Melatonine 5Mg	1 dosage form / 1 Days	Sleep disorder NOS	Propranolol	Headache	-	Drug Withdrawn	
7	NL-LRB-29987 male, 30-40 Years Pharmacist	Melatonine 0,1Mg	2 / 1 Days	Sleep disorder NOS		Confusion Consciousness decreased	- -	Drug Withdrawn	Recovered Recovered
8	NL-LRB-31080 female, 60-70 Years Physician	Melatonine 1Mg	4 / 1 Days	Sleep disorder NOS	Ipratropium	Vaginal discharge	6 Months	Dose Not Changed	Unknown
9	NL-LRB-33979 male, 7-10 Years Pharmacist	Melatonine 1Mg	3 / 1 Days	Disorder sleep	Beclometason	Abdominal pain upper Restlessness marked Irritability	2 Days 7 Days 7 Days	Dose Not Changed	Not Recovered Not Recovered Not Recovered

10	NL-LRB-34529 male, 10-20 Years Pharmacist	Melatonine 5Mg	5 milligr am / 1 Days			Mouth dry Taste alteration Thirst	3 Days 3 Days 3 Days	Dose Not Changed	Unknow n Unknow n Unknow n
11	NL-LRB-35887 male, 10-20 Years Pharmacist	Melatonine 5Mg	5 milligr am / 1 Days	Attention deficit/hy peractivit y disorder		Urinary incontinence	-	Dose Not Changed	Not Recover ed
12	NL-LRB-48727 male, 70 Years and older Consumer	Melatonine 5Mg	20 milligr am / 1 Days	Insomnia	Fluvoxamine Oxazepam Desloratadine Losartan Chloorthiazide	Depressed state Drowsiness	2 Days 2 Days	Drug Withdrawn	Recover ed Recover ed
13	NL-LRB-49403 female, 50- 60 Years Consumer	Melatonine 5Mg	5 milligr am / 1 Days	Sleep difficult		Vertigo Drug withdrawal syndrome	14 Days 14 Days	Drug Withdrawn	Recover ed Recover ed
14	NL-LRB-50161 male, 10-20 Years Consumer	Melatonine 5Mg	5 milligr am /	Sleep disorder	Methylfenidaat	Aggressive reaction	7 Days	Drug Withdrawn	Recover ed
15	NL-LRB-50476 female, 7- 10 Years Pharmacist	Melatonine 1Mg	1 milligr am / 1 Days			Rash	1 Weeks	Unknown	Unknow n
16	NL-LRB-50715 female, 40- 50 Years Physician	Melatonine 1Mg (la) Phenobarb italum Tablet 100Mg - Non- Current Drug (la)	3 dosag e form / 1 Days 300 milligr am / Days			Convulsions	3 Hours 3 Hours	Drug Withdrawn, Dose Not Changed	Recover ed
17	NL-LRB-52534 male, 10-20 Years Pharmacist	Melatonine 3Mg Tablet	3 milligr am / 1 Days	Sleep disorder		Skin discolouration	3 Month s	Dose Not Changed	Not Recover ed
18	NL-LRB-54059 male, 50-60 Years Physician	Melatonine 5Mg	5 milligr am / 1 Days	Sleep disorder	Sotalol Acenocoumarol	Diarrhoea	3 Weeks	Drug Withdrawn	Recover ed
19	NL-LRB-56389 male, 7-10 Years Pharmacist	Ritalin Tablet 10Mg Melatonine 0,1Mg	20 milligr am / 1 Days 1 dosag e form	Attention deficit hyperacti vity disorder Sleep disorder		Tooth disorder	1 Years 8 Month s	Dose Not Changed, Dose Not Changed	Not Recover ed

			/ 1 Days						
20	NL-LRB-59844 male, 60-70 Years Pharmacist	Melatonine 5Mg	1 dosage form / 1 Days	Sleep disorder	Zopiclon Clonazepam Piroxicam- Betadex Hydrokinine Ranitidine	Paraesthesia Hyperhidrosis Stomach upset	3 Hours 3 Hours 3 Hours	Drug Withdrawn	Recovered Recovered Recovered
21	NL-LRB-61023 female, 60-70 Years Pharmacist	Melatonine 0,1Mg	milligram /			Dizziness Fall	2 Weeks 2 Weeks	Drug Withdrawn	Recovered Recovered
22	NL-LRB-61255 male, 50-60 Years Pharmacist	Melatonine 3Mg Tablet	3 milligram / 1 Days	Insomnia	Gabapentine Diazepam Nitrazepam Tramadol	Depressed reaction Breathlessness Insomnia	1 Days 1 Days 1 Days	Drug Withdrawn	Unknown Unknown Unknown
23	NL-LRB-63417 male, 50-60 Years Physician	Melatonine 1Mg (la) Acenocoumarol Teva Tablet 1Mg (la)	2 milligram / 1 Days /	Insomnia		INR decreased Drug interaction inhibition	3 Weeks 3 Weeks -	Drug Withdrawn Dose Not Changed	Recovered Unknown
24	NL-LRB-63559 male, 50-60 Years Pharmacist	Melatonine 5Mg	10 milligram / 1 Days		Doxepine Diclofenac/Misoprostol Valsartan Zolpidem Oxazepam Metoprolol	Dizziness	-	Dose Not Changed	Unknown
25	NL-LRB-65818 male, 10-20 Years Pharmacist	Melatonine Capsule 2Mg	2 milligram / 1 Days	Sleep disorder	Methylfenidaat	Drug dependence	30 Days	Dose Not Changed	Not Recovered
26	NL-LRB-66230 female, 40-50 Years Consumer	Melatonine	1 dosage form / 1 Days	Insomnia		Diarrhoea	2 Weeks	Drug Withdrawn	Recovered
27	NL-LRB-70166 male, 10-20 Years Pharmacist	Melatonine 10Mg	10 milligram / 1 Days	Sleep disorder	Methylfenidaat	Weight increase	-	Drug Withdrawn	Unknown
28	NL-LRB-70286 male, 10-20 Years Pharmacist	Melatonine 5Mg	5 milligram / 1 Days	Sleep disorder	Methylfenidaat	Nocturnal enuresis	3 Years	Not Applicable	Unknown
29	NL-LRB-71551 female, 10-20 Years Physician	Melatonine 0,1Mg	1 dosage form /			Headache	-	Drug Withdrawn	Recovered

30	NL-LRB-73911 female, 50-60 Years Consumer	Melatonine 1Mg	5 dosage form / 1	Insomnia		Palpitations	3 Days	Drug Withdrawn	Unknow n
31	NL-LRB-74019 female, 60-70 Years Pharmacist	Melatonine 10Mg	10 milligram /		Calciumcarbonaat/Lactogluconaat Bruistab Levothyroxine	Abdominal cramp Diarrhea	- -	Drug Withdrawn	Recover ed Recover ed
32	NL-LRB-75016 female, 10-20 Years Consumer	Melatonine 5Mg	1 dosage form / 1 Days	Sleep disorder		Growth retarded Constipation	10 Years 8 Years	Not Applicable	Not Recover ed Not Recover ed
33	NL-LRB-77004 female, 4-7 Years Physician	Melatonine 1Mg	1 milligram / 1 Days	Insomnia		Stools abnormal	1 Days	Dose Not Changed	Not Recover ed
34	NL-LRB-81606 female, 50-60 Years Pharmacist	Melatonine 5Mg	5 milligram / 1 Days	Sleep disorder	Atenolol Sumatriptan Temazepam Estriol Ovule Acetazolamide Betahistine Acetylsalicylzuur/ Metoclopramide	Diarrhoea	3 Month s	Drug Withdrawn	Recover ed
35	NL-LRB-82408 male, 70 Years and older Consumer	Circadin® Tablet Mva 2Mg	1 dosage form /	Sleep disorder	Acenocoumarol Amiodaron Bumetanide Fosinopril Metoprolol Spironolacton Lactulose Pantoprazol Simvastatine	Dizziness Fall	4 Days 4 Days	Drug Withdrawn	Unknow n Unknow n
36	NL-LRB-83070 female, 10-20 Years Physician	Melatonine 1Mg	1 milligram /	Sleep disorder	Promethazine	Galactorrhoea not associated with childbirth	5 Days	Drug Withdrawn	Recover ed
37	NL-LRB-83648 female, 70 Years and older Pharmacist	Schiff Sleep Support® Melatonine 3Mg	6 milligram /		Ureum Creme Acetylsalicylzuur Chloortalidon Hydroxyzine Simvastatine Calciumcarb/Col ecalc Temazepam Levothyroxine Levothyroxine Alendroninezuur	Therapeutic effect unexpected	14 Days	Unknown	Unknow n
38	NL-LRB-85427 female, 60-70 Years Pharmacist	Circadin® Tablet Mva 2Mg	2 milligram / 1 Days	Insomnia	Oxazepam Citalopram	Upper abdominal pain	30 Minute s	Drug Withdrawn	Recover ed

39	NL-LRB-86176 female, 50-60 Years Pharmacist	Circadin® Tablet Mva 2Mg	2 milligram / 1 Days	Drug withdrawal syndrome		Tearing eyes Nausea Headache Malaise	2 Days 1 Days 1 Days 1 Days	Drug Withdrawn	Recovering Recovering Recovering Recovered with sequelae
40	NL-LRB-87176 female, 50-60 Years Pharmacist	Melatonine 5Mg	5 milligram / 1 Days	Drug withdrawal syndrome	Oxazepam Paroxetine Atorvastatine Metoprolol Acetylsalicylzuur Dispertablet Nitroglycerine Hydrochloorthiazide Salmeterol/Fluticasone	Hyperhidrosis Nightmares	- 1 Hours	Drug Withdrawn	Recovered Recovered
41	NL-LRB-87811 female, 50-60 Years Pharmacist	Melatonine 5Mg	5 milligram / 1 Days		Desloratadine	Anxiety Hyperhidrosis Dreaming abnormal Restlessness	3 Days 3 Days 3 Days 3 Days	Drug Withdrawn	Recovered Recovered Recovered Recovered
42	NL-LRB-88221 male, 10-20 Years Physician Physician	Melatonine 5Mg	5 milligram / 1 Days	Sleep disorder	Dexamfetamine	Syncope Drug interaction	5 Days 5 Days	Dose Not Changed	Recovered Recovered
43	NL-LRB-88491 female, 60-70 Years Pharmacist	Melatonine 0,1Mg	milligram / 1 Days	Insomnia		Psoriasis Rash Abscess Pain in face	2 Months 2 Months 2 Months 2 Months 2 Months	Drug Withdrawn	Recovered Recovered Recovered Recovered
44	NL-LRB-89696 female, 50-60 Years Consumer	Circadin® Tablet Mva 2Mg	/		Levothyroxine	Arthralgia Myalgia General malaise	14 Days 14 Days 14 Days	Dose Not Changed	Recovered Recovered Recovered
45	NL-LRB-89729 female, 7-10 Years Pharmacist	Melatonine 5Mg (la) Depakine Enteric Tablet Msr 300Mg (la)	5 milligram / 1 Days 600 milligram / Days	Sleep disorder Epilepsy	Salbutamol Salmeterol/Fluticasone	Insomnia Drug interaction potentiation Convulsions aggravated	- - - - -	Dose Reduced, Dose Increased	Unknown Unknown Unknown

46	NL-LRB-90206 female, 50-60 Years Physician	Melatonine 1Mg	1 milligr am /	Insomnia		Visual hallucinations	1 Hours	Drug Withdrawn	Recover ed
47	NL-LRB-90336 male, 60-70 Years Physician	Circadin® Tablet Mva 2Mg	75 milligr am / Days	Anxiety disorder	Metformine	Oesophageal pain Palpitations	1 Hours 1 Hours	Dose Not Changed	Recoveri ng Recoveri ng
48	NL-LRB-90951 female, 7-10 Years Physician	Risperdal Tablet Omhuld 0,5Mg Depakine Enteric Tablet Msr 150Mg Melatonine 0,1Mg	1 milligr am / 1 Days 2 dosag e form / 1 Days 1 dosag e form /	Pervasiv e develop mental disorder NOS Epilepsy Sleep disorder		Puberty precocious	2 Month s 3 Years 2 Years	Dose Reduced, Unknown, Not Applicable	Not Recover ed
49	NL-LRB-91419 female, 4-7 Years Pharmacist	Circadin® Tablet Mva 2Mg	2 milligr am / 1 Days	Sleep disorder		Abdominal pain Diarrhea	1 Days 1 Days	Not Applicable	Not Recover ed Recover ed
50	NL-LRB-101696 female, 70 Years and older Pharmacist	Melatonine 5Mg	10 milligr am / 1 Days	Sleep disorder	Ursodeoxycholzu ur Omeprazol Plantago Ovata Fluvastatine Diltiazem Carbasalaatcalci um	Dreaming abnormal	-	Dose Reduced	Recover ed
51	NL-LRB-101996 male, 30-40 Years Physician	Melatonine 5Mg	5 milligr am /	Sleep disorder		Loose stools Defaecation urgency	1 Days 1 Days	Unknown	Unknow n Unknow n
52	NL-LRB-103123 male, 40-50 Years Pharmacist	Circadin® Tablet Mva 2Mg	4 milligr am / 1 Days	Sleep disorder		Hepatitis Insomnia Abdominal pain Flushing	1 Days 1 Days 1 Days 1 Days	Drug Withdrawn	Recoveri ng Recoveri ng Recoveri ng Recoveri ng
53	NL-LRB-104684 male, 10-20 Years Pharmacist	Circadin® Tablet Mva 2Mg	2 milligr am / 1 Days	Sleep disorder		Headache Therapeutic response unexpected with drug substitution	1 Days 1 Days	Drug Withdrawn	Recover ed Recover ed
54	NL-LRB-105538 female, 70 Years and older Pharmacist	Fragmin 5000 Injvlst 25.000Ie/M lWwsp 0,2Ml Circadin Tablet Mva 2Mg	1 dosag e form / 1 Days / /	Hip surgery Sleep disorder	Sotalol Omeprazol Hydrochlorthiazide	Diarrhoea	14 Days 14 Days	Dose Not Changed, Dose Not Changed	Unknow n

55	NL-LRB-105541 female, 30-40 Years Consumer	Melatonine 5Mg	5 milligram / 1 Days	Sleep difficult	Ethinylestradiol/Levonorgestrel(Trinor/Trigynon)	Heaviness in limbs Nausea Hyperhidrosis Hyperhidrosis	2 Hours 12 Hours 2 Hours	Drug Withdrawn	Recovering Recovering Recovered Recovered
56	NL-LRB-106914 male, 7-10 Years Consumer	Melatonine 5Mg	3 milligram /			Drug effect decreased Therapeutic response unexpected with drug substitution	- -	Unknown	Unknown Unknown
57	NL-LRB-109545 female, 40-50 Years Pharmacist	Circadin® Tablet Mva 2Mg	2 milligram / 1 Days	Sleep disorder		Facial flushing	2 Days	Drug Withdrawn	Recovered
58	NL-LRB-110415 female, 7-10 Years Physician	Melatonine 1Mg	1 milligram /	Sleep disorder	Clonazepam Felbamaat Lamotrigine Macrogol (Movic/Molax/Laxt/Gen) Bisacodyl	Constipation	-	Drug Withdrawn	Not Recovered
59	NL-LRB-110531 male, 10-20 Years Pharmacist	Melatonine 1Mg	1 dosage form /		Fluticason	Sleep disturbance Abnormal dreams	3 Days 3 Days	Drug Withdrawn	Unknown Unknown
60	NL-LRB-118084 female, 60-70 Years Pharmacist	Melatonine	1 dosage form / 1 Days	Sleep problem	Enalapril Solifenacine Domperidon Pantoprazol	Urine odour abnormal	2 Months	Dose Not Changed	Not Recovered
61	NL-LRB-120003 male, 30-40 Years Physician	Melatonine Capsule 5Mg Nvza	5 milligram /	Sleep disturbance		Hidradenitis suppurativa	-	Unknown	Recovered
62	NL-LRB-122283 female, 60-70 Years Physician	Melatonine 5Mg	5 milligram / 1 Days	Sleep disorder		Diarrhoea Abdominal cramps	14 Days 14 Days	Drug Withdrawn	Recovered Recovered
63	NL-LRB-125357 female, 60-70 Years Consumer	Sintrom Mitis Tablet 1Mg - Non-Current Drug Melatonine 0.2Mg Acai 1500Mg	/ milligram / 3000 milligram / 1 Days 1 dosage	Thrombosis Sleep disorder		Dizziness Balance impaired NOS Mental dullness Somnolence Therapeutic response unexpected with drug substitution	4 Days 4 Days 4 Days 4 Days	Dose Not Changed, Dose Not Changed, Dose Not Changed, Dose Not Changed, Dose Not Changed,	Unknown Unknown Unknown Unknown Recovering

		Vitamine B Complex Dragee Bruin Kw - Non-Current Drug Nitrazepam Tablet 5Mg	e form / 1 Days 5 milligram / 1 Days						
64	NL-LRB-127413 male, 10-20 Years Physician	Melatonine 0,3Mg	milligram / 1 Days	Sleep disorder		Hyperactivity Difficulty sleeping	14 Days 14 Days	Drug Withdrawn	Recovered Recovered
65	NL-LRB-129906 female, 40-50 Years Physician	Dogmatil Capsule 50Mg Spiriva Respimat Inhopl 2,5Mg/Do Patr 60Do+Inh Melatonine 5Mg	300 milligram / 1 Days 1 dosage form / 1 Days 5 milligram / 1 Days	Vertigo	Pramipexol Triamtereen/Epitizide Domperidon Esomeprazol Levocetirizine Naproxen Fluticason Duloxetine Paracetamol/Codine	Galactorrhoea	11 Years 11 Years 11 Years	Not Applicable, Unknown, Unknown	Not Recovered
66	NL-LRB-130715 female, 50-60 Years Consumer	Melatonine	/	Sleep disorder	Oxazepam Budesonide/Formoterol	Muscle cramp Bone pain	4 Days 4 Days	Drug Withdrawn	Recovering Recovering
67	NL-LRB-132098 male, 70 Years and older Pharmacist	Melatonine 5Mg	5 milligram / 1 Days		Betahistine Nitrazepam Bromazepam	Hearing decreased	10 Minutes	Drug Withdrawn	Unknown
68	NL-LRB-133293 female, 40-50 Years Physician	Melatonine 1Mg	1 milligram / 1 Days	Sleep disorder	Methylfenidaat	Nightmare	1 Days	Drug Withdrawn	Recovered
69	NL-LRB-136653 female, 40-50 Years Pharmacist	Melatonine Capsule 5Mg Nvza	5 milligram / 1 Days	Sleep disorder		Constipation	1 Days	Dose Reduced	Unknown
70	NL-LRB-137765 male, 60-70 Years Physician	Melatonine 5Mg	5 milligram / 1 Days	Insomnia		Hallucination visual Dreaming abnormal	1 Days 1 Days	Drug Withdrawn	Recovered Recovered
71	NL-LRB-140104 male, 4-7 Years Pharmacist	Melatoninum	1 dosage form /	Sleep disorder	Valproïnezuur	Aggression	1 Days	Drug Withdrawn	Recovered
72	NL-LRB-141677 male, 50-60 Years Consumer	Melatonine Capsule 2Mg	2 milligram /	Insomnia	Lithiumcarbonaat Quetiapine	Weakness of limbs Dizziness Confusion Stomach discomfort	- - - -	Drug Withdrawn	Recovered Recovered Recovered

									Recovered
73	NL-LRB-144892 male, 10-20 Years Physician	Methylfenidaat Tablet 10Mg Melatonine 1Mg	3 dosage form / 1 Days 1 milligram / 1 Days	Attention deficit hyperactivity disorder Sleep disorder		Hyperpigmentation skin	10 Months 3 Years	Drug Withdrawn, Drug Withdrawn	Recovering
74	NL-LRB-146153 male, 7-10 Years Physician	Melatonine 1Mg	1 milligram / 1 Days	Sleep disorder		Nocturnal enuresis	1 Days	Dose Reduced	Recovering
75	NL-LRB-148663 male, 60-70 Years Physician	Melatonine Capsule 5Mg Nvza	5 milligram /	Sleep disorder	Fluvoxamine Metoprolol Hydrochlorothiazide Enalapril	Diarrhoea	1 Days	Drug Withdrawn	Unknown
76	NL-LRB-149613 female, 20-30 Years Pharmacist	Melatonine 3Mg Tablet	3 milligram / 1 Days	Insomnia	Ethinylestradiol/ levonorgestrel Colecalciferol	Crying Anxiety Decreased appetite Insomnia Listlessness Depression	4 Hours 4 Hours 4 Hours 4 Hours 4 Hours 4 Hours	Dose Not Changed	Not Recovered Not Recovered Not Recovered Not Recovered Not Recovered Not Recovered Not Recovered
77	NL-LRB-150413 female, 40-50 Years Consumer	Melatonine 1Mg	1 milligram / 1 Days	Attention deficit disorder	Methylfenidaat	Restless legs	1 Hours	Dose Not Changed	Unknown
78	NL-LRB-151414 male, 60-70 Years Consumer	Circadin® Tablet Mva 2Mg	2 milligram / 1 Days	Insomnia		Erythema facial Burning sensation skin Swelling face	10 Hours 10 Hours 10 Hours	Drug Withdrawn	Recovering Recovering Recovering
79	NL-LRB-153624 female, 60-70 Years Physician	Melatonine Capsule 1Mg	1 dosage form / 1 Days	Sleep disorder	Maprotiline Paroxetine Valproinezuur	Visual hallucinations	2 Days	Drug Withdrawn	Recovered

83	NL-LRB-158942 male, 50-60 Years Pharmacist	Melatonine Tablet 5Mg (Ia) Temazepam Capsule 10Mg (Ia)	5 milligram / 1 Days 10 milligram / 1 Days	Sleep disorder Sleep disorder	Citalopram Valproïnezuur	Hypersomnia Drug interaction potentiation	1 Month s 1 Month s 1 Month s 1 Month s	Dose Not Changed, Dose Reduced	Recover ed Recover ed
84	NL-LRB-160366 female, 20-30 Years Physician	Melatonine Tablet 3Mg	1 dosage form /	Sleep disorder		Mood altered	-	Drug Withdrawn	Recover ed
85	NL-LRB-160438 male, 4-7 Years Physician	Melatonine	1 dosage form / 1 Days	Sleep disorder		Melaena	2 Days	Drug Withdrawn	Recover ed
86	NL-JNJFOC-201311046 70 years and older female, Physician	Risperdal Tablet Omhuld 0,5Mg Melatonine	/ /	Drug use for unknown indication Product used for unknown indication		Scleroderma like change Creatine kinase increased Contracture	- - - - -	Unknown, Unknown	Unknow n Unknow n Unknow n
87	NL-LRB-165925 male, 7-10 Years Physician	Melatonine Tablet Mga 2Mg	/	Sleep disorder		Upper abdominal pain Therapeutic response unexpected with drug substitution	2 Weeks 2 Weeks	Drug Withdrawn	Recover ed Recover ed
88	NL-LRB-171174 female, 20-30 Years Consumer	Sleepzz @Melatonine 1,5 Mg (Otc)	10 dosage form / 1 Days	Sleep disorder		Itchy rash	30 Minute s	Drug Withdrawn	Not Recover ed
89	NL-LRB-171607 female, 70 Years and older Pharmacist	Circadin® Tablet Mva 2Mg	2 milligram / 1 Days	Insomnia	Metoprolol Oxazepam	Feeling abnormal Poor vision Urination impaired Blood pressure high	- - - -	Drug Withdrawn	Recover ed Recover ed Recover ed Recover ed
90	NL-LRB-173417 female, 50-60 Years Consumer	Circadin® Tablet Mva 2Mg	2 milligram / 1 Days	Insomnia	Verapamil Acetylsalicylzuur Irbesartan Ranitidine Lithiumcarbonaat Levocetirizine Macrogol	Chest pain	4 Hours	Unknown	Recover ed
91	NL-LRB-178742 female, 40-50 Years Physician	Melatonine Capsule 5Mg	5 milligram / 1 Days	Sleep disorder		Diarrhoea	14 Days	Drug Withdrawn	Recover ed
92	NL-LRB-179180 male, 40-50 Years Pharmacist	Melatonine	2 milligram / 1 Days	Somnolence		Myalgia Arthralgia	12 Hours 12 Hours	Drug Withdrawn	Recover ed Recover ed

93	NL-LRB-181962 female, 40-50 Years Consumer	Melatonine	1 dosage form /	Sleep disorder		Paranoid reaction	2 Hours	Drug Withdrawn	Recover ed
94	NL-LRB-182050 female, 60-70 Years Consumer	Melatonine Tablet 5Mg	5 milligram / 1 Days	Poor sleep	Levothyroxine Liothyronine Clonidine Omeprazol Trazodon	Diarrhoea	14 Days	Drug Withdrawn	Recover ed
95	NL-LRB-182562 female, 30-40 Years Consumer	Melatonine Capsule 3Mg	1 dosage form /			Palpitations	20 Minutes	Drug Withdrawn	Recover ed
96	NL-LRB-183162 female, 40-50 Years Pharmacist	Melatonine 10Mg	10 milligram / 1 Days	Insomnia		Dizziness Chest pressure Insomnia Dyspnoea	1 Days 1 Days 1 Days 1 Days	Drug Withdrawn	Recover ing Recover ing Recover ing Recover ing
97	NL-LRB-183552 female, 10-20 Years Consumer	Melatonine	1 dosage form / 1 Days	Insomnia		Aggression Depression Fatigue	24 Hours 24 Hours 24 Hours	Drug Withdrawn	Recover ed Recover ed Recover ed
98	NL-LRB-186744 male, 50-60 Years Consumer	Ascorbinezuur Tablet 250Mg Bisoprolol Tablet 2,5Mg Melatonine Tablet 5Mg Spironolacton Tablet 25Mg Thiamine Tablet 25Mg Vitamine B Complex Tablet Omhuld - Non- Current Drug Fenprocoumon Tablet 3Mg Metoclopramide Tablet 10Mg Chloordiazepoxide Dragee 25Mg	500 milligram / 1 Days 3 milligram / 1 Days 5 milligram / 1 Days 25 milligram / 1 Days 100 milligram / 1 Days 1 dosage form / 1 Days 1 dosage form /			Polyneuropathy	- - - - - - - -	Unknown, Unknown, Unknown, Unknown, Unknown, Unknown, Unknown, Unknown	Unknow n

		Paracetamol Tablet 500Mg	milligram / 2000 milligram / 1						
99	NL-LRB-188075 male, 70 Years and older Physician	Melatonin Tablet 1Mg	2 milligram / 1 Days	Sleep disorder	Allopurinol Thiamine Vitamine B Complex Colecalciferol Cetomacrogol Creme	Hyperbilirubinaemia Hepatic function disorder	- -	Drug Withdrawn	Recovering Recovering
100	NL-LRB-197984 male, 70 Years and older Consumer	Melatonin Tablet 3Mg	3 milligram / 1 Days	Drug use for unknown indication		Nocturia	-	Dose Reduced	Not Recovered
101	NL-LRB-199912 female, 30-40 Years Consumer	Melatonin Capsule 1Mg	2 milligram / 1 Days	Sleep problem		Palpitations Insomnia	30 Minutes 30 Minutes	Drug Withdrawn	Recovered Recovered
102	NL-LRB-201631 female, 20-30 Years Consumer	Melatonin 0.1Mg	milligram / 1 Days	Insomnia	Rupatadine Montelukast	Feeling drunk Dizziness	7 Hours 7 Hours	Drug Withdrawn	Recovering Recovering
103	NL-LRB-202772 female, 4-7 Years Consumer	Melatonin Tablet 1Mg	1 milligram / 1 Days	Sleep disorder		Abnormal behaviour	2 Days	Drug Withdrawn	Recovering
104	NL-LRB-203665 male, 40-50 Years Consumer	Melatonin Tablet 3Mg	3 milligram / 1 Days	Sleep disorder		Abnormal dreams	1 Hours	Drug Withdrawn	Recovered
105	NL-LRB-206153 female, 40-50 Years Physician	Melatonin	1 milligram / 1 Days	Sleep disorder		Muscle spasms Leg edema	8 Hours 8 Hours	Drug Withdrawn	Recovered Recovered
106	NL-LRB-206385 male, 40-50 Years Consumer	Melatonin	2 dosage form / 1 Days	Insomnia		Dizziness Anxiety Heart rate irregular	4 Years 4 Years 4 Years	Drug Withdrawn	Recovered with sequelae Recovered with sequelae Recovered with sequelae
107	NL-LRB-209713 female, 50-60 Years Consumer	Melatonin	1 dosage form / 1 Days	Sleep disorder	Irbesartan	Diarrhoea	8 Hours	Drug Withdrawn	Recovered
108	NL-LRB-211041 male, 10-20 Years Pharmacist	Melatonin Capsule 3Mg	6 milligram / 1 Days	Insomnia		Jaw stiffness	60 Minutes	Dose Reduced	Recovered

109	NL-LRB-211194 female, 10-20 Years Physician	Melatonine Tablet 1Mg	1 milligram / 1 Days	Sleep disorder	Pantoprazol	Fear Hallucination Unstable feeling Tearing eyes Blurred vision Photopsia Pruritus	5 Hours 5 Hours 5 Hours 5 Hours 5 Hours 5 Hours 5 Hours	Drug Withdrawn	Recovered Recovered Recovered Recovered Recovered Recovered Recovered
110	NL-LRB-211205 female, 20-30 Years Consumer	Melatonine 0,3Mg	milligram / 1 Days	Trouble falling asleep		Menstrual irregularity	6 Hours	Dose Reduced	Recovered
111	NL-LRB-212444 female, 20-30 Years Consumer	Ranitidine Hydrochloride Melatonine Capsule 1Mg	2 dosage form / 1 Days 2 milligram / 1 Days	Gastrointestinal discomfort Insomnia	Etonogestrel Implantaat 68Mg	Sleep disturbance	1 Days 1 Days	Dose Not Changed, Dose Not Changed	Unknown
112	NL-LRB-212624 female, 50-60 Years Consumer	Melatonine	1 dosage form / 1 Days	Insomnia		Headache	6 Hours	Drug Withdrawn	Unknown
113	NL-LRB-213364 female, 20-30 Years Consumer	Melatonine Tablet 3Mg	3 milligram / 1 Days	Poor sleep	Citalopram	Headache	2 Days	Drug Withdrawn	Recovered
114	NL-LRB-213586 male, 20-30 Years Consumer	Melatonine 5 Mg Kruidvat®	5 milligram / 1 Days	Insomnia		Bladder pain	10 Hours	Drug Withdrawn	Recovered
115	NL-LRB-214975 female, 70 Years and older Pharmacist	Circadin® Tablet Mva 2Mg	2 milligram / 1 Days	Sleep disorder	Estradiol Pleister Temazepam Timolol	Nausea	2 Hours	Drug Withdrawn	Recovered
116	NL-LRB-216717 female, 50-60 Years Consumer	Sleepzz Melatonine Time Release®	3 milligram / 1 Days	Anxiety		Palpitations	4 Hours	Drug Withdrawn	Recovered
117	NL-LRB-217846 male, 30-40 Years Pharmacist	Melatonine Capsule 3Mg (la) Fluvoxamine Tablet 50Mg (la)	3 milligram / 1 Days 50 milligram / 1 Days	Insomnia Depression		Palpitations Hyperhidrosis Drug interaction	1 Days 1 Days 1 Days 1 Days	Drug Withdrawn, Dose Not Changed	Recovering Recovering Recovering
118	NL-LRB-218279 male, 30-40 Years Consumer	Melatonine Capsule 1Mg	1 milligram / 1 Days	Sleep disturbance		Abnormal dreams Polyuria	2 Days 2 Days	Drug Withdrawn	Not Recovered Not Recovered

119	NL-LRB-219281 male, 70 Years and older Pharmacist	Melatonine Tablet 5Mg	5 milligram / 1 Days	Insomnia	Hypromellose Carbasalaatcalcium Bruistablet Atorvastatine Levocetirizine Methylfenidaat Pantoprazol Paroxetine	Nausea Hyperhidrosis Palpitations	2 Hours 2 Hours 2 Hours	Dose Reduced	Recovered Recovered Recovered
120	NL-LRB-220099 male, 20-30 Years Physician	Melatonine Tablet 5Mg	5 milligram / 1 Days	Sleep disorder		Feeling bad Poor sleep Concentration impaired Forgetfulness Anger	7 Days 7 Days 7 Days 7 Days	Drug Withdrawn	Recovering Recovering Recovering Recovering
121	NL-LRB-220675 female, 60-70 Years Consumer	Melatonine Capsule 5Mg	5 milligram / 1 Days	Sleep problem	Escitalopram	Night sweats Headache Restlessness	- - -	Drug Withdrawn	Recovering Recovering Recovering
122	NL-LRB-221366 female, 30-40 Years Consumer	Melatonine Capsule 3Mg	3 milligram / 1 Days	Sleep rhythm reversal	Valproïnezuur	Mania	2 Days	Drug Withdrawn	Recovered
123	NL-LRB-223714 female, 60-70 Years Consumer	Melatonine Tablet 5Mg	5 milligram / 1 Days	Insomnia		Diarrhoea	5 Weeks	Unknown	Recovering
124	NL-LRB-225000 female, 30-40 Years Consumer	Melatonine Tablet 1Mg	1 milligram / 1 Days	Insomnia		Sleep walking	6 Hours	Dose Reduced	Not Recovered
125	NL-LRB-227057 female, 60-70 Years Consumer	Melatonine Tablet 5Mg	5 milligram / 1 Days	Insomnia	Omeprazol	Headache	2 Months	Drug Withdrawn	Recovered
126	NL-LRB-227968 male, 10-20 Years Consumer	Melatonine Capsule 3Mg	3 milligram / 1 Days	Insomnia		Constipation Abdominal pain	8 Hours 8 Hours	Dose Not Changed	Not Recovered Not Recovered
127	NL-LRB-228720 female, 20-30 Years Consumer	Melatonine Tablet 3Mg	3 milligram / 1 Days	Sleep rhythm reversal		Anxiety	3 Days	Drug Withdrawn	Not Recovered
128	NL-LRB-229380 female, 30-40 Years Consumer	Melatonine Tablet 3Mg	9 milligram / 1 Months	Insomnia		Nightmares	5 Hours	Dose Not Changed	Recovered
129	NL-LRB-230437 female, 60-70 Years Consumer	Melatonine Forte	1 dosage form / 1 Days	Insomnia		Epileptiform attacks (NOS)	18 Hours	Drug Withdrawn	Recovering
130	NL-LRB-230885 female, 60-70 Years Consumer	Melatonine Capsule 1Mg	2 milligram / 1 Days	Insomnia	Paroxetine	Dizziness Flushing Nausea	30 Minutes 30 Minutes	Drug Withdrawn	Recovered Recovered Recovered

							30 Minute s		
13 1	NL-LRB- 233836 female, 10- 20 Years Pharmacist	Melatonine	1 dosage form / 1 Days	Sleepless ness	Methylfenidaat Valproïnezuur)	Epileptiform attacks (NOS)	4 Years	Dose Not Changed	Recover ed
13 2	NL-LRB- 236082 female, 50- 60 Years Pharmacist	Melatonine	25 milligram / 1 Days	Drug use for unknown indication	Sumatriptan Colecal/Menaqui	Myalgia Bone pain	- -	Drug Withdrawn	Recover ed with sequelae Recover ed with sequelae
13 3	NL-LRB- 238095 male, 30-40 Years Consumer	Melatonine Tablet 3Mg	3 milligram / 1 Days	Trouble falling asleep	Duloxetine	Constipation	1 Days	Dose Not Changed	Not Recover ed
13 4	NL-LRB- 239072 female, 10- 20 Years Consumer	Arkorelax®	1 milligram / 1 Days	Sleep difficult		Abdominal cramps Flatulence Diarrhoea	15 Minute s 15 Minute s 15 Minute s	Drug Withdrawn	Not Recover ed Not Recover ed Not Recover ed
13 5	NL-LRB- 241907 male, 7-10 Years Consumer	Concerta Tablet Mva 36Mg Methylfeni daat Tablet 10Mg Melatonine Tablet 3Mg	36 milligram / 1 Days 10 milligram / 1 Days 3 milligram / 1 Days	ADHD ADHD Sleep disorder	Colecalciferol	Raynaud's syndrome	2 Weeks 2 Weeks 2 Weeks	Dose Not Changed, Dose Not Changed, Dose Not Changed	Recoveri ng
13 6	NL-LRB- 242035 female, 30- 40 Years Consumer	Melatonine	1 dosage form / 1 Days	Sleepless ness		Malaise Sweating Feeling hot Shaking Rash	10 Minute s 10 Minute s 10 Minute s 10 Minute s 10 Minute s 10 Minute s	Drug Withdrawn	Recover ed Recover ed Recover ed Recover ed Recover ed
13 7	NL-LRB- 243018 female, 50- 60 Years Consumer	Melatonine Capsule 5Mg	5 milligram / 1 Days			Feeling abnormal Feeling drunk Nausea Dizziness	10 Minute s 10 Minute s 10 Minute s 10 Minute s	Drug Withdrawn	Recover ed Recover ed Recover ed Recover ed

138	NL-LRB-244305 female, 30-40 Years Physician	Melatonine Tablet 1Mg	1 milligram / 1 Days	Sleep difficult	Levothyroxine Chloorhexidine	Leukocyte count decreased	-	Drug Withdrawn	Not Recovered
139	NL-LRB-248110 female, 40-50 Years Consumer	Melatonine Tablet 1Mg	1 milligram / 1 Days	Sleep problem	Sertraline Ethinylestradiol/ evonorgestrel	Diarrhoea	1 Days	Dose Not Changed	Not Recovered
140	NL-LRB-248324 male, 4-7 Years Consumer	Melatonine	2 milligram / 1	Trouble falling asleep		Behaviour hyperactive	-	Dose Not Changed	Not Recovered
141	NL-LRB-250043 female, 20-30 Years Consumer	Melatonine Capsule 1Mg	1 dosage form /	Insomnia		Headache	8 Hours	Drug Withdrawn	Not Recovered
142	NL-LRB-212150 female, 50-60 Years Consumer	Melatonine Tablet 5Mg	3 milligram / 1 Days	Insomnia		Palpitations Pruritus	2 Weeks 2 Weeks	Drug Withdrawn	Recovering Recovering
143	NL-LRB-00254756 female, 40-50 Years Physician	Melatonine Tablet 3Mg	3 milligram / 1 Days	Sleep disorder		Depressed mood Sleepiness	3 Weeks 3 Weeks	Drug Withdrawn	Recovered Recovered
144	NL-TEVA-2017-NL-834113 male, 60-70 Years Other health professional	Melatonine	1 milligram / 1 Days	Difficulty sleeping	Acetylsalicylzuur Formoterol Fluticason- Ciclesonide	Premature ventricular contractions	- -	Drug Withdrawn	Recovered
145	NL-TEVA-2017-NL-834114 male, 70 Years and older Other health professional	Melatonine	1 milligram / 1 Days	Difficulty sleeping	Sitagliptine Atorvastatine Candesartan Metformine	Premature ventricular contractions	- -	Drug Withdrawn	Recovered
146	NL-LRB-00270196 female, 20-30 Years Pharmacist	Melatonine Tablet 5Mg	1 dosage form / 1 Days	Sleep disorder	Diazepam Tablet 5Mg	Sleep paralysis Hallucination	30 Minutes 30 Minutes	Not Applicable	Recovered Recovered

147	NL-LRB-00277123 male, 70 Years and older Other health professional	Melatonine Capsule 3Mg	3 milligram / 1 Days	Sleep disorder NOS	Furosemide Isosorbidedimononitrat Pantoprazol Betamethason Isosorbidedinitrat Natriumchloride Blaasspoeling	Chest pain	4 Days	Drug Withdrawn	Fatal
148	NL-LRB-00278929 female, 40-50 years Consumer	Melatonine Tablet 1Mg	1 dosage form /	Initial insomnia		Jaw pain	1 Days	Drug Withdrawn	Recovering
149	NL-LRB-00251803 female, 7-10 Years Other health professional	Melatonine Tablet 1Mg	1 milligram / 1 Days	Drug use for unknown indication		Lack of drug effect Pharmaceutical product complaint	15 Days 15 Days	Unknown	Unknown Unknown
150*	NL-LRB-00292433 female, 60-70 Years Pharmacist	Melatonine Capsule 25Mg	25 milligram / 1 Days	Immune enhancement therapy	Anastrozol	Sleeplessness	2 Years	Dose Not Changed	Unknown
151	NL-LRB-00299763 female, 10-20 Years Consumer	Melatonine Tablet 5Mg	5 milligram / 1 Days	Myalgic encephalomyelitis		Memory impairment Headache	- -	Drug Withdrawn	Not Recovered Not Recovered
152	NL-LRB-00299881 female, 10-20 Years Consumer	Melatonine Capsule 5Mg	5 milligram / 1 Days	Insomnia		Palpitations Headache Dizziness Agitated Polyuria Mood swings Blurred vision Breast tenderness Nightmares Flatulence	7 Weeks 7 Weeks 7 Weeks 7 Weeks 7 Weeks 7 Weeks 7 Weeks 7 Weeks 7 Weeks 7 Weeks 7 Weeks	Dose Reduced	Not Recovered Not Recovered Not Recovered Not Recovered Not Recovered Not Recovered Not Recovered Not Recovered Not Recovered Not Recovered Not Recovered
153	NL-LRB-00300118 female, 70 Years and older Consumer	Melatonine Capsule 1Mg	1 dosage form / 1 Days	Insomnia	Imipramine Bromazepam	Constipation Nausea Somnolence Depressed mood Malaise Restlessness	3 Days 3 Days 3 Days 3 Days 3 Days	Drug Withdrawn	Unknown Unknown Unknown Unknown Unknown

									Unknown Unknown
154	NL-LRB-00300179 male, 30-40 Years Consumer	Melatonin Tablet 5Mg	3 milligram / 1 Days	Sleep problem		Feeling anxious Irritability Depressed mood	8 Hours 8 Hours 8 Hours	Drug Withdrawn	Recovering Recovering Recovering
155	NL-LRB-00301230 female, 60- 70 Years Consumer	Melatonin Tablet 5Mg	5 milligram / 1 Days	Sleep disorder	Progesteron Estradiol	Heart rate increased Chest pain Dizziness Light headedness	8 Hours 8 Hours 8 Hours 8 Hours	Drug Withdrawn	Recovered Recovered Recovered Recovered
156	NL-LRB-00301562 female, 7- 10 Years Consumer	Melatonin Tablet 1Mg	/	Sleep disorder		Facial rash	5 Days	Dose Not Changed	Not Recovered
157	NL-LRB-00301654 female, 50- 60 Years Consumer	Melatonin Tablet 1Mg	1 milligram /	Insomnia		Palpitations Tinnitus Headache Heart rate increased Blood pressure increased	30 Minutes 30 Minutes 30 Minutes 30 Minutes 30 Minutes 30 Minutes	Drug Withdrawn	Recovered Recovered Recovered Recovered Recovered
158	NL-LRB-00302800 female, 30- 40 Years Consumer	Melatonin Capsule 1Mg	1 milligram / 8 Hours	Sleep disorder		Nausea Band like headache Feeling of warmth	20 Minutes 20 Minutes 20 Minutes 20 Minutes	Not Applicable	Recovered Recovered Recovered
159	NL-LRB-00306453 female, 4-7 Years Consumer	Circadin® Tablet Mva 2Mg	1 dosage form / 1 Days	Delayed sleep phase		Awakening early	-	Dose Not Changed	Not Recovered
160	NL-LRB-00313761 female, 10- 20 Years Consumer	Melatonin Tablet 1Mg	1 dosage form / 1 Days	Sleep difficult		Low back pain Bowel sounds abnormal Feeling abnormal	12 Hours 2 Hours 12 Hours	Drug Withdrawn	Recovered Recovering Recovered

161	NL-LRB-00312678 female, 60-70 Years Physician Physician	Melatonine Tablet 3Mg	3 milligram / 1 Days	Sleep difficult	Sotalol Omeprazol Colecalciferol Risedroninezuur	Tongue disorder Feeling strange Blood pressure low Dyspnea Bradycardia	1 Seconds 1 Seconds 1 Seconds 1 Seconds 1 Seconds	Drug Withdrawn	Recovered Recovered Recovered Recovered Recovered
162	NL-LRB-00314367 female, 30-40 Years Consumer	Melatonine Tablet 3Mg	3 milligram / 1 Days	Sleep difficult		Dizziness Headache	5 Days 5 Days	Dose Not Changed	Recovered Recovered
163	NL-SZ09-PHHY2014 NL104190 female, 10-20 Years Other health professional	Risperidon Tablet Omhuld 0,5Mg Haloperidol Promethazine Capsule 25Mg - Non-Current Drug Trazodon Tablet 100Mg Levomopromazine Tab 25Mg (Als Waterstof maleaat) Melatonine Tablet 3Mg	3 milligram / 1 Days 1 milligram / 1 Days 25 milligram / 100 milligram / 1 Days / 3 milligram / 1 Days		Immunoglobuline Normaal Infusiepoeder 0 5G -	Drug ineffective	- - - - -	Unknown, Unknown, Unknown, Unknown, Unknown	Unknown
164	NL-LRB-00318183 female, 30-40 years Consumer	Melatonine Tablet 3Mg	1 dosage form / 1 Days	Sleep disturbance		Depression Fatigue extreme Anxiety Irritability Weight gain Panic attacks	1 Weeks 1 Weeks 1 Months 1 Weeks 2 Weeks 1 Months	Drug Withdrawn	Recovered Recovered Recovered Recovered Recovering Recovered
165	NL-LRB-00318389 female, 10-20 Years Physician	Melatonine Tablet 5Mg	5 milligram / 1 Days	Sleep disorder		Galactorrhea Hyperprolactinaemia	2 Years 2 Years	Drug Withdrawn	Recovering Recovering

166	NL-JNJFOC-201902079 50-60 female, Consumer	Risperdal Consta Injpd Flacon 25Mg + Solv 2Ml Melatonine	38 milligr am / milligr am /	Product used for unknown indication Product used for unknown indication		Behavior disorder Hypersomnia Tiredness Drug interaction	- - - - - -	Unknown, Drug Withdrawn	Unknow n Unknow n Recoveri ng Unknow n
167	NL-LRB-00322821 female, 10-20 Years Physician	Melatonine Tablet 5Mg	1 dosag e form /	Sleep disturban ce	Quetiapine Haloperidol Tablet	Acne vulgaris	5 Days	Dose Reduced	Recoveri ng
168	NL-LRB-00322899 male, 50-60 Years Consumer	Melatonine Tablet 3Mg	1 dosag e form / 1 Days	Insomnia		Depressed mood Fatigue Listlessness	12 Hours 12 Hours 12 Hours	Unknown	Not Recover e Not Recover ed Not Recover ed
169	NL-RADNeurim Pharmaceu ticals EEC Limited- NEU- 001099- 2019 female, Physician	Circadin® Tablet Mva 2Mg	2 milligr am /	Sleep difficult		Drug level in blood increased	-	Drug Withdrawn	Unknow n
170	NL-LRB-00329763 male, 10-20 Years Consumer	Melatonine Pharma Nord Tablet Filmomhul d 3Mg	3 milligr am / 1 Days	Sleep disturban ce		Nausea Hangover Feeling of warmth Shoulder pain Dry mouth	20 Minute s - 15 Minute s 2 Hours 1 Hours	Dose Reduced	Not Recover ed Not Recover ed Not Recover ed Not Recover ed
171	NL-LRB-00332213 female, 10-20 Years Consumer	Temazepam Capsule 10Mg Melatonine	2 dosag e form / 1 dosag e form /	Sleep difficult Sleep difficult		Nightmares Feeling drunk	15 Minute s - 1 Minute s -	Dose Not Changed, Drug Withdrawn	Not Recover ed Not Recover ed
172	NL-LRB-00335651 female, 40-50 Years Consumer	Melatonine Capsule 3Mg	1 dosag e form / 1 Days	Sleep difficult		Palpitations	4 Hours	Drug Withdrawn	Recover ed
173	NL-LRB-00336968 male, 30-40 Years Consumer	Melatonine Tablet 3Mg		Initial insomnia		Salivary hypersecretion	30 Minute s	Drug Withdrawn	Recoveri ng
174	NL-002147023 -	Melatonine				Lack of drug effect	-	Unknown,	Unknow n

	PHHY2019 NL161319 female, 60-70 Years Physician	+ 32 other suspect drugs				Drug use for unapproved indication			Unknow n
17 5	NL-LRB- 00345438 female, 10-20 Years Consumer	Melatonine	1 dosag e form / 1 Days	Autism spectrum disorder		Behavior hyperactive Bleeding Dry skin Aggressive behavior Behavior abnormal	4 Weeks 4 Weeks 4 Weeks 4 Weeks 4 Weeks	Drug Withdrawn	Unknow n Unknow n Unknow n Unknow n Unknow n
17 6	NL-LRB- 00347699 male, 7-10 years Consumer	Melatonine	1 dosag e form / 1 Days	Sleep disorder		Bed wetting	2 Hours	Dose Not Changed	Not Recover ed
17 7	NL-LRB- 00349128 female, 10-20 Years Physician	Melatonine	1 dosag e form /	Sleep difficult	Macrogol Levothyroxine	Epileptic seizure	3 Hours	Drug Withdrawn	Recover ed
17 8	NL-LRB- 00354238 female, 30-40 Years Consumer	Melatonine	2 dosag e form / 1 Days	Sleep disorder		Abdominal pain Awakening early	60 Minute s 6 Hours	Drug Withdrawn	Recover ed Recover ed
17 9	NL-LRB- 00359954 male, 40-50 Years Consumer	Melatonine Tablet 0,5Mg	milligr am / 1 Days	Sleep phase rhythm disturban ce	Citalopram Ketoconazol Triamcinolonacet onide	Fatigue aggravated Somnolence Malaise Body dysmorphic disorder Condition aggravated	2 Weeks 2 Weeks 2 Weeks 2 Weeks 2 Weeks	Drug Withdrawn	Recover ed Recover ed Recover ed Recover ed Recover ed
18 0	NL-LRB- 00362096 female, 10-20 Years Consumer	Circadin® Tablet Mva 2Mg	2 milligr am / 1 Days	Sleep disorder		Headache Depressed mood Dreams abnormal Alopecia Withdrawal reaction	2 Days 2 Days 2 Days 2 Days 2 Days	Drug Withdrawn	Not Recover ed Not Recover ed Not Recover ed Not Recover ed Not Recover ed
18 1*	NL-LRB- 00365707 male, 0-1 years Physician	Citalopram Tablet Omhuld 20Mg Melatonine Tablet 5Mg	20 milligr am / 1 Days 3 milligr am / 1 Days	Depressi on Sleeples sness	Levothyroxine	Talipes congenital Congenital hydronephrosis SSRICongenital hepatomegaly Maternal exposure during pregnancy	- - - - - - -	Unknown, Unknown	Not Recover ed Unknow n Recover ed Unknow n

* immune enhancement therapy in cancer, dosage 25mg
**SSRIs (Citalopram) suspect, based on case-reports in the literature