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National Children's Commissioner examines intentional self-harm and suicidal behaviour in children

I am the administrator and creator of a website called **Awareness of Singulair Side Effects for Australian Families and Individuals** (<https://www.facebook.com/montelukastsideeffects>) and I am also the Founder of the **International SINGULAIR (Montelukast) Side Effects Action Group** and an Administrator for the Facebook support page titled **Making the Side Effects of Singulair Aware to Parents of Children & Teens**. These groups are made up of parents of affected children and individuals suffering the side effects of Singulair (active ingredient Montelukast) from all over the world including the US, UK, Ireland, Malaysia, Canada, Mexico, Romania, Philippines, Singapore, Vietnam, France, Brazil, Morocco, Argentina, New Zealand, Netherlands Antilles, South Africa, Norway, Israel and Australia.

Attached in Appendix A. you will read personal accounts of the impact Singulair (Montelukast) has had on many children. These accounts have been written by members of the **Making the Side Effects of Singulair Aware to Parents of Children & Teens**¹ Facebook support page. This page has recently exceeded 400 members and is growing daily.

In April 2013, the Australian Therapeutic Goods Administration posted the Medicines Safety Update, Volume 4, Number 2, April 2013. In this update it officially recognised that Montelukast (Singulair), which is an asthma prevention medication, has neuropsychiatric risks. It reads as follows:

Health professionals are reminded of the possibility of neuropsychiatric adverse events, including suicidal ideation, in children, adolescents and adults treated with Montelukast. Health professionals should be aware of these potential adverse effects and advise patients and parents to seek medical advice should they occur².



¹<https://www.facebook.com/groups/40378158644/>

²<http://www.tga.gov.au/hp/msu-2013-02.htm>

The US Food and Drug Administration have an alert on their website dated 12 June 2009 that states:

The reported neuropsychiatric events include postmarket cases of agitation, aggression, anxiousness, dream abnormalities and hallucinations, depression, insomnia, irritability, restlessness, suicidal thinking and behavior (including suicide), and tremor³.

Singulair is an asthma preventer medication, which is administered on a daily basis to prevent asthma attacks; it can also be used to manage allergies. Singulair has been used for approximately 15 years to manage asthma and approximately 10 years to manage allergies. The tablets come in three different dosages 4mg, 5mg and 10mg, there are also granules, which can be used in babies. Medication brands available in Australia, which contain the active ingredient Montelukast can be found at Appendix G.

Children as young as six months in some countries and age two in Australia can be prescribed Singulair (Montelukast), at this young age they are unable to adequately communicate the side effects they may be experiencing.

Many parents or affected individuals do not make the link between this medication (that they perceive is targeting the respiratory system) and the neuropsychiatric side effects, which can include suicidal thoughts and aggression.

Singulair's US label carries a warning for the following neuropsychiatric side effects: agitation, aggressive behavior or hostility, anxiousness, depression, disorientation, disturbance in attention, dream abnormalities, hallucinations, insomnia, irritability, memory impairment, restlessness, somnambulism, suicidal thinking and behavior (including suicide), and tremor; systemic eosinophilia/vasculitis. ⁴

The Australian side effects, as listed in MIMS are as follows. Please note that I have not altered the order of this list, however I have highlighted the side effects that I feel are relevant to your review. Please refer to Appendix B. for a visual representation of this listing.

- Fluid retention
- Nose bleed
- Headache, dizziness, drowsiness
- Feeling unusually weak or tired
- Upper respiratory tract infection
- Muscle aches or cramps, joint pain
- Decreased feeling or sensitivity, especially in the skin
- Pins and needles
- Stomach pain
- Nausea, vomiting
- Diarrhoea
- **Agitation**, including **aggressive behaviour** and/or **hostility**

³<http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHealthcareProfessionals/ucm165489.htm>

⁴http://www.merck.com/product/usa/pi_circulars/s/singulair/singulair_ppi.pdf

- Tremor
- Irritability, restlessness, **feeling anxious**
- **Depression**
- Disorientation
- Disturbances in attention
- Seeing, feeling or hearing things that are not there (also called hallucinations)
- Memory impairment
- Dream abnormalities, difficulty sleeping
- Sleep walking
- Skin rashes or itchiness
- Increased tendency to bleed, bruising
- Fast or irregular heart beats, also called palpitations
- Symptoms of liver disease such as nausea, vomiting, loss of appetite, feeling generally unwell, fever, itching, yellowing of the skin and eyes, and dark coloured urine
- **Suicidal thoughts and actions**
- Swelling of the face, lips mouth, throat or tongue which may cause difficulty breathing or swallowing
- Pinkish, itchy swellings on the skin, also called hives or nettle rash, severe skin reactions that may occur without warning
- Seizure

As a group our members have experienced that the vast majority of medical professionals we have encountered have been uneducated about the acknowledged side effects of Singulair (Montelukast). This includes general practitioners, pediatricians, neurologists, pharmacists, psychologists and psychiatrists. The answer from many professionals is to prescribe other medications such as antidepressant or antipsychotic medication to cover the side effects of the Singulair. The lack of education of parents and doctors is concerning since this is a widely prescribed drug with no intended psychotropic action, most consumers are not aware of potential side effects unless they are advertised or they are warned about them by their prescribing physicians.

An increase in the amount of alerts to Medical professionals would be beneficial to the education process. Some examples from other countries include alerts from the Association for Medical Ethics (USA) '*Singulair does have side effects, some of them very dangerous*' (Appendix E) and the Canadian Paediatric Surveillance Program - '*Montelukast (Singulair) Risk of psychiatric adverse reactions*' (Appendix. F).

According to the US Food and Drug Administration - FDA, the clinical trials conducted prior to Singulair's approval were not designed to evaluate neuropsychiatric events. More investigation of Singulair's side effects is desperately needed. Although Merck (the makers of Singulair) insists that these side effects are extremely rare, even the FDA has acknowledged that Adverse Event Reports in children that are reported to the FDA likely represent just a portion of the actual events.

Adverse Drug Reaction Reports ADRR's (filed by doctors or the general public) are collected and assessed by the Australian Therapeutic Goods Administration. ADRR's are only filled out when the 'link' between the medication and the side effects are established. In the case of

Singulair, which has such a low professional education rate within the medical community, it is possible to assume that many affected individuals are not being captured in the statistics.

Asthma affects a large group of children within Australia. In many cases Singulair (Montelukast), which is a chewable tablet, is a preferred method of medicating a child. Administering Singulair is easier than the alternatives, which usually require the use of a spacer and timed breathing for maximum efficacy. This can be very challenging for both children and parents and Singulair is therefore appealing to medical professionals. Please refer to Appendix I. which outlines the most common Singulair side effects by age, as lodged to the US FDA via the Adverse Drug Reaction reporting system. It is disturbing to note that children aged 2-9 years of age, reported suicidal ideation however by age 10-19 the adverse reaction reports include suicidal ideation and suicide attempts.

The National Asthma Council Australia (NACA) have a website called kidswithasthma.com.au. It is a key information and education site for parents, which fails to inform of the risks associated with the use of Montelukast (Singulair). I note that the content on this website was developed by the NACA with support from an unrestricted educational grant from Merck Sharp and Dohme (Australia) Pty. Ltd. While the NACA claims to have retained editorial control, the website is published by Merck Sharp and Dohme (Australia) Pty. Ltd., who are fully aware of the many adverse side effects that are linked to Singulair (Montelukast) including neuropsychiatric episodes and severe behavioural issues.

In August 2013, I approached the National Asthma Council Australia (NACA) via e-mail to express my concerns regarding the lack of transparency and the possible conflict of interest in regards to the kids with asthma website. Whilst there are no adverse side effects or concerns listed about the use of Singulair; there are detailed negatives listed regarding the use of the alternative preventer options. *"Inhaled corticosteroids – What you should know – Certain doses might reduce a child's growth by up to 1cm in height, but uncontrolled asthma might also reduce a child's growth. High doses can cause problems with the adrenal gland"; "These medications can be sticky and the inhaler mouthpiece needs to be cleaned regularly"*.

Kristine Whorlow, the Chief Executive Officer of the National Asthma Council Australia responded on the 26 August 2013. I replied to her e-mail and have received no response. The website does not appear to have been updated in any way to reflect these concerns. More needs to be done to ensure that parents of children on Singulair are aware of the potential side effects, monitoring of an educated medical professional throughout the use of Singulair is vital for it's safety.

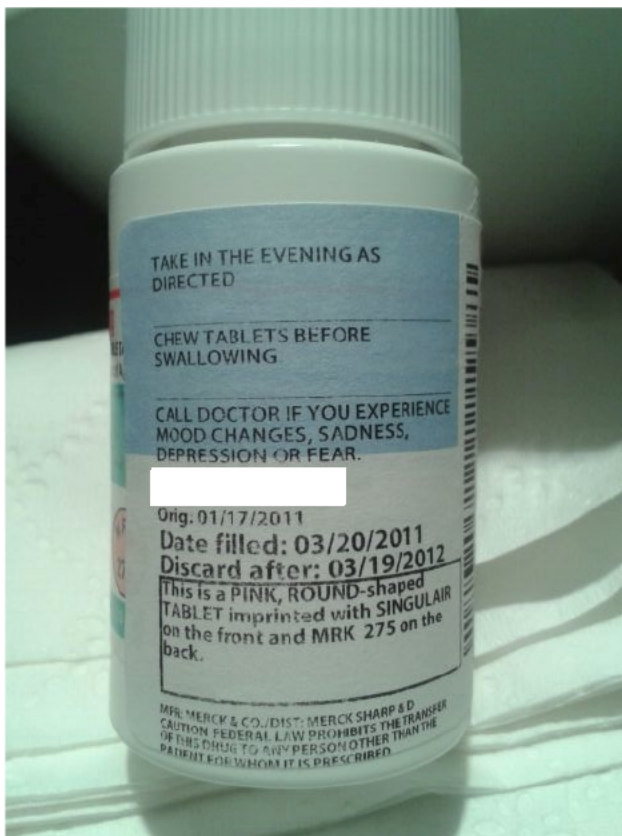
Our group's aim is not to have this medication taken off the shelves as we understand how complex and life threatening asthma can be; however, we do hope that full transparency and education of these side effects will be prioritised. The impacts of Singulair side effects are detrimental to young children and to the community as a whole including teachers, health practitioners and families.

It needs to be recognised that the use of Singulair, like asthma, can lead to death as it did in the case of 15 year old Cody Miller who committed suicide after just 17 days on Singulair. Cody had no prior mental health issues and had become anxious, agitated and was suffering panic attacks in the weeks leading up to his suicide. Appendix H. highlights adverse drug reaction report data from the US FDA from 2004 to 2012. The graph shows a substantial number of deaths have been reported as a result of Singulair use.

Following are some ideas that may assist affected children

Department of Education – Educate teachers to be on the lookout for children that are suffering the side effects of their asthma medication. Severe behavioral issues are a common sign however many of our members have reported severe issues with handwriting, memory and concentration, some have reported these as ongoing issues once Singulair is discontinued. Teachers could play a very important role in assisting parents to make the link between this medication and a child's educational and behavioural struggles.

The Australian Therapeutic Goods Administration – In an effort to educate parents and to protect vulnerable children that have no voice regarding the side effects of this medication, we suggest that the Australian Government introduce labeling on the outside of the Singulair/Montelukast packaging with a warning that '***This medication may cause neuropsychiatric episodes including suicidal thoughts and behavioural issues***'.



This image is a Singulair bottle from the US, please note that it states 'Call doctor if you experience mood changes, sadness, depression or fear'.

Steps should be taken in Australia to ensure patients receive consistent and accurate information about their prescription medications and are aware of the potential risks and benefits of those drugs when they pick them up at a pharmacy. A compulsory warning label on the outside of the Singulair and Montelukast packaging would achieve this goal, as product information is not always provided with the prescription and when it is, people do not always read through all information provided and may only look at it once throughout the duration they take the medication or dispense it to their child. Updates to the product information are continuous by the drug company and people are not always aware that they should regularly read through the product information for changes.

In the US, a bill has been lodged called the “Cody Miller Initiative for Safer Prescriptions Act.” The bill would ensure patients receive consistent and accurate information about their prescription medications and are aware of the potential risks and benefits of those drugs when they pick them up at a pharmacy.

The legislation is named for teenager Cody Miller who, on August 4, 2007, committed suicide after starting on Singulair.⁵

A register of medications taken within 12 months of an individual’s suicide could assist in observing patterns of concern regarding suicide risk and specific medications of concern.

Other Medications of Concern

There are other medications of concern, which should also be considered in the context of links between young people, suicide and self harm. Following is a snippet from a Sydney Morning Herald article about Strattera, which is prescribed for ADHD.

Suicide Link To ADHD Drug⁶ **Amy Corderoy** October 04, 2013

A nine-year-old boy has killed himself and two other children have attempted suicide while taking a drug used to treat attention deficit hyperactivity disorder, federal drug authorities have said.

In a safety update, the Therapeutic Goods Administration urged doctors to ensure parents are aware that suicidal thoughts can be an extremely rare but disastrous side-effect of the ADHD medication Strattera.

The news comes as figures obtained by Fairfax Media show NSW is Australia's ADHD drug capital, with medication use continuing to rise.

A snippet of another article of interest is as follows:

Psychiatrists Fear Link With Prescription Meds And Violent Shootings⁷ Written by John O’Sullivan

*In a ‘**Statement on the Connection Between Psychotropic Drugs and Mass Murder**’ (January 4, 2013) the International Society For Ethical Psychology and Psychiatry (ISEPP) calls for an inquiry into the connection between acts of mass murder and the use of psychotropic drugs. The evidence of a link is found in the paper, ‘*Prescription Drugs Associated with Reports of Violence Towards Others*’ that also shows violence towards others is a seldom-studied adverse drug event and an atypical one because the risk of injury extends to others.*

The plea by the Board of Directors and membership of the International Society For Ethical Psychology and Psychiatry reflects a growing body of evidence as detailed in an important 2011 study showing a link between prescription medication and violence.

⁵ <http://owens.house.gov/news/documentsingle.aspx?DocumentID=330898>

⁶ <http://m.smh.com.au/national/health/suicide-link-to-adhd-drug-20131004-2uzut.html> - _ =

⁷ <http://www.principia-scientific.org/Current-News/psychiatrists-fear-link-with-prescription-meds-and-violent-shootings.html>

*Among the drugs with warnings about aggressive behaviors are varenicline, zolpidem, **Montelukast**, and all antidepressant drugs. The respected international body cited a sorry list of cases where anti-depressants may have played a part. They include:*

- *Eric Harris, one of the gunmen in the Columbine school shooting, was taking Luvox and Dylan Klebold, his partner, had taken Zoloft and Paxil.*
- *Doug Williams, who killed five and wounded nine of his fellow Lockheed Martin employees, was on Zoloft and Celexa.*
- *Michael McDermott was on three antidepressants when he fired off 37 rounds and killed seven of his fellow employees in the Massachusetts Wakefield massacre.*
- *Christopher Pittman was on antidepressants when he killed his grandparents.*
- *Kip Kinkel was on Prozac when he killed his parents and then killed 2 children and wounded 25 at a nearby school.*
- *In fourteen recent school shootings, the acts were committed by persons taking or withdrawing from psychiatric drugs, resulting in over 100 wounded and 58 killed.*
- *In other school shootings, information about the shooter's prescription drug use and other medical history were kept from public records.*

Interesting research is currently being conducted in Europe, which is specifically linked to Montelukast and suicide – <http://www.stop-study.com/index.php/project-summary/>

Details can be found at Appendix C for the STOP (Suicidality Treatment Occurring in Paediatrics) project.

Alarming data which was released in January 2014 by The **Institute for Safe Medication Practices** (USA) highlighted the most frequent suspect drugs in serious adverse drug events reported in normal medical use 2008 -2012 (Appendix D.) The rankings showed -

SINGULAIR (Montelukast) RANKED 1 for suicidal ideation
SINGULAIR (Montelukast) RANKED 2 overall

On the 2nd May 2014 members of our group provided submissions and testified in person at the US Food and Drug Administrations Non-prescription drugs Advisory Committee meeting in regards to a submission from Merck (the drug company) to have 10mg Montelukast tablets, branded as Singulair Allergy, sold over the counter (OTC) without a prescription. The advisory panel members voted 4 in favour and 11 against Singulair Allergy being made available OTC. We are currently awaiting the final decision which is made by an independent member of the US FDA. The advisory panel provided multiple reasons for their panel's decision one of which was the concerns surrounding the neuropsychiatric side effects of Singulair.^{8 9}

⁸ <http://www.fda.gov/AdvisoryCommittees/Calendar/ucm393018.htm>

⁹ <http://www.medscape.com/viewarticle/824583?src=stfb>

Please assist me in protecting Australian children that don't have a voice and Australian families that still have not made the 'link' between the medication and their children's severe behavioural and health issues. It is vital that education regarding the neuropsychiatric side effects of Singulair (Montelukast) is highlighted to the medical and general community in order to save more children from committing suicide.

Kind regards,

Vanessa Sellick

Founder of International SINGULAIR (Montelukast) Side Effects Action Group
Administrator of Awareness of Singulair Side Effects for Australian Families and Individuals

APPENDIX A.

PERSONAL ACCOUNTS

Following are some brief personal accounts.

stories are from members of our Singulair side effects support group.

Personal Account 1.

I have two sons that in my opinion have suffered significantly as a result of daily doses of Singulair to manage their asthma. My oldest son took the medication for three years and my youngest two and a half years. At age four, my oldest son began to have suicidal thoughts and at one stage threw himself out in front of a car; he would often bite himself and punch or slap his head. He often begged me to kill him or asked me to break his legs when he is in the water so that he would drown.

He suffers from OCD, germ phobia, severe anxiety, sporadic anorexia thought processes and has short periods of memory loss and disorientation. He struggles to get to sleep at night, has very low personal self-image and gets angry and agitated easily. His physical side effects included intense stomach pains, vomiting, headaches, dizziness, severe nose bleeds, leg muscle pain, bedwetting and heart palpitations, all recognised Singulair side effects, some of which he still experiences. Despite his extreme struggles, he is an exceptionally loving and affectionate child, he cares for others and shows great empathy for those around him.

My youngest has issues with toileting, which is consistent with other children that have been on Singulair and was discussed by medical professionals at the recent FDA Advisory Panel Meeting; however his largest struggle is long bouts of crying for no reason. He also suffers from a short temper and agitation. We are a loving and supportive family but no amount of love can overcome these destructive thought processes that are born from these side effects. It makes me fear greatly for children that have no support in their lives and that are struggling with the horror of these side effects.

Many Australian medical professionals were involved in trying to pinpoint why my oldest son had so many struggles and no one made the link between his suicidal thoughts, severe anxiety, multiple other symptoms and his use of Singulair. The link between Singulair and these side effects is well known in the US; however, in Australia many doctors, pharmacists and psychologists do not seem to know about them.

Personal Account 2.

My son was 13 when first prescribed Montelukast, a county level rugby player, happy go lucky and laid back lad. Within a few weeks of taking this drug he became increasingly anxious, stopped sleeping and started to experience alarming mood swings. At this time he was also going through adolescence and recently changed schools - we put many of these symptoms down to this. After several months where moods could be so black that we were receiving concerning messages from school about bizarre behaviour that we realised he was self harming and becoming obsessed with suicide and death. This all came to a head when he had a major psychotic episode at school and I started looking for reasons, found the side effects of Montelukast on Google and realised what was happening. In the UK at that time, there were no warnings on the drug advice. We stopped and there was a dramatic improvement but the effects have been long

term. He still does not sleep, he was never able to complete his education due to inability to cope with stress and concentration. He has found a way through life by working with others who struggle but this drug significantly changed his personality - permanently. It is vital that it is not available without due warning - in my opinion it should be removed from the market as no-one can have any idea whether a child will be effected or not.

is now 19 and was on the drug for approximately 9 months, stopping when he was 14.

Personal Account 3.

My son started on Singulair when he was 6.5 years of age for allergies. Prior to this he was what society would label as a well adjusted happy little boy. He could recite the alphabet and the months of year and remember the words to songs taught at school. By age 10 we found he was no longer able to do this. He suffered with tics, dark urine, aching joints and pins & needles. Some days he would not be able to walk far at all and would sit on the pavement refusing to move. The neurological change was the most concerning. Uncontrollable temper tantrums, hallucinations - he would hear his name being whispered in his ear, he would not spend any time alone in his room as he would say things were jumping and forming out of the wall. At the point of stopping Singulair when he was 11 years of age he was having suicidal thoughts and used to bite himself and bang his head against the wall and complain of a fuzzy head. It has been 3 years since he last took a Singulair tablet and although the suicidal, dark thoughts, self harming has ceased he still suffers with an extreme lack of concentration and ability to digest information.

Personal Account 4.

Singulair can and does cause neuropsychiatric side effects. My son took Singulair for approximately five years starting at about the age of three. He struggled with agitation, aggression, hostility, anxiousness, disturbance in attention, insomnia, irritability, memory impairment, and restlessness while taking it. His symptoms worsened after a dosage increase from 4mg-5mg and continued to intensify with continued use, culminating in depression and suicidal ideation. After I learned about Singulair's side effects and stopped giving it to my son, I observed a dramatic improvement in his mood, demeanor and behavior within days. I also used Singulair for a short period of time and experienced mood and behavior changes.

It is unknown how or why Singulair causes these side effects, how it affects a child's developing brain and whether or not it can cause long term problems. Since 2009, Parents United for Pharmaceutical Safety and Accountability has been receiving inquiries from parents wanting to know how long it takes for Singulair's side effects to resolve. Reports have also been received that, weeks, months or more after stopping Singulair, children continued to experience some of the problems they developed while taking it.

Personal Account 5.

Our now 10 year old twin daughters were on Singulair (Montelukast) for almost five years. At age 8 we noticed our daughter, _____, acting very depressed and having nightmares. Our pediatrician told us to take her off Singulair immediately. That was December 7, 2012. It was after we took her off we started to notice even more very extreme behavior changes: severe anxiety, night terrors, manic type behaviors and depression. Some of our biggest concerns have centered

around her thoughts of dying. She has often mentioned in the last 17 months, "I want to die" or "I want to go to heaven so I don't feel this way anymore." I cannot not stress enough that these words are highly unusual for our child. When we look at the timeline of events that have occurred in her life in the last 17 months, we can clearly see a correlation to her behavioral changes and her time taking Singulair. We hope that this issue is researched

further and we can help prevent this from happening to anyone else.

Personal Account 6.

Our son took Singulair for 4 years from May 2007 to May 2011. His mood and behavior started to change very gradually several months after starting Singulair. He started to have mood swings, became anxious and was easily upset by things. He started to have night terrors every time he got sick and had a fever. He worried about everything and had separation anxiety at night when he had thoughts and fears of dying. In the Spring of 2011, after stopping Singulair for a few days and then restarting, the side effects escalated to a very serious level with increasing anxiety, bad dreams, hostility, severe sleep issues, visual distortions, difficulty concentrating, extreme mood swings with inconsolable crying and restlessness. We knew something was terribly wrong and this culminated on May 6, 2011 with him having severe hallucinations and an almost psychotic reaction during a fever caused by a strep infection. We rushed him to Urgent Care and by chance we saw an advertisement for Singulair on an electronic registration pad which listed all of the side effects that he was having. We stopped the Singulair cold turkey (with the advice of our doctor) and we began to see our son change in front of our eyes. If we had known about the side effects we would have more quickly realized that the changes we were seeing in our son were being caused by Singulair and could have prevented all of this much earlier.

Recovery has been a long road. Just three days after stopping our son was a different child, he became affectionate rather than hostile, he started to laugh and joke, he showed a renewed interest in things, he stopped chewing his shirt, he stopped bedwetting, his handwriting improved, he started to draw, and he stopped having uncontrollable meltdowns. Our son told us that while on Singulair he always worried that something bad was going to happen. Even though we saw immediate positive changes in his behavior, that were without question as a result of him stopping the medication, he had lingering symptoms of anxiety, restlessness and severe sleep issues as a result of this traumatic experience which took 1.5 years to resolve. Ever since the Spring of 2011, after the side effects of Singulair escalated, we began to notice that he also had developed a heightened sensitivity to other medications and food additives. This multiple chemical sensitivity has caused setbacks in his recovery which no one has been able to explain and we continue to believe that this was caused by the long term use of Singulair which caused changes in his body and brain. (He did not have these sensitivities until after his side effects escalated.) We have been trying to work with doctors for the last three years to try to better understand why it seems that after taking Singulair his body metabolizes things differently. To this day we have no answers and believe that if further studies were conducted on the neuropsychiatric effects of Singulair doctors would better know how to help our son and hundreds of other children and adults recover.

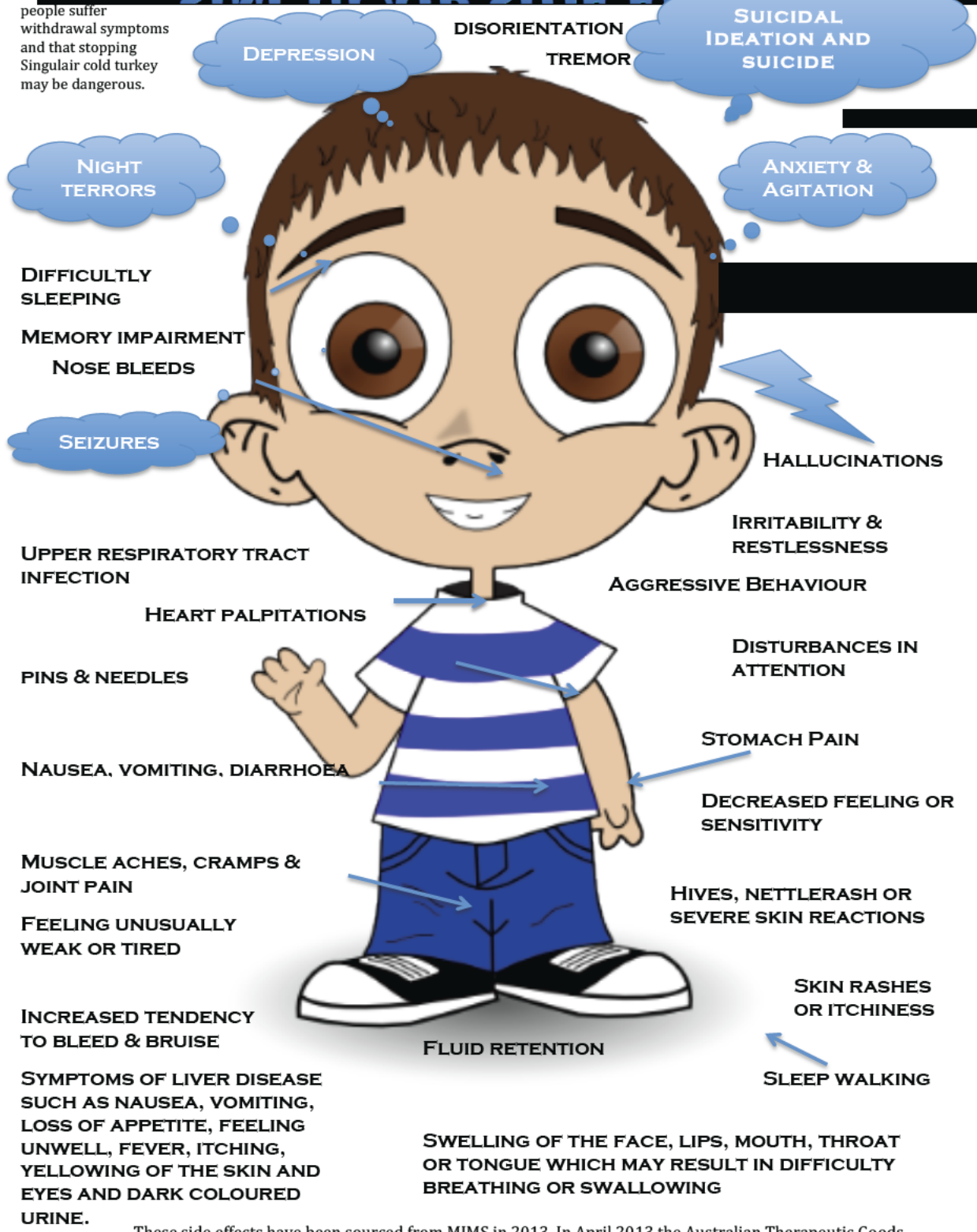
APPENDIX B.

Please ensure that you consult your GP to

<http://www.facebook.com/montelukastsideeffects>

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people suffer withdrawal symptoms and that stopping Singulair cold turkey may be dangerous.

SINGULAIR SIDE EFFECTS



These side effects have been sourced from MIMS in 2013. In April 2013 the Australian Therapeutic Goods Administration released an alert linking Singulair and neuropsychiatric episodes.

APPENDIX C.



STOP – A comprehensive evaluation of suicidality

The STOP project aims to develop a comprehensive web-based methodology for the assessment and monitoring of suicidality in children and adolescents. The STOP consortium brings together renowned researchers from across Europe, each with a strong scientific and clinical background in this innovative child and adolescent psychiatry network. It has a mixed and balanced expertise with respect to paediatric psychopharmacology, suicidality, regulatory issues, and use of new technologies and infrastructure.

Project Summary Background

There is insufficient data available about safety of using many medications in children and adolescents who may have an illness that itself predispose them to suicidality. There is also insufficient data available about the time-course of medication related suicidality and what happens to it over the long-term. Further, there is insufficient data available about the long-term safety, in particular about medication related suicidality, especially since there is evidence to suggest that paediatric populations may represent a vulnerable group compared to adults.

The STOP project arises from the collaboration of a group of experts in paediatric psychopharmacology within the framework of the European Child and Adolescent Paediatric Network (ECAPN). ECAPN is supported by the European College of Neuropsychopharmacology (ECNP) (www.ecnp.eu) and its network initiative (EcnpNI).

Objectives

The STOP project aims to develop a comprehensive web-based methodology for the assessment and monitoring of suicidality in children and adolescents. Four domains are of importance for this purpose: assessment and monitoring of suicidality, assessment of putative risk and protective factors but also mediators (intermediate outcomes contributing to treatment effects), assessment of psychiatric and physical symptoms and medication characteristics.

This assessment methodology will be used in three clinical samples to identify characteristic features of medication-related suicidality (MRS): children and adolescent receiving an atypical antipsychotic, children receiving fluoxetine for depression and children treated with **Montelukast** for bronchial asthma. These medications were targeted because they have been related to suicidality.

APPENDIX D.



The **Institute for Safe Medication Practices** - Adverse Drug Events in Children Under Age 18 - Psychiatric side effects prominent in 10 of 15 most frequently reported drugs. Most Frequent Suspect Drugs in Adverse Drug Events Reported in Medical Use 2008 - 2012 (US FDA) -

SINGULAIR (Montelukast) RANKED 1 for suicidal ideation
SINGULAIR (Montelukast) RANKED 2 overall

16 January 2014

<http://www.ismp.org/quarterwatch/pdfs/2013Q1-Kids-Special.pdf>

Table 1. Most frequent suspect drugs in serious adverse drug events reported in normal medical use, 2008-2012

Rank	Drug name	Brand name*	Cases	Medical use*	Psych**	Most freq ADE	2d most freq ADE
1	Infliximab	REMICADE	1772	Crohn's Disease	N	Crohn's disease	Ulcerative colitis
2	Montelukast	SINGULAIR	944	Asthma	Y	Suicidal ideation	Aggression
3	Somatropin	NUTROPIN	606	GH deficiency	N	Headache	Convulsion
4	Baclofen	LIORESAL	579	Muscle spasticity	N	Hypertonia	Drug ineffective
5	Isotretinoin	CLARAVIS	447	Acne	Y	Suicidal ideation	Depression
6	Methylphenidate	CONCERTA	418	ADHD	Y	Sudden death	Aggression
7	Lamotrigine	LAMICTAL	335	Epilepsy	Y	Convulsion	Stevens-Johnson synd
8	Lisdexamfetamine	VYVANSE	314	ADHD	Y	Suicidal ideation	Aggression
9	Aripiprazole	ABILIFY	297	Bipolar disorder	Y	Weight increased	Dystonia
10	Ibuprofen	MOTRIN	242	Pyrexia	N	Hypersensitivity	Renal failure acute
11	Etanercept	ENBREL	231	Juvenile arthritis	N	Injection site pain	Vomiting
12	Atomoxetine	STRATTERA	227	ADHD	Y	Suicidal ideation	Chest pain
13	Quetiapine	SEROQUEL	210	Bipolar disorder	Y	Weight increased	Tardive dyskinesia
14	Levetiracetam	KEPPRA	206	Epilepsy	Y	Convulsions	Drug ineffective
15	Risperidone	RISPERDAL	195	Bipolar disorder	Y	Aggression	Weight increased

* Most frequently cited in case reports. **Psychiatric side effects > 25% of reports.

GH = Growth hormone. ADHD = Attention deficit hyperactivity disorder. Additional note in Methods Summary

APPENDIX E.


ASSOCIATION FOR MEDICAL ETHICS (USA)



'Singulair does have side effects, some of them very dangerous'.
<http://www.ethicaldoctor.org/ame-articles/articles-americas-popular-drugs/singulair>

APPENDIX F.

CANADIAN PAEDIATRIC SURVEILLANCE PROGRAM -Montelukast (Singulair) - Risk of psychiatric adverse reactions 05/2010.



CANADIAN PAEDIATRIC
SURVEILLANCE PROGRAM

ADR

Tip of the Month

Montelukast (Singulair™)

Risk of psychiatric adverse reactions

Montelukast sodium (Singulair™), a leukotriene-receptor antagonist, is used in the treatment of asthma and seasonal allergic rhinitis. Adverse reactions related to self-injury, suicidality, depression, hostility or psychosis, suspected of being associated with the use of montelukast, were reported.

Physicians should:

- Be aware of the risk of suicidality and other psychiatric adverse reactions with the use of montelukast.
- Reduce or stop the drug immediately if psychiatric signs and/or symptoms appear.
- Realize that, in some patients, the adverse reactions can reappear upon re-introduction of the drug. Very close observation is recommended.

Reference
www.hc-sc.gc.ca/dhp-mps/medeff/bulletin/cam-bcei_v19n3-eng.php#a1

Please report all serious adverse drug reactions (ADRs).

05/2010

APPENDIX G.

MEDICINE BRANDS AVAILABLE IN AUSTRALIA THAT CONTAIN MONTELUKAST (the active ingredient in Singulair).

APO-Montelukast Chewable tablets
APO-Montelukast Tablets
Auro-Montelukast Tabs Chewable tablets
Chemmart Montelukast Chewable tablets
Lukair Chewable tablets
Lukair Tablets
Montair Chewable tablets
Montair Tablets
Montelukast GH Chewable tablets
Montelukast RBX Chewable tablets
Montelukast Sandoz Chewable tablets
Pharmacor Montelukast Chewable tablets
Respikast Chewable tablets
Singulair Chewable tablets
Singulair Tablets
Terry White Chemists Montelukast Chewable tablets

<http://www.nps.org.au/medicines/respiratory-system/other-respiratory-medicines-and-devices/montelukast-other-respiratory-medicines-and-devices>

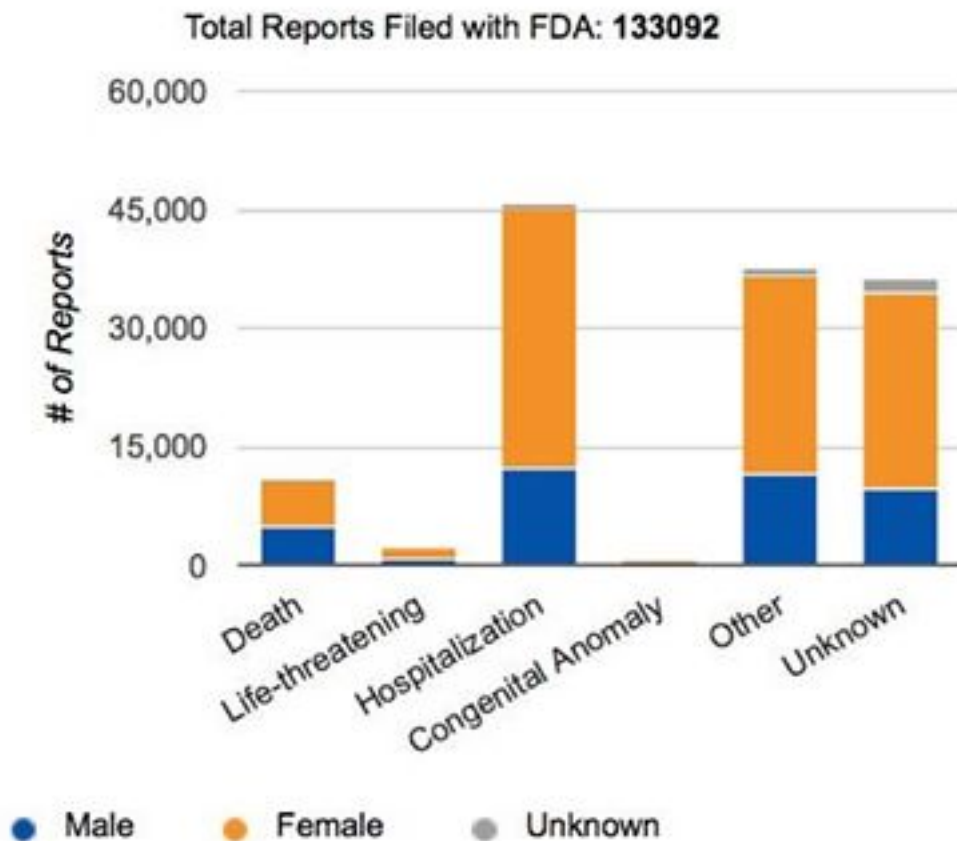
APPENDIX H.

US FOOD AND DRUG ADMINISTRATION

Adverse Events Summary for SINGULAIR (Montelukast sodium) based on 133092 reports filed with the FDA between 2004 and 2012.

<http://www.askapatient.com/adverse-events.asp?drug=SINGULAIR>

Types of Adverse Events for SINGULAIR



APPENDIX I.

US FDA DATA COMPILED ON eHealthMe.com

On May, 18, 2014: 41,147 people who reported to have side effects when taking Singulair are studied - <http://www.ehealthme.com/singulair/singulair-side-effects>

Most common side effects by age:

0-1	2-9	10-19
Hypoglycaemia	Aggression	Depression
Drug Exposure During Pregnancy	Abnormal Behaviour	Suicidal Ideation
Hypotension	Suicidal Ideation	Anxiety
Diarrhoea	Crying	Asthma
Convulsion	Anxiety	Headache
Irritability	Depression	Suicide Attempt
Agitation	Anger	Aggression
Aggression	Nightmare	Abnormal Behaviour
Henoch-schonlein Purpura	Insomnia	Nausea
Insomnia	Agitation	Fatigue

Please note that this data is only for Singulair branded Montelukast, additional data is available on Montelukast branded products.