

Safe Prescribing in Frailty Tackling Medicine Overuse & Anticholinergic Risks

Graham Stretch
9th October 2024

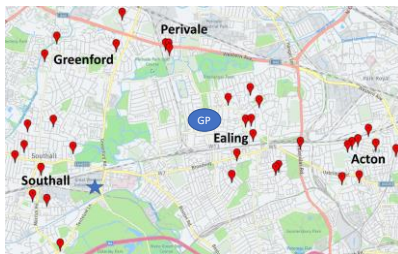


Session Plan

- Background
- Frailty
- Polypharmacy
- Consequences
- Cognitive impairment and ACB
- Strategies
- Resources
- Cases

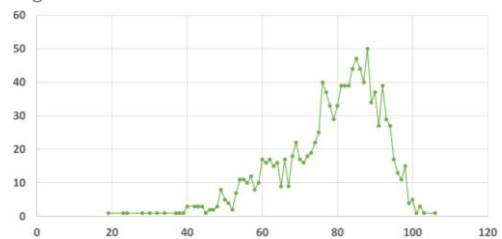


The Care Home Service



- **34 Homes**
- **1200 Residents**
- **08-20**
- **365**

Age

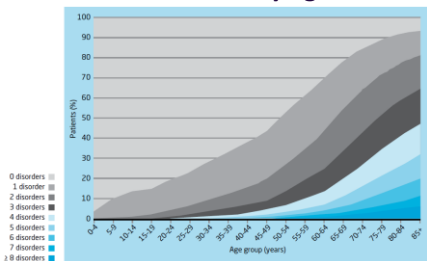


- 18-108**
- Frailty****
- Generalist**
- Dementia**
- Neuro**
- Physical**

ePACT2 : Yr to July 2024 : 191k items : £1.8Mn : 98% Pharmacy



Number of chronic conditions by age



Barnett et al, Lancet, 2012, 380, pp 37-43



Clinical Frailty Scale¹

- 1 Very Fit** - People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.
- 2 Well** - People who have no active disease symptoms but are less fit than category 1. Often, they exercise or are very active occasionally, e.g. seasonally.
- 3 Hanging In** - People whose medical problems are well controlled, but are not regularly active beyond routine walking.
- 4 Vulnerable** - While not dependent on others for daily help, often symptoms limit activities. A common complaint is being "sloved up" and/or being tired during the day.
- 5 Mildly Frail** - These people often have more evident slowing and need help in high order IADLs (finances, transportation, heavy housework, medications). Typically mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.
- 6 Moderately Frail** - People need help with all outside activities and with keeping house. Usually, they often have problems with tasks and need help with bathing and might need minimal assistance (cuing, standby) with dressing.
- 7 Severely Frail** - Completely dependent for personal care, from showering (bath or shower or hygiene). Even so, they seem stable and not at high risk of dying (within ~ 6 months).
- 8 Very Severely Frail** - Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.
- 9 Terminally Ill** - Approaching the end of life. This category applies to people with a life expectancy < 6 months, who are not otherwise evidently frail.

Scoring frailty in people with dementia.
The degree of frailty corresponds to the degree of dementia. Common symptoms in mild dementia include forgetting the details of events, such as, though still remembering the main part, repeating the same question and/or social withdrawal. In moderate dementia, recent memory is very impaired, even though they sometimes can remember their past life events well. They can do personal care with prompting. In severe dementia, they cannot do personal care without help.

¹ 1. Gobbler Study on Health & Aging Research 2006.
2. Gobbler Study on Health & Aging Research 2006.
3. Gobbler Study on Health & Aging Research 2006.
4. Gobbler Study on Health & Aging Research 2006.
5. Gobbler Study on Health & Aging Research 2006.
6. Gobbler Study on Health & Aging Research 2006.
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9. Gobbler Study on Health & Aging Research 2006.

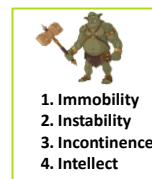


Definition of Comprehensive Geriatric Assessment

“ A multi-dimensional, interdisciplinary diagnostic process to determine the medical, physiological and functional capabilities of a frail older person in order to develop a coordinated and integrated plan for treatment and long-term follow-up. ”



Source: Book: 'Medical Assessment of Older People', British Geriatrics Society (BGS), 2011



1. Immobility
2. Instability
3. Incontinence
4. Intellect

The giants of geriatrics are immobility, instability, incontinence and intellectual impairment. They have in common multiple causation, chronic course, deprivation of independence and no simple cure.

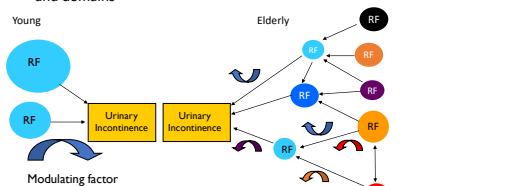
— Bernard Isaacs, The Challenge of Geriatric Medicine, Oxford University Press, 1997



Bernard Isaacs
in: Isaacs B., An Introduction to Geriatrics, London: Baillière, Tindall and Cox, 2005

Urinary incontinence as a geriatric syndrome

- Multiple risk factors (RF), across multiple organ systems and domains^{1,2}



1. Adapted from Tammis EM et al. *JAMA* 1991; 275: 1348-53.
2. Adapted from Toussaint R et al. *Age Geriatr Soc* 2007; 35: 789-93.

With thanks to Catherine O'Leary for software



Urge urinary incontinence increases the risk of falls (instability) and fracture

- 6049 community dwelling women
- Weekly / more frequent episodes of URGE incontinence
- Independent risk factor for falls and non-vertebral fractures
- Not stress incontinence
- Urinary frequency, nocturia, and rushing to the bathroom to avoid urge urinary incontinence episodes
- Continence assessment routine as part of falls prevention

26 Brown et al. *J Am Geriatr Soc* 2005; 43:4615-21-5



Bidirectional association between urinary incontinence and (im)mobility

- Hip fracture – increased risk of incontinence pre/post-op
- Urge urinary incontinence increases risk for falls/hip fracture
- Improving mobility and balance in cognitively impaired patients reduces daytime incontinence

Palmer et al. *J Gerontol A Biol Sci Med Sci* 2002; 57(7):M673-7.
Hasegawa et al. *Arch Gerontol Geriatr* 2012; 55(1):77-81.
Brown MM. *Int J Nurs Stud* 1991; 28(2):149-152.



Association between urinary incontinence and white matter changes in the brain

- Studies in community-dwelling elderly link structural white matter changes on magnetic resonance imaging of the brain with:¹
 - Mobility impairment
 - Cognitive impairment
 - Urinary incontinence
- Elderly individuals with greater white matter hyperintensity burden also show increased prevalence of detrusor overactivity and difficulty maintaining continence on urodynamic studies²

1. Kuchel GA et al. *J Gerontol A Biol Sci Med Sci* 2009; 64A: 932-9.
2. Sakakibara B et al. *J Neurol Neurosurg Psychiatry* 1999; 67: 658-60.



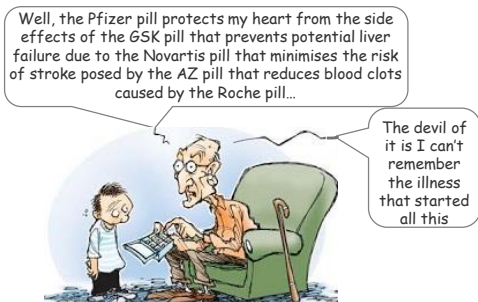
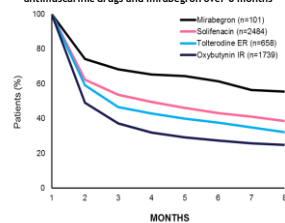
Breaking the chain of events / recognising the risk factors

- Holistic / MDT approach (CGA)
- MDG Meetings
- Improved screening for osteoporosis – primary and secondary (OG service)
- Falls and referral to falls service / IC/ICE/OT/Physio
- Cognitive screening and OPA memory services
- Improved continence screening / OPRAC
- Training

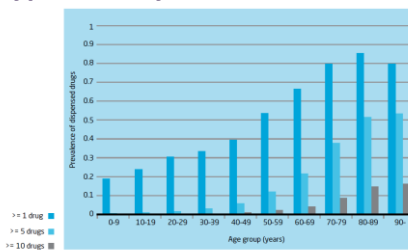


Persistence data

Persistence rates of all doses of the most prescribed antimuscarinic drugs and mirabegron over 8 months¹



Polypharmacy - Sweden 2005-08



Hovstadius et al, 2010, BMC Clinical Pharmacology, 10, 16





POLYPHARMACY

“...should be conceptually perceived as a ‘disease’ with potentially more serious complications than those of the diseases these different drugs have been prescribed for”

Gafni et al
Arch Intern Med. 2010;170(18):1648-1654



How?

- ‘Therapeutic enthusiasm’ - the ‘Illusion’
Thomas, BMJ 1978;20;1(6123):1327-8
 - 200 patients treat / No treatment
 - Same outcome
- The patients’ or their relatives’ demands
- An inappropriate response to non-medical problems
- Deprivation
- Unrealistic expectations by the prescriber, patient or both
- A failure to individualise treatment and to consider their overall needs
- Inadequate review

Contemporary Themes

The consultation and the therapeutic illusion

K. B. THOMAS

Brick Medical Journal, 1974, 1, 101-108

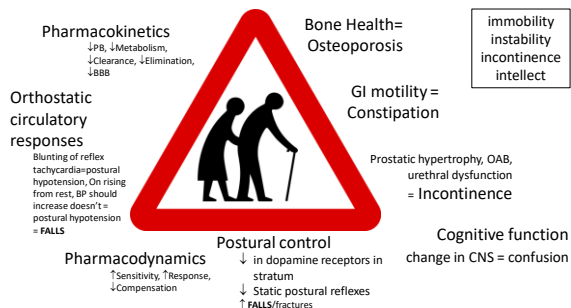
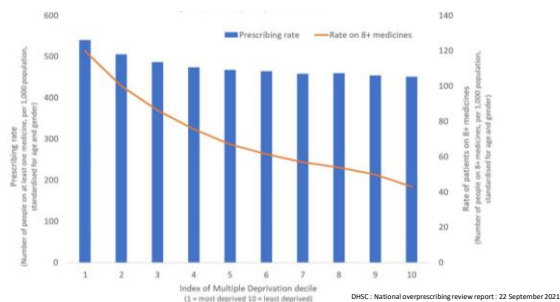


Good for you, good for us, good for everybody

A plan to reduce overprescribing to make patient care better and safer, support the NHS, and reduce carbon emissions

Published 22 September 2021





ADRs

Up to 20% of all admissions
Up to 50% preventable

2004 : Most common drug groups associated with admission - 6.5%:

1. NSAIDs 29.6%
2. Diuretics 27.3%
3. Warfarin 10.5%
4. ACE 7.7%
5. Antidepressants 7.1%
6. Beta blockers 6.8%
7. Opiates 6.0%
8. Digoxin 2.9%
9. Prednisolone 2.5%
10. Clopidogrel 2.4%

Pirmohamed et al., BMJ 2004;329:15

2022 : Most common drug groups associated with admission - 18.4%:

1. Diuretics 14%
2. Steroid inhaler 12%
3. Anticoagulants 10%
4. Proton Pump Inhibitor 8%
5. Antiplatelets 7%
6. Chemotherapy 7%
7. ACE-I /ARB 6%
8. Antidepressants & antipsychotics 6%
9. Opiates 6%
10. Beta blockers 4%

Olanou, Pirmohamed et al. BMJ 2022;12:e055551.

ADRs : 10-20% Admissions

Constipation	Opiates, antihistamines, iron, calcium channel blockers, anticholinergics
Nausea and vomiting	Many drugs
Postural hypotension, falls	Sedatives, Antiparkinson drugs, antihypertensives, alcohol, psychotropics, anticholinergics
Impaired cognition	Most CNS drugs, anticholinergics
Blood disorders	Metformin, Clozapine, orphenazazine
GI bleeds	Aspirin, NSAIDs, Warfarin, SSRIs, Prednisolone
Confusion	Cimetidine, hypnotics, anticholinergics
Blurred vision	Anticholinergics, antihistamines, TCAs
Renal failure	ACEI, NSAIDs
Hypertension	NSAIDs
Extrapyramidal effects	Metoclopramide, prochlorperazine, antipsychotic
Anorexia	Digoxin
Altered taste	ACEIs, metronidazole, zopiclone

“Higher cumulative anticholinergic use is associated with an increased risk for dementia”

Gray *et al.* Cumulative use of strong anticholinergics and incident dementia: a prospective cohort study.
 JAMA Intern Med. 2015;175:401-7

The Headlines
 Study suggests sleeping drugs can increase risk of Alzheimer's. The Guardian, 27 January 2015
 Popular sleep remedies and hay fever pills increase risk of Alzheimer's by more than 50%. Daily Mail, 26 January 2015
 Hay fever and sleeping tablets can increase risk of Alzheimer's and dementia. Daily Mirror, 26 January 2015
 Routine drugs for elderly 'raise risk of dementia'. The Times, 26 January 2015
 Hay fever pills and sleeping aids can 'significantly increase' risk of Alzheimer's, says US study. The Independent, 26 January 2015
 Hay fever drugs raise risk of Alzheimer's disease, say scientists. The Daily Telegraph, 26 January 2015
 Dementia 'linked' to common over-the-counter drugs. BBC News, 27 January 2015

Risk for incident dementia and Alzheimer disease with 9-year cumulative anticholinergic use with 2-year lag time

TSD0	Follow-up time (person-years)	Dementia		Alzheimer Disease	
		Number of Events	HR (95% CI)	Number of Events	HR (95% CI)
0	6137	154	1.00 Reference	124	1.00 Reference
1-90	7861	208	0.89 0.71-1.11	172	0.94 0.74-1.20
91-365	4849	171	1.21 0.96-1.52	128	1.19 0.92-1.55
366-1095	2461	94	1.15 0.88-1.52	80	1.30 0.96-1.75
>1095	3712	170	1.49 1.17-1.89	133	1.59 1.22-2.08

n=3434, mean follow-up 7.3y

Gray *et al.* JAMA Intern Med. 2015;175:401-7



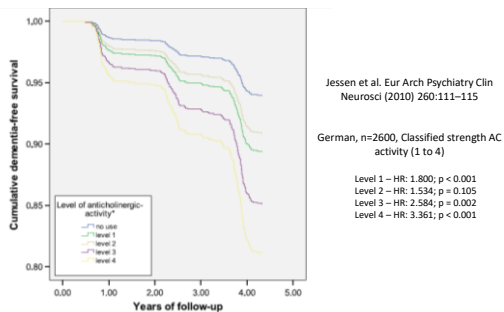
“The use of medications with anticholinergic activity increases the cumulative risk of cognitive impairment and mortality.”

Fox *et al.* Anticholinergic medication use and cognitive impairment in the older population: the medical research council cognitive function and ageing study.
 J Am Geriatr Soc. 2011 Aug;59(8):1477-83

Fox *et al.* 2011

- Thirteen thousand and four participants from UK aged 65 and older.
- Worsening brain function: participants ACB score 5 + scored lower test (MMSE).
- Increased death rate:
 - End year 2: 20% people scoring 4 + vs. 7% scoring 0.
 - Every extra ACB point scored odds dying ↑ 26%
- Cumulative risk both no. anticholinergic drugs & strength each drug's anticholinergic effect





April 2016

Association Between Anticholinergic Medication Use and Cognition, Brain Metabolism, and Brain Atrophy in Cognitively Normal Older Adults

Figure 1. Association of Anticholinergic (AC) Medication Use With Cognition and Glucose Metabolism Among Participants From the Alzheimer's Disease Neuroimaging Initiative (ADNI)

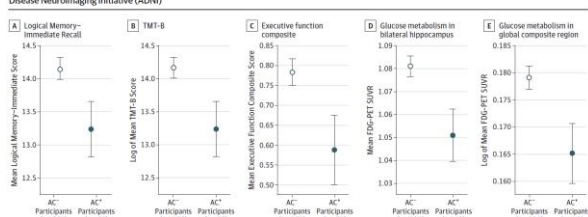


Figure 2. Effect of Anticholinergic (AC) Medication Use on Brain Atrophy Measures

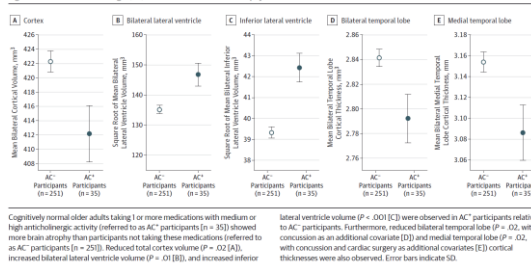
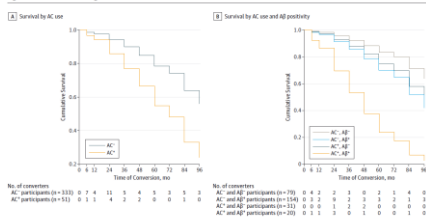


Figure 4. Effect of Anticholinergic (AC) Medication Use on Clinical Conversion



No. of converters
 AC participants (n=132) 0 2 4 11 5 4 5 3 1 0
 no AC participants (n=132) 0 1 1 4 2 2 0 0 1 0

No. of converters
 AC+ Aβ+ participants (n=75) 0 0 2 2 3 0 0 0 0 0
 AC- Aβ+ participants (n=154) 0 2 2 0 2 0 2 2 1 1
 AC+ Aβ- participants (n=122) 0 0 0 1 2 1 0 0 0 0
 AC- Aβ- participants (n=220) 0 1 1 3 0 1 0 0 1 0

A. A significant association between AC use and future progression of Alzheimer's Disease Neuroimaging Initiative participants to mild cognitive impairment and/or Alzheimer's Disease was observed (P < .05, hazard ratio [HR], 1.25).
 B. Total number of medications, cardiac surgery, total number of comorbid conditions, and other psychiatric conditions as additional covariates.
 C. When evaluating the interaction between AC use and Aβ positivity, we found that participants taking no more medications with medium or high AC activity who are positive for Aβ-on florbetapir F-18-position emission tomographic (PET) scan or cerebrospinal fluid (CSF) samples (compared to AC- and Aβ- participants) showed a higher risk of conversion relative to participants not taking these medications who are negative for Aβ-on florbetapir F-18-positron emission tomography or CSF samples (relative to AC- and Aβ- participants) (P < .005, HR, 4.26).
 D. When evaluating the interaction between AC use and Aβ positivity, we found that participants taking no more medications with medium or high AC activity and participants who are positive for either AC use or Aβ (P < .005, HR, 4.26).



Alzheimer's & Dementia: Translational Research & Clinical Interventions 3 (2017) 471-479



Featured Article

Midlife anticholinergic drug use, risk of Alzheimer's disease, and brain atrophy in community-dwelling older adults

Yi-Fang Chuang^{a,b,c}, Palchamy Elango^d, Christopher E. Gonzalez^e, Madhav Thambisetty^{a,b}

"In conclusion, we found that exposure to medications with possible AC activity as early as midlife is associated with increased risk of AD and accelerated atrophy in brain regions vulnerable to AD pathology before cognitive impairment. Our results have important public health implications."



RESEARCH



Anticholinergic drugs and risk of dementia: case-control study

Kathryn Richardson,¹ Chris Fox,² Ian Maidment,³ Nicholas Steel,³ Yoon K Loke,² Antony Arthur,¹ Phyo K Myint,⁴ Carlota M Grossi,⁵ Katharina Mattishent,⁶ Kathleen Bennett,⁷ Noll L Campbell,⁸ Malaz Boustani,⁹ Louise Robinson,⁹ Carol Brayne,⁹ Fiona E Matthews,¹⁰ George M Savva¹

WHAT THIS STUDY ADDS

Antidepressant, urological, and antiparkinson drugs with definite anticholinergic activity are linked to future dementia incidence, with associations persisting up to 20 years after exposure

doi: 10.1136/bmj.k1315



COMMENTARY

Anticholinergic drugs and risk of dementia: Time for action?

Brian Bell¹ | Anthony Avery¹ | Della Bishara² | Carol Coupland¹ | Darren Ashcroft³ | Martin Orrell⁴

¹Department of Primary Care, University of Nottingham, Nottingham, UK
²NIHR Maudsley Biomedical Research Centre, South London and Maudsley NHS Trust, London, UK
³School of Pharmacy and Pharmaceutical Sciences, University of Manchester, Manchester, UK
⁴Institute of Mental Health, University of Nottingham, Nottingham, UK

"In summary, it appears that the use of anticholinergics like Razaford Hill criteria for establishing a causal link with the development of dementia and this may also be the case for other anticholinergics that easily cross the blood-brain barrier. Should doctors and pharmacists make the case for avoiding anticholinergics associated with risk of dementia? The precautionary principle would suggest that we should act now and advise colleagues not to use anticholinergics associated with dementia for bladder symptoms when there are alternatives that appear to be safer"

Pharmacol Res Perspect. 2021;9:e00793. doi.org/10.1002/prp2.793
 Published online 04 June 2021



Handwritten notes on a lined paper. At the top, it says "RECEIVED" with a date stamp "13/7/20". Below that, there are several lines of handwritten text, including "Mrs G", "1987", and a list of medical conditions and treatments such as "X1. Diabetes Mellitus 10mg 1000", "X2. Hypertension 10/500mg tabs", "X3. Chronic Pain 5mg tabs", "X4. WAGNER'S ANGINA 25/300 R 100 (UK SUPPLY THREE MONTHS ONLY)", "X5. IBS 60mg MR Capsule", "X6. SALAZOPYRIN EN-Tabs 500mg", "X7. LEVOTHYROXINE Sodium 50mcg tablets", "X8. LEVOTHYROXINE Sodium 25mcg tablets", "X9. SCHIZOPHRENIA DISORDER SERENIDE 125 Evohaler", "X10. SERENIDE 125 Evohaler", "X11. SALAZOPYRIN 100mg CFC INHALER", "X12. NEURONTIN 100mg Half (600) Capsules", "X13. PARACETAMOL 500mg Tabs BUTRANS 20".



- | | | |
|--|---|--|
| 20 Mar 2000 Essential hypertension (XE0Uc) | 04 Aug 2007 Glaucoma (18 Dec 2007 Serum cholesterol raised (44P3.)) | 19 Mar 2015 Osteoarthritis Hip pain (X75rv) |
| 10 May 2002 Hypothyroidism (X40IQ) | 18 Dec 2007 Hyperlipidaemia (14AC) | 25 Sep 2016 Dry eyes (1B88.) |
| 02 Sep 2002 Deep vein phlebitis (XE0VY) | 18 Dec 2007 Indigestion (1954.) | 07 Jun 2020 Microcytic hypochromic anaemia (D00y1) |
| 02 Sep 2002 H/O: pulmonary embolus (14AC) | 01 Feb 2008 Indigestion (1954.) | 07 Jun 2021 Anaemia - iron deficiency (Xa0K6) |
| 24 Nov 2005 Urinary incontinence (1A23.) | 01 Feb 2009 Rheumatoid Arthritis (N040.) | 27 Mar 2022 Supraventricular tachycardia (Xa0K6) |
| 24 Oct 2006 Knee joint operations (7K3.) | 01 Feb 2010 Dyspepsia (X40YQ) | |
| 13 Dec 2006 Asthma monitoring (XM1Xb) | 27 Jun 2010 Morbid obesity (X40YQ) | |
- Repeat File**
- | | | |
|---|--|--|
| • Amitriptyline 10mg Tablets | • Lactulose 3.1-3.7g/5ml oral solution | • Salbutamol 100micrograms/dose inhaler CFC free |
| • Buprenorphine 10micrograms/hour transdermal patches | • Latanoprost 50micrograms/ml eye drops | • Scheriproct ointment (Bayer Plc) |
| • Cellulvic 1% eye drops 0.4ml unit dose (Allergan Ltd) | • Levothyroxine sodium 25microgram tablets | • Seretide 125 Evohaler (GlaxoSmithKline UK Ltd) |
| • Co-diydamol 10mg/500mg tablets | • Levothyroxine sodium 50microgram tablets | • Simvastatin 40mg tablets |
| • Dileem XL 180 capsules (Teva UK Ltd) | • Omeprazole 20mg gastro-resistant capsules | • Solifenacin 5mg tablets |
| • Domperidone 10mg tablets | • Oramorph 10mg/5ml oral solution (Boehringer Ingelheim Ltd) | • Trospium chloride 60mg MR capsules |
| • Folic acid 5mg tablets | • Paracetamol 500mg tablets | • Warfarin 1mg tablets |
| • Gabapentin 100mg capsules | • Promethazine 25mg Tablets | • Warfarin 3mg tablets |
| | • Salazopyrin EN-Tabs 500mg (Pfizer Ltd) | • Warfarin 5mg tablets |



Alternatives?

- | | | |
|--|--|--|
| <p>TCI</p> <ul style="list-style-type: none"> • Depression <ul style="list-style-type: none"> - SSRI - SNRI - Duloxetine - Trazodone • Neuropathic <ul style="list-style-type: none"> - gabapentin - pregabalin - duloxetine | <p>Antihistamine</p> <ul style="list-style-type: none"> • '1st Gen' <ul style="list-style-type: none"> - chlorpheniramine - diphenhydramine - promethazine • Current Indication? • '2nd Gen' <ul style="list-style-type: none"> - loratadine - cetirizine | <p>OAB</p> <ul style="list-style-type: none"> • Anti-Chol <ul style="list-style-type: none"> - oxybutynin - tolterodine - solifenacin - trospium - darfenacin • SNRI <ul style="list-style-type: none"> - duloxetine • B₃ agonist <ul style="list-style-type: none"> - mirabegron |
|--|--|--|



Optimise

- Try mirabegron for OAB - replace anti cholinergics.
 - No INR recorded requested warfarin - indication? stop
 - Pain relief Butrans 20, paracetamol 2 qds and oramorph 2.5-5mg 4hr prn record usage
 - Stop amitriptyline / promethazine / domperidone
 - repeat levothyroxine, salazopyrin, salbutamol and seretide.
 - Simvastatin to be reviewed non-concordant - stop?
- New Rx**
- Buprenorphine 20micrograms/hour transdermal patches - 4 patch - apply one as directed
 - Gabapentin 100mg capsules - 100 capsule - 1 tds
 - Mirabegron 50mg MR Tabs - 30 tabs - 1 OD
 - Oramorph 10mg/5ml oral solution (Boehringer Ingelheim Ltd) - 300 ml - 5MLS WHEN REQUIRED UP TO 4-6 HOURLY
 - Scheriproct ointment (Bayer Plc) - 30 gram - apply twice daily as needed
 - (R) Levothyroxine sodium 25microgram tablets - 56 tablet - EVERY DAY
 - (R) Levothyroxine sodium 50microgram tablets - 56 tablet - OD
 - (R) Paracetamol 500mg tablets - 224 tablet - 2 FOUR TIMES A DAY regularly
 - (R) Salazopyrin EN-Tabs 500mg (Pfizer Ltd) - 224 tablet - 2 TABLETS TWICE DAILY
 - (R) Salbutamol 100micrograms/dose inhaler CFC free - 200 dose - 1-2 PUFFS PRN
 - (R) Seretide 125 Evohaler (GlaxoSmithKline UK Ltd) - 120 dose - ONE PUFF TWICE A DAY



Questions

