

Stability of Drugs in Compliance Aids

August 2006

(Cover letter)

Dear Pharmacist,

Multi-compartment Compliance Aids (MCAs) are increasingly being used in the primary and secondary care settings to aid patient compliance with medication intake.

At Pinderfields General Hospital, most MCA dispensing is carried out by pharmacy staff. Patients who are discharged into the community are given the MCA on the understanding that, either the patient themselves, a carer or a local community pharmacy will be able to refill the MCA on a continual basis.

Despite routine dispensing of drugs in MCAs, we are unaware of any standard guidance available on the actual stability of drugs in compliance aids.

Many manufacturers are quick to point out that their drug(s) are not licensed for inclusion in a compliance aid based on the absence of any stability studies, and that this **will affect their liability**. Hence they cannot/will not advise on the suitability of inclusion in a compliance aid. Some manufacturers whilst pointing out the absence of stability information in MCAs, provide guidance based on the physical and chemical properties of the drug. The final decision on whether to include or exclude a drug from a compliance aid is therefore left up to the enquirer.

HOW TO USE THIS GUIDE

In response to demand from our pharmacy dispensaries, Medicines Information at Pinderfields General Hospital have over the years, accumulated information on a vast number of drugs and their stability in compliance aids. There are many different types of compliance aids available on the market. We routinely use the "Medidos No 1 Daily Dose Reminder" and the "Medimax No 1 Daily Dose Reminder" and the information presented takes these devices into consideration.

The tabulated guide is self-explanatory. It is an alphabetical list of drugs sorted by generic name. Defined against each drug name are the Trade Name, Source of information (usually the manufacturer) and the Date on which the information was last reviewed.

Under the heading "Stability", information has been tabulated in two columns. The **first column** refers to information received from the manufacturer and the **second column** refers to local practice at Pinderfields General Hospital. It is important to note that our local practice is not based on "in-house stability" data and is merely included for awareness.

Either a tick ✓ or a cross ✗, followed by a row of numbers indicates each response. The numbers are indexed and represent a given statement.

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General Rules: Drugs excluded from MCAs:

- Dispersible formulations
- Non-tablet/capsule formulations i.e. suppositories, liquids, powders, wafer formulations etc
- Drugs which may cause skin reactions / hypersensitivity reactions on prolonged contact e.g. chlorpromazine.
- All drugs with cytotoxic potential.
- Drugs requiring special temperature control i.e. fridge, freezer.
- Blister packs or containers containing drying agents usually indicate the relative instability of the drug when exposed to moisture. Only dispense into a MCA if advised by the manufacturer.

It is also important to note that the information presented is regularly being updated and it is up to each individual to ensure that they have access to the most up to date information.

Hope you find the information useful.

Yours sincerely,

Rania Ishak
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Stability of items in Compliance Aids -

*in particular Medidos No 1 Daily Dose Reminder / Medimax No 1 Daily Dose Reminder-
supplied by Dudley Hunt*

Drug	Source of Information	Date	Brand	Stability	
				Manufacturer recommendation	Current Practice at Pinderfields General Hospital

A

Acetazolamide tablets	Wyeth	10/01	Diamox	✗ ₁	
Acetazolamide SR capsules	Wyeth	10/01	Diamox SR	✓ _{4,5}	
Aciclovir	GSK	10/97	Zovirax	✓ _{4,5,7}	
Aciclovir (dispersible)	GSK	12/01	Zovirax	✗ ₁	
Allopurinol 100mg	GSK	12/01	Zyloric		✓ ₄
Alfuzosin	SS	05/02	Xatral	✓ _{4,8}	
Alfuzosin XL	SS	05/02	Xatral XL	✓ _{4,8}	
Alendronate	MSD	10/01	Fosamax	✓ _{3,10}	
Amiodarone	SS	04/01	Cordarone X	✓ _{4,5,7,8}	
Amitriptyline	APS	08/03	Generic	✗ ₂	
Amisulpride	SS	10/01	Solian	✗ ₂	✗ ₂
Amlodipine	Pfizer	10/01	Istin	✗ ₁	✗ ₁
Anastrozole	AstraZeneca	10/01	Arimidex	✗ ₂	
Arthrotec 50	Searle	04/99	Arthrotec 50	✗ ₁	✗ ₁
Aspirin e/c	Eli Lilly	12/01	Nu-Seal	✗ ₂	✗ ₂
	Sinclair Pharm	12/01	Caprin e/c	✓ _{4,5}	
Atenolol	AstraZeneca	10/01	Tenormin	✗ ₁	✓ ₇
Atorvastatin	Pfizer	10/01	Lipitor	✗ ₂	
Azathioprine	GSK	07/04	Imuran	✓ _{4,7,9}	

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B

Baclofen	APS	05/01	Generic		✗ ₂
Bendrofluazide	APS	08/03	Generic	✗ ₂	
Benperidol tablets	Concord	10/01	Anquil	✓ _{4,5,7}	
Betahistine	Solvay	10/01	Serc	✓ _{3,8}	
Bisoprolol	Merck	02/01	Cardicor	✓ ₄	

C

Calcium Carbonate D3	Shire	10/01	Calcichew D ₃	✓ _{3,5,8}	
	Strakan	05/03	Adcal / Adcal D ₃	✗ ₂	
Carbamazepine Normal Release	Cephalon	02/06	Tegretol	✗ ₂	
Carbamazepine MR	Novartis	12/01	Tegretol Retard	✗ ₂	
Cefaclor capsules	Eli Lilly	12/01	Distaclor	✓ _{3,5,7,10}	
Cefaclor m/r tablets	Eli Lilly	12/01	Distaclor m/r	✗ ₁	
Cefradine caps	BMS	11/01	Velosef	✗ ₂	✓ ₄
Celiprolol	Pantheon Healthcare Ltd	06/02	Celectol	✓ ₄	
Celecoxib	Pfizer	10/01	Celebrex	✗ ₂	
Chloral Betaine tabs	Smith & Nephew	08/00	Welldorm		✗ ₂
Chlorambucil	GSK	09/02	Leukeran	✗ ₁	
Chlorpromazine	Hawgreen	10/01	Largactil	✗ ₁	✗ ₂
Citalopram	Lundbeck	08/99	Cipramil	✓ _{3,9}	
Clarithromycin	Abbott	12/01	Klaricid	✗ ₂	
Clarithromycin XL	Abbott	12/01	Klaricid XL	✗ ₂	
Clonazepam	Roche	01/00	Rivotril		✓ _{4,9}
Clopidogrel	SS	07/01	Plavix	✓ ₄	
Clozapine	Novartis	12/01	Clozaril	✗ ₂	✓ ₆
Co-amilofruse 5/40	Cox	03/02	Generic	✗ ₂	

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Co-amilozide 5/50	APS	07/01	Generic	✓ ₄	
Co-Beneldopa (disp tabs)	Roche	06/06	Madopar	✓ _{3,7,9}	
Co-Beneldopa capsules	Roche	06/06	Madopar	✗ ₁	
Co-careldopa	Dupont	03/00	All Sinemets		✓ ₇
Co-danthrusate Caps	Evans Medical	08/00	Normax		✗ ₂
Codeine Phosphate	CP Pharm	01/02	Generic	✗ ₂	
Combivir (Lamivudine/Zidovudine)	GSK	03/02	Combivir	✓ ₃	
Co-Rifater	Aventis	11/01	Rifater	✓ _{1,5,7,10}	
Co-trimoxazole	GSK	03/02	Septrin	✓ _{3,7,8}	
Cyclizine	CeNeS	01/01	Valoid	✓ ₄	
Cyclosporin	Novartis	12/01	Neoral	✗ ₂	✗ ₂

D

Dantrolene	P&G	10/01	Dantrium	✓ _{4,5}	
Desloratidine	Schering Plough	10/01	Neo-Clarityn	✗ ₂	
Diclofenac dispersible tabs	Novartis	12/01	Voltarol	✗ ₂	✗ ₂
Diclofenac EC	Novartis	12/01	Voltarol	✗ ₂	✓ ₅
Diclofenac SR	Novartis	10/01	Voltarol Retard	✗ ₂	✓ ₅
Didanosine capsules	BMS	10/03	Videx	✓ ₄	
Didanosine chewable tablets	BMS	10/03	Videx	✗ ₁	
Digoxin	GSK	07/01	Lanoxin	✓ _{3,10}	
Diltiazem SR	Napp Labs	01/02	Adizem SR	✗ ₂	✓ _{5,6,7,8}
Diltiazem XL	Napp Labs	01/02	Adizem XL	✗ ₂	✓ _{5,6,7,8}
Dipyridamole S/R	Boehr. Ingelheim	02/01	Persantin Retard	✓ _{3,5,10}	
Docusate Sodium	Schwarz	10/01	Dioctyl	✓ ₃	
Donepezil tablets	Pfizer	10/01	Aricept	✓ _{4,5,9}	
Dothiepin Capsules	Abbott	10/01	Prothiaden	✗ ₂	✓ ₁₁
Doxazosin	Pfizer	01/02	Cardura	✗ ₂	

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Doxazosin XL	Pfizer	01/02	Cardura XL	✗ ₁	
Doxycycline	Pfizer / APS	12/02	Vibramycin	✗ ₂	

E

Efavirenz	BMS	03/02	Sustiva	✓ _{4,5,7,8}	
Enalapril	MSD	10/99	Innovace		✗ ₂

F

Felodipine	AstraZeneca	12/02	Plendil	✗ ₂	
Flucloxacillin	GSK	10/01	Floxapen	✓ _{4,8}	
Fluconazole	Pfizer	10/01	Diflucan	✓ _{4,8}	
Fludrocortisone	BMS	10/00	Florinef	✓ _{4,8}	
Fluvastatin	Novartis	12/03	Lescol	✓ ₄	
Fluoxetine	Eli Lilly	12/01	Prozac	✓ _{4,5,7,10}	
Frusemide	CP	12/01	Generic	✗ ₂	✓ _{6,14}

G

Gabapentin	Pfizer	10/01	Neurontin	✗ ₂	✓ _{6,14}
Gliclazide	Servier	12/99	Diamicon	✓ _{4,5,7,10}	✓ _{7,8}
Glipizide	Pfizer	10/01	Glibenese	✓ ₄	

H

Haloperidol tablets	Janssen-Cilag	11/01	Haldol	✗ ₂	✓ ₄
Hydroxyzine	Pfizer	10/01	Atarax	✓ _{4,5,7,8}	
Hyoscine Hydrobromide	Roche Consumer Health	08/02	Kwells	✓ ₄	

I

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Indomethacin	MSD	10/02	Indocid	✓ _{4,6}	
Isosorbide mononitrate	Norton	04/01	Generic	✓ _{4,5,7}	
	Cox	04/01	Generic	✓ _{4,5,6,7}	
Isosorbide mononitrate LA	Schwarz	01/02	Elantan LA	✓ _{4,5,7,8}	
Isosorbide mononitrate SR 60mg	AstraZeneca	10/98	Imdur	✓ _{3,10}	

L

Lamivudine	GSK	12/01	Epivir	✗ ₂	✓ _{4,7}
Lamivudine	GSK	12/01	Zeffix	✗ ₂	
Lamotrigine	GSK	12/01	Lamictal	✗ ₂	✗ ₂
Lansoprazole	Wyeth	10/01	Zoton	✓ _{3,5,10}	
	Teva	06/06	Generic	✗ ₂	
Lisinopril	AstraZeneca	12/01	Zestril	✗ ₂	✓ _{4,6}
Lithium Carbonate m/r	SS	10/01	Priadel	✓ ₄	
Loperamide	Jansen-Cilag	12/01	Imodium	✗ ₂	
Losartan	MSD	10/01	Cozaar	✗ ₂	✗ ₂
Loxapine	Wyeth	10/01	Loxapac	✗ ₂	✓ _{4,8}

M

Meloxicam	Boehr. Ingelheim	08/00	Mobic		✓ _{4,8}
Mesalazine	P&G Pharm	06/02	Asacol	✓ _{5,7,8}	
Metformin	Merck	07/01	Glucophage	✓ _{4,8,13}	
Methotrimeprazine	Link	10/03	Nozinan	✓ ₄	
Methylprednisolone	P&U	10/01	Medrone	✗ ₂	✓ _{4,11}
Metolazone	Borg	11/01	Metenix 5	✗ ₂	✓ _{4,7}
Minocycline MR caps	Wyeth	10/01	Minocin MR	✓ _{4,8,5}	
mirtazapine	Organon	05/02	Zispin	✓ _{4,8}	

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		08/06	Zispin SolTab	✗ ₁	
Morphine Sulphate m/r (MST)	Napp	08/00	MST	✗ ₂	
Moxonidine	Solvay	07/03	Physiotens	✓ ₄	

N

Naftidrofuryl	Merck	03/02	Praxilene	✓ _{4,5,7}	
Nefazodone	BMS	11/01	Dutonin	✗ ₂	✓ _{4,8}
Nevirapine	Boehringer	02/01	Viramine	✓ _{4,8}	
Nicorandil	Aventis	11/01	Ikorel	✓ ₄	
Nifedipine	Bayer	11/01	All Adalat preps	✗ ₁	✗ ₁
Nizatidine	Eli Lilly	12/01	Axid	✓ _{4,5,7,10}	

O

Olanzapine tablets	Eli Lilly	12/01	Zyprexa	✓ _{3,10}	
Olanzapine orodispersible	Eli Lilly	12/01	Zyprexa Velo	✗ ₁	✗ ₁
Omeprazole capsule	AstraZeneca		Losec	✗ ₁	
Omeprazole MUPS	AstraZeneca	11/99	Losec MUPS	✓ ₃	
Oxybutynin	SS	10/01	Ditropan	✗ ₁	✗ ₁
Oxybutynin XL	SS	10/01	Ditropan XL	✗ ₁	

P

Pancreatin	Solvay	10/01	Creon	✓ _{3,8}	
Paroxetine tablets	GSK	10/01	Seroxat	✗ ₂	✓ _{4,8}
Penicillamine	Eli Lilly	12/01	Distamine	✗ ₂	
Pergolide	Eli Lilly	12/01	Celance	✗ ₁	✗ ₁
Perindopril	Servier	03/02	Coversyl	✓ _{4,8}	
Phenytoin	Pfizer	10/01	Epanutin	✗ ₂	4,8
Piroxicam	Pfizer	10/01	Feldene Melt	✗ ₁	
Potassium Chloride m/r	Alliance	07/01	Slow K		✓ _{4,5,6}

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Pravastatin	BMS	03/01	Lipostat	✓ _{4,8}	
Prednisolone EC	Wockhardt	07/04	Generic	✗ ₂	
Prochlorperazine	Castlemead Generic	12/02	Stemetil	✗ ₂	
Pyridostigmine	ICN	12/99	Mestinon	✓ _{4,10}	

Q

Quetiapine	Astra Zeneca	10/01	Seroquel	✓ _{4,8}	
Quinine Sulphate	Cox	05/01	Generic	✓ _{4,8}	

R

Rabeprazole	Janssen-Cilag	10/01	Pariet	✗ ₂	✗ ₂
Raloxifene	Eli Lilly	12/01	Evista	✗ ₂	
Ramipril	Aventis	07/01	Tritace	✗ ₂	
	Teva	06/06	Generic	✗ ₂	
Ranitidine tabs	GSK	10/01	Zantac	✗ ₂	✗ ₂
Risedronate	P&G	04/01	Actonel	✗ ₂	✓ _{4,6}
Risperidone	Janssen-Cilag	10/01	Risperdal	✓ ₄	
Rivastigmine	Novartis	08/02	Exelon	✓ ₄	
Rofecoxib	MSD	07/01	Vioxx	✗ ₁	
Ropinirole	GSK	10/01	Requip	✓ _{4,5,7,10}	

S

Salbutamol SR	GSK	12/01	Volmax	✗ ₁	✗ ₁
Saquinovir	Roche	10/01	Invirase	✗ ₂	✓ _{4,7}
Sennosides tabs	Reckitt & Coleman	10/01	Senokot	✗ ₂	
Sertindole	Lundbeck	10/01	Serdolect	✗ ₁	✗ ₁
Sertraline	Pfizer	02/06	Lustral		✓ _{4,8}

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Simvastatin	MSD	12/01	Zocor	✗ ₂	✗ ₂
Spirolactone 25mg	Norton	12/01	Generic	✗ ₂	✓ _{4,7}
Stilboestrol	APS	10/03	Generic	✗ ₂	

T

Tamoxifen	APS	02/02	Generic	✗ ₂	
Tamsulosin m/r	Yamanouchi	11/01	Flomax m/r	✗ ₂	
Tenofovir	Gilead	08/05	Viread	✗ ₁	
Terbinafine	Novartis	10/01	Lamisil	✗ ₂	✓ _{4,7}
Tetrabenazine	Cambridge	03/02	Xenazine	✗ ₂	
Theophylline SR	3M Health Care	12/01	Nuelin	✗ ₂	✗ ₂
Theophylline SR capsule	Merck	10/01	Slo-Phyllin	✓ _{4,5,8}	
Thioridazine	Novartis	10/01	Melleril	✗ ₂	
Thyroxine 100microg	Cox	11/01		✗ ₁	✓ _{4,8}
Tizanidine 2mg	Elan	12/01	Zanaflex	✓ ₄	✓ _{4,9}
Tramadol	P&U	10/01	Zydol	✗ ₂	✓ _{4,8}
Tranexamic acid	P&U	10/01	Cyklokapron	✗ ₂	
Trazodone	Aventis	11/01	Molipaxin	✓ _{3,5,10}	
Trifluoperazine	Goldshield	05/02	Stelazine	✗ ₁	
Trimipramine	Aventis	12/01	Surmontil	✓ _{3,5,7}	
Tropium	Galen Ltd	06/02	Regurin	✗ ₂	

V

Valproate Sodium	SS	03/01	Epilim	✗ ₁	✗ ₁
Valproic Acid	SS	06/02	Depakote	✗ ₂	
Valsartan	Novartis	12/01	Diovan	✓ _{4,5,7}	
Venlafaxine 37.5mg & 75mg	Wyeth	10/01	Efexor	✗ ₁	

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Venlafaxine S.R.	Wyeth	10/01	Efexor XL	✓ _{3,8}	
Verapamil m/r	Abbott	10/01	Securon SR	✗ ₂	✓ _{4,8}

W

Warfarin	Goldshield	02/02	Generic	✗ ₂	
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Z

Zidovudine	GSK	10/01	Retrovir	✗ ₁	
Zolpidem	SS	10/02	Stilnoct	✓ ₄	
Zopiclone	Aventis	11/01	Zimovane	✓ _{3,5,7,10}	

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Key to type and source of data on which the information is based

Category	Explanation
X	Stability Data.....
1	... <i>available</i> which indicates that the drug is not suitable for inclusion
2	... <i>not available</i> therefore can not recommend inclusion into a dosette box
✓	Stability Data.....
3	... <i>available</i> from manufacturer therefore ok to use
4	... <i>not available</i> from manufacturer but happy to use it anyway
5	Need moisture proof conditions
6	Need to monitor for changes in appearance
7	Need to protect from light
8	Use for up to 7 days in a dosette box
9	Use for up to 2 weeks in a dosette box
10	Use for up to 4 weeks in a dosette box
11	Same formulation used to be in bottles therefore do not foresee a problem
12	Pharmacy has done this for years therefore monitor for changes in appearance
13	This drug has a strong smell
14	Information received from other Medicines Information centres

Abbreviations of Pharmaceutical Companies

APS - Approved Prescription Services Ltd,

BMS - Bristol-Myers Squibb Pharmaceuticals Ltd

GSK - GlaxoSmithKline

MSD-Merck Sharp & Dohme Ltd

P&G Pharm - Proctor & Gamble Pharmaceuticals UK Ltd,

SS - Sanofi-Synthelabo

Disclaimer: This guide may be used as a reference source by **pharmacists** involved in the dispensing of drugs in compliance aids, on the understanding that the information provided is **based on that received from the manufacturers and not on in-house stability studies carried out by Pinderfields General Hospital**. This information should not be used by members of the public or patients as specialist knowledge is required for the interpretation of such information. This information is issued on the understanding that it is the best available from the resources at our disposal at the time of issue.

Prepared and updated by Medicines Information, Pharmacy Department, Pinderfields General Hospital, Wakefield. January 2006.

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