

How stable are medicines moved from original packs into compliance aids?

In this article, Claire Church and Jane Smith have compiled a table based on information received from manufacturers about the possible stability of their medicines after removal from their packaging and placement in compliance aids

The use of compliance aids has increased in both primary and secondary care over recent years. Compliance aids aim to act as a reminder for patients to take their medicines, enabling them to manage their own often complex and confusing drug regimens. They also act as a visual prompt for carers, indicating that patients have taken their medicines, or at least removed them from the device.

The use of these aids involves the transfer of medicines from the manufacturer's original packaging to the compliance aid. The original packaging is designed to protect the contents to appropriate pharmacopoeial and quality standards for a variety of criteria, eg, water vapour transmission, as required in the product licence. However, the compliance aid cannot guarantee the same level of protection.

Many systems are not disposable and are frequently reused without cleaning. The hazards associated with physical, chemical and microbiological cross-contamination could be a major risk factor. All other dispensing containers are designed for single use.

Compliance aids have limited available space for each dose, are not airtight and offer less moisture and light protection than original packs. Doubts are raised as to the stability of medicines that have been transferred to compliance aids: is there a deterioration in quality and can this result in a reduction of efficacy to an unacceptable level?

Despite the increased dispensing of medicines in this way, guidance on their stability in these systems is limited and little new information has been published in recent years. Certain products are particularly unsuitable for transferring into compliance aids, but even this information is often not readily available.

The Royal Pharmaceutical Society, in its "Medicines, ethics and practice" guide (section 3.4.7) says that "medicines should not be left in sealed monitored dosage systems for

longer than eight weeks" and that "certain medications should not be placed in monitored dosage systems. These include effervescent tablets, dispersible tablets, buccal tablets, sublingual tablets, significantly hygroscopic preparations and solid dose cytotoxic preparations."

A general article by Roger Walker in *The Pharmaceutical Journal* in 1992² contained information on around 70 products from 53 pharmaceutical manufacturers. The leading article in the same journal discussed the lack of data and concluded: "Manufacturers and regulatory authorities urgently need to catch up with current practice."³ In response to these articles a series of letters appeared a few weeks later.⁴

A medicines and prescribing bulletin for health care professionals in East Lancashire published data on approximately 30 products in November 2000.⁵

The medicines information department at Pinderfields General Hospital has collated data that are largely derived from pharmaceutical manufacturers and not in-house stability data. This was last updated in January 2004 and contains information on 176 products. This currently unpublished document is available to other medicines information departments and may be available in the future on the UK Medicines Information website: www.ukmi.nhs.uk.

In an attempt to provide clearer updated guidance on potential stability problems, we approached pharmaceutical manufacturers for their opinion on the stability of their products in compliance aids.

Data collection

Fifty medical information departments of pharmaceutical companies in the UK were contacted by telephone during November and December 2002 and asked whether their solid oral dosage forms could be transferred to a compliance aid. No specific brand of aid was specified.

Information in writing was received from all the pharmaceutical companies contacted and these data covered 243 products. A further exercise to confirm data was carried out in September 2004 and we now have information on 392 products (see Table).

All but one company agreed to their data to be used in this article provided the following disclaimer is included and strongly emphasised: "It is important to note that the individual manufacturers do not endorse this practice of transferring medicines from the

original packs to compliance aids as it may be outside the terms of their product licence. For the majority of manufacturers any information they provide is based on anecdotal evidence or in-house studies as no formal studies would have been carried out."

Wyeth Laboratories requested its own disclaimer to be used as well, since it believed this would be a more accurate reflection of its products and is as follows: "The product information provided in this article has been provided by the marketing authorisation holders for these products. The marketing authorisation holders only recommend that their products are stored in accordance with the summary of product characteristics for each product and that storage of products in any other way is entirely at the pharmacist's own risk." These products are highlighted in the Table by an asterisk (*) in the additional information column.

Data presentation

The Table now contains a list of 392 products in alphabetical order by generic name. Defined against each name is the brand name (if applicable), company, stability code and any other additional information relating to stability. The stability data have been classified into six groups according to the data received. Each group was allocated a code for ease of numbering in the Table linked to the extent of suitability for use in a compliance aid. Stability codes were allocated as follows:

1. Do not put into a compliance aid.
2. No stability data available, therefore company does not recommend putting in a compliance aid. (Refer to SPC for additional stability information.)
3. No stability data available, therefore company does not recommend putting in a compliance aid. Reason for concern is stated, eg, light-sensitive. Individual pharmacists must accept responsibility for putting in a compliance aid. Risks can be minimised by additional safeguards, eg, use of a black bag.
4. No stability data available, but it is probably suitable to put in a compliance aid.
5. Stability data available in an alternative container, but not necessarily in a compliance aid.
6. Stability data available which state that it is suitable to put in a compliance aid.

The additional information that relates to stability is based on that received from the

Claire Church, BPharm, MRPharmS, is community liaison pharmacist at Southmead Hospital, Bristol.

Jane Smith, MSc, MRPharmS, is acting principal pharmacist, service development, at North Bristol NHS Trust (formerly senior pharmacist, patient services at Southmead Hospital).

Correspondence to: Mrs Church (e-mail claire.church@nbt.nhs.uk).

manufacturers and is the best available from the resources at the time of compilation.

The Table does not represent an exhaustive list and many companies were keen to remind professionals that the most suitable and current source of information regarding the stability of a medicinal product can be obtained direct from the medicine information department of the respective pharmaceutical companies.

SPCs may be a reference source for determining the stability of a product within the original packaging. These can be accessed online on the Electronic Medicines Compendium website at www.medicines.org.uk.

Omission of a medicine from the Table does not mean that the medicine is suitable for putting in a compliance aid.

Discussion

Out of 392 products investigated, none had had stability tests carried out on them within a compliance aid. The Medicines and Healthcare products Regulatory Agency (MHRA), which issues product licences, requires companies to provide evidence of stability of the medicine in its original pack until its stated expiry date, if stored as recommended. The licence only covers storage in the original packaging and transfer to any other container cannot be advocated without extensive stability testing being carried out.

Most companies will not recommend transferring medicines from original packs to compliance aids due to the absence of stability studies. They cannot guarantee the bioavailability, efficacy or palatability of any formulation that is stored outside its original container. Many companies indicated that they do not have any stability data to support the storage in compliance aids, and therefore cannot recommend the practice. Some stated that storage in such devices would be an unlicensed use of their product and as such would remain the responsibility of the pharmacist or physician.

Most companies were sympathetic to pharmacists' position and appreciate the fact that the use of compliance aids is becoming increasingly popular or indeed necessary and that it is obviously impractical to prevent the use of them. Some companies replied with more useful comments that included: "We do not have any relevant stability studies, but these tablets are generally stable and we are not aware of any specific reason why they should not be stored in a compliance aid for x number of days."

Even more useful replies were from the companies that provided information on the chemical and physical properties of their drug, eg, hygroscopicity, light sensitivity. This at least enables a pharmacist to make a judgement on whether to include or exclude a drug from a compliance aid in the absence of hard evidence.

Several companies offered a solution to avoid removal from their packaging by suggesting cutting around the blister and putting the dosage form (still in the blister) into the

General exclusions

Using the information obtained, more general guidelines for the transfer of solid oral dosage forms from original packs to compliance aids have been written. They assume that all compliance aids will be stored at ambient temperature, in a dry environment and away from direct sunlight.

However, we would suggest some general exclusions, based on the published and unpublished data reviewed:

- Medicinal products which are likely to be susceptible to the effects of moisture, including
 - Effervescent, dispersible, and soluble products, which are unsuitable for packing in compliance aids owing to their hygroscopic nature. Ingress of moisture into the compliance aid may impair dispersal or dissolution properties of the product, or chemical drug degradation of the product may occur.
 - Buccal and mucosal products, which may be unsuitable since they are formulated to dissolve and so are sensitive to moisture.
 - Significantly hygroscopic products, which are generally unstable, as either the formulation or the active component is sensitive to moisture.
- Medicinal products that are susceptible to the effects of prolonged exposure to light
- Medicinal products that are required to be kept refrigerated
- Medicinal products the handling of which is likely to be harmful to individuals

compliance aid. However, this practice is avoided in our dispensary since the publication of a warning in *The Pharmaceutical Journal* which concerned two incidents, one fatal, when the patients concerned swallowed a whole blister resulting in intestinal perforation.⁶ It is also more difficult to remove the dose from a small area of packaging.

It was interesting that different companies sometimes offered conflicting advice for the same product, eg, omeprazole. This may be due to different production processes, different stability testing or one manufacturer being more cautious than another.

The survey carried out suggests that most solid oral dosage forms can be safely transferred to a compliance aid for a short period. There are, however, both general and specific exceptions to this and it is important that pharmacists, patients and carers are aware of these (see Panel above).

As the practice of using compliance aids continues to grow, with an ageing population and greater care in patient's homes, there is a necessity for short-term stability data for all medicines.

We would encourage manufacturers, when applying for a new product licence, to provide data on the stability of the product when redispensed into a compliance aid. This would be particularly useful for products that

are unstable. This information could be made available in the SPC. It is essential that action is taken now to fill this information gap and so benefit patients and practice in the future.

Conclusion

This survey has revealed that although some information can be obtained from the pharmaceutical companies there is still a shortage of short-term stability data for the transfer of medication to compliance aids. Since the publication of the leading article in *The Pharmaceutical Journal* in 1992³ little appears to have changed in the availability of this stability information. It is impracticable to prevent the use of compliance aids until such data becomes available. It is hoped that this collection of data in a compact format will provide some assistance in the interim.

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References

1. Royal Pharmaceutical Society of Great Britain. Medicines, ethics and practice: a guide for pharmacists (number 27). London: The Society; 2003.
2. Walker R. Stability of medicinal products in compliance devices. *Pharmaceutical Journal* 1992;248:124-6.
3. Dealing with dosage aids (leading article). *Pharmaceutical Journal* 1992;248:99.
4. Stability of medicines dispensed in compliance devices (letters). *Pharmaceutical Journal* 1992;248:174-5.
5. Stability of medicines in compliance aids and monitored dose systems. *Interface* 2000; no 45.
6. Blister-strip warning. *Pharmaceutical Journal* 1996;256:85.

Future research

- We have initiated joint research with our regional quality assurance officer to carry out in-house stability testing of specific drugs in compliance aids that we routinely use. At the time of writing, the stability of dispersible and enteric coated aspirin has been investigated. This was carried out in various compliance aids at normal (35-50%) and high (up to 85%) humidity. We hope to extend this to other products and publish the data.
- We have liaised with the other two Bristol hospitals and the local primary care trusts with the aim of developing a common policy. This will reduce the problems that arise when patients using compliance aids are transferred between primary and secondary care.
- We plan to work with medicines information pharmacists to ensure that the resources we and Pinderfields have developed are presented in a suitable format for web presentation.

The stability of drugs in compliance aids, based on information provided by manufacturers (acarbose to co-careldopa)

Generic name	Brand name	Company	Code	Additional information	Generic name	Brand name	Company	Code	Additional information
Acarbose	Glucobay	Bayer	4	Should be stable for 7 days	Buspirone	Buspar	BMS	2	
Acetazolamide	Diamox / SR	Goldshield	2		Cabergoline	Cabaser	Pfizer	4	Probably stable for 7 days
Aciclovir	Zovirax	GSK	2		Cabergoline	Dostimex	Pfizer	1	Should be stored with desiccant
Aciclovir dispersible	-	Pfizer	2		Calcium carbonate	Cacit	P&G	1	Effervescent tablet is moisture sensitive
Aciclovir dispersible	Zovirax dispersible	GSK	1	Dispersible tablet	Calcium carbonate	Didromel PMO	P&G	1	Cacit is moisture sensitive
Alendronate 5mg	Fosamax	MSD	5	Stable for 3 months at 40C and 75% relative humidity	Canesartan	Amlas	AstraZeneca	2	
Alendronate 10mg/70mg	Fosamax	MSD	2		Captopril	Acepril	BMS	2	
Alfacalcidol	One Alpha	Leo	1	Moisture sensitive; can become sticky out of original packaging and congeal with other tablets in the compliance aid	Captopril	Capoten	BMS	2	
Alfacalcidol	One Alpha	Leo	1		Captopril/ hydrochlorothiazide	Acezide	BMS	2	
Alifuzosin	Xatral / XL	SS	2		Capozide	Capozide	BMS	2	
Allopurinol	Zyloric	GSK	2		Carbamazepine	Tegretol / Retard	Cephalon UK	1	Susceptible to moisture
Amlodipine/ hydrochlorothiazide	Moduretic	BMS	2		Carbenoxolone sodium	Pyrogastrone	SS	2	
Amiodarone	Cordarone	SS	2		Carvedilol	EuCARDIC	Roche	3	Protect from light
Amisulpride	Solian	Alpha	2		Cefaclor	Distiaclor	Lilly	4	Probably stable for up to 4 weeks
Amitriptyline	Istin	Pfizer	1	Hygroscopic	Cefactor MR	Distiaclor MR	Lilly	1	Sensitive to moisture
Amphotericin	Fungilin	BMS	2	Disintegrates in the presence of small amounts of water	Cefadroxil	Baxan	BMS	2	
Anastrozole	Arimidex	AstraZeneca	4		Cefprozil	Cefzil	BMS	2	
Apomorphine	Uprima	Abbott	2	Probably ok for short term storage in a compliance aid	Cefradine	Velosef	BMS	1	Powder is hygroscopic
Aripiprazole	Abilify	BMS	1	Hygroscopic	Celecoxib	Celebrex	Pfizer	2	
Aspirin	Angettes	BMS	1	Hygroscopic	Chloridazepoxide	Librium	Valeant	2	
Aspirin	-	Alpha	1	Hygroscopic	Chloroquine phosphate/ proguanil HCl	Avloclor/Paludrine	AstraZeneca	2	
Aspirin EC	Nu-Seals	Lilly	2	Not suitable as sensitive to atmospheric moisture	Chlorpromazine	Largactil	Havgreen	3	Can cause contact dermatitis when handled (wear gloves); must be protected from light
Atenolol	Caprin	Pinewood	1	Probably not suitable as sensitive to moisture	Ciclosporin	Neoral	Novartis	1	Ethanol vaporises out of the capsule when out of the original packaging
Atenolol	Teromin	AstraZeneca	2	Potential to be hygroscopic	Cinnarizine	Stugeron/Forte	Janssen-Cilag	2	Not known to be hygroscopic
Atenolol	-	CP	2		Ciprofibrate	Modalim	SS	2	
Atenolol/chlortalidone	Teroretic/Tenoret 50	AstraZeneca	2		Ciprofloxacin	Ciproxin	Bayer	1	May absorb a small amount of water over time; light sensitive over time
Atenolol/co-amiloride	Kalten	AstraZeneca	2		Citalopram	Cipramil	Lundbeck	4	Probably stable for 6 months
Atenolol/nifedipine	Tenif	AstraZeneca	2		Clarithromycin	Klaricid	Abbott	3	Protect from light
Atazanavir sulphate	Reyataz	BMS	2		Clarithromycin XL	Klaricid	Abbott	2	
Atorvastatin	Lipitor	Pfizer	3	Disintegrates in bright sunshine	Clobazam	Frisium	Sanofi Aventis	4	Probably stable for 4 weeks
Auranofin	Ridaura	Yamanouchi	1		Clomethiazole	Heminevrin	AstraZeneca	1	Should only be dispensed in glass bottles
Baclofen	Lioresal	Cephalon UK	1	Protect from moisture	Clomipramine	Anafranil	Cephalon UK	2	Protect from moisture
Baclofen	-	APS	2		Clonazepam	Rivotril	Roche	3	Store in dark
Bambuterol HCl	Bambec	AstraZeneca	2		Clopidogrel	Plavix	SS	2	
Benperidol	Benquili	Hansam	2		Cloral Betaine	Wellnorm	Alphashow	4	
Beta-cardone	Sotalol	Celltech	2		Clozapine	Clozaril	Novartis	2	
Bethahistine	Serc	Solvay	2		Co-amiloride 5/40	-	Generics (UK)	4	Probably stable for 7 days
Betamethasone	Bethnel	Celltech	2		Co-amiloride	Lasoride	Borg	3	Protect from light
Betamethasone	Bethesol	Celltech	2		Co-amiloride	-	CP	2	
Bexarotene	Targretin	Zeneus Pharma	4		Co-amiloride	-	APS	2	
Bicalutamide	Casodex	AstraZeneca	2		Co-amiloride	-	CP	2	
Bisoprolol	Cardicor	Merck	2		Co-beneldopa	Madopar	Roche	4	Probably stable for 14 days
Bisoprolol	-	APS	2		Co-beneldopa dispersible	Madopar dispersible	Roche	5	Stable for at least 14 days
Bisoprolol	-	IVAX	4	Probably stable for 7 days	Co-careldopa	Sinemet	BMS	1	Powder is hygroscopic
Bumetanide	Burinex	Leo	4						
Buprenorphine HCl	Temgesic	RB	2						
Buprenorphine HCl	Subutex	RB	2						

The stability of drugs in compliance aids, based on information provided by manufacturers (co-careldopa to hydroxyzine)

Generic name	Brand name	Company	Code	Additional information	Generic name	Brand name	Company	Code	Additional information
Co-careldopa	Sinemet CR	BMS	1	Powder is hygroscopic	Ergometrine	-	Celltech	2	
Co-careldopa	Sinemet 110/250	BMS	1	Blue dye can fade on light exposure; also moisture will cause levodopa to turn black on prolonged exposure	Erythromycin	Erymax	Zeneus Pharma	4	
Co-danthrusate	Normax	Celltech	2		Erythromycin BP	Erythromid	Abbott	3	Protect from light
Co-trimoxazole	Seprin	GSK	2		Erythromycin	Erythroped A	Abbott	2	
Codine phosphate	-	CP	2		Ethylsuccinate	-	Abbott	2	
Colchicine	-	Celltech	2		Erythromycin stearate	Erythocin	Abbott	2	
Cyclizine	Valoid	Amdipharm	3	Light sensitive	Escitalopram	Cipraxel	Lundbeck	4	Probably stable for 6 months
Danazol	Danoi	SS	2		Esomeprazole	Nexium	Astrazeneca	5	Stable for 6 months at 25°C and relative humidity of 60%
Dantrolene sodium	Dantrium	P&G	2		Etidronate disodium	Didronel	P&G	2	
Demeclocycline	Ledermycin	Goldshield	2		Ethamsylate	-	SS	2	
Desloratadine	Neoclaritin	Schering Plough	4	Unlikely to be hygroscopic	Ethinylestradiol	-	Celltech	2	
Dexamethasone	-	Organon	4	Unlikely to be any issues	Etoposide	Vepesid	BMS	1	Cytotoxic
Dexamfetamine sulphate	Dexedrine	Celltech	2		Felodipine	Plendil	Astrazeneca	2	
Diazoxide	Eudemine	Celltech	2		Ferrous fumarate/folic acid	Pregaday	Celltech	2	
Diclofenac EC/SR/Retard	Voltarol	Novartis	2		Ferrous sulphate	-	Alpharma	4	Probably stable for maximum of 14 days (could taint other tablets)
Diclofenac and misoprostol	Arthrotec	Pfizer	1	Misoprostol is extremely moisture sensitive and may degrade	Ferrous sulphate	Ferrograd	Abbott	2	
Didanosine chewable	Videx	BMS	1	Hygroscopic	Ferrous sulphate/sodium ascorbate	Ferrograd C	Abbott	2	
Didanosine EC	Videx EC	BMS	2		Ferrous sulphate/folic acid	Ferrograd folic	Abbott	2	
Didronel PMO	-	P&G	1	See Calcium carbonate and etidronate	Finasteride	Proscar	MSD	1	Women should not handle crushed or broken tablets when they are or potentially may be pregnant (if the dispenser and/or carer is male or not pregnant the stability code can be changed to 2)
Digitoxin	-	Celltech	2		Fluocloxacillin	Floxapen	GSK	2	
Digoxin	Lanoxin	GSK	4	Probably stable for 14 days	Fluconazole	Diflucan	Pfizer	4	
Diltiazem hydrochloride	Dilzem	Zeneus Pharma	4		Fludrocortisone	Florinef	BMS	2	
Diltiazem	Slozem	Merck	2		Fluphenazine HCl	Moditen	SS	2	
Diltiazem SR/XL	Adzem SR/XL	Napp	2	Probably stable for 4 weeks	Fluphenazine/nortriptyline	Motival	SS	2	
Diltiazem	Angiill SR/XL	Trinity	4		Fluoxetine	Prozac	Lilly	4	Probably stable for up to 4 weeks
Diltiazem	Tildiem/LA/Retard	SS	2		Flupentixol	Depixol	Lundbeck	4	Probably stable for 4 weeks
Dipyridamole MR	Persantin Retard	BI	5	Moisture sensitive; stable for 30 days out of the original container, eg. plastic dispensing bottle	Flunarolol	Flunarol	Lundbeck	4	Probably stable for 4 weeks
Dipyridamole MR/aspirin	Asasantin Retard	BI	5	Stable for 30 days out of the original container, eg. plastic dispensing bottle	Flurazepam	Dalmane	Valeant	2	
Dipyridamole	Persantin	BI	3	Protect from light	Flurbiprofen	Froben/SR	Abbott	2	
Disopyramide	Rythmodan	Borg	2		Flutamide	Drogenil	Schering Plough	2	
Docusate sodium	Diocyl	Schwartz	4		Fosinopril	Staril	BMS	2	Probably stable for 4 weeks
Domperidone	Motilium	SS	2		Furosemide	-	Alpharma	4	
Domperidone/paracetamol	Domperamol	Servier	4	Probably stable for 8 days	Furosemide/potassium	-	CP	2	
Donepezil	Aricept	Pfizer	4	Probably stable for 14 days	Gabapentin	Lasikal	Borg	3	Protect from light
Dosulepin tablets and capsules	-	Generics (UK)	4	Probably stable for 7 days	Gemfibrozil	Neurontin	Pfizer	2	
Dosulepin	Prothiaden	Abbott	2		Glacialide	Lipid	Pfizer	2	
Doxazosin	Cardura	Pfizer	2		Glipizide	Diamicron/MR	Servier	4	Probably stable for 8 days
Doxazosin	Cardura XL	Pfizer	1	Not recommended for inclusion in compliance aid; SPC states "must be stored in the original package"	Glutamine	Glibenese	Pfizer	2	
Doxepin	Sinequan	Pfizer	2		Glutamine	Glunenorm	SS	2	
Efavirenz	Sustiva	BMS	2		Haloperidol	-	IVAX	4	Probably stable for 7 days
Enalapril	Innovace	MSD	1	May hydrolyse at high temperature and in the presence of moisture; 10% loss of potency occurred when exposed to 40°C and 75% humidity for 13 weeks	Hydroxycarbamide	Hydrea	BMS	1	Cytotoxic
Ergocalciferol	-	Celltech	2		Hydroxychloroquine	Plaquenil	SS	2	
					Hydroxyzine	Atarax	Pfizer	4	Probably stable for 7 days

The stability of drugs in compliance aids, based on information provided by manufacturers (ibuprofen to paracetamol/codeine)

Generic name	Brand name	Company	Code	Additional information	Generic name	Brand name	Company	Code	Additional information
Ibuprofen	Brufen/Relard	Abbott	2		Mefenorex	Flagyl	Hawgreen	3	Must be protected from light
Indapamide	Natrilix/SR	Servier	4	Probably stable for 8 days	Minocycline	Minocin MR	Wyeth	4	Probably stable for 7 days*
Inositol nicotinate	Hexopal	SS	2		Minoxidil	Loniten	Pfizer	2	
Iribesartan	Apravel	BMS	2		Mirtazapine	Zispin	Organon	1	Hygroscopic; as an alternative, can write days of the week on lidding paper of each tablet pouch
Iribesartan /hydrochlorothiazide	CoApravel	BMS	2		orodispersible				Moisture sensitive and may degrade
Isoniazid	-	Celltech	2		Misoprostol	Cytotec	Pfizer	1	
Isonorbide mononitrate	-	Alpha	4	Probably stable for up to 14 days	Modafinil	Provigil	Cephalon UK	2	
Isonorbide mononitrate	-	IVAX	4	Probably stable for 7 days	Morphine sulphate	MST Continus	Napp	2	
Isonorbide mononitrate	Cedocard Relard	Pfizer	2		Moxifloxacin	Avelox	Bayer	4	Should be stable for 7 days
Isonorbide mononitrate	Elantam LA	Schwartz	2		Nadolol	Corgard	SS	2	
Isonorbide mononitrate	Imdur	Astrazeneca	5	Stable for one month	Nafidofuryl	Praxilene	Merck	2	
Isonorbide mononitrate	Monomax SR/XL	Trinity	4	Probably stable for 4 weeks	Nalidixic acid	Negram	SS	2	
Ketoprofen	Ketocid	Trinity	4	Probably stable for 4 weeks	Naloxone	Naloxe	BMS	2	
Ketoprofen	Orudis	Hawgreen	3	Must be protected from light	Naproxen and misoprostol	Neptratec	Pfizer	2	
Ketoprofen	Oruvail	Hawgreen	3	Must be protected from light	Nevirapine	Viramune	BI	4	
Labelolol hydrochloride	Trandate	Hawgreen	2		Nicardipine	Cardene	Yamanouchi	2	
Lamivudine	Epivir	Celltech	2		Nicardipine	Cardene SR	Yamanouchi	3	Protect from light.
Lamotrigine	Lamictal	GSK	2		Nicorandil	Ikorel	Sanofi Aventis	5	Stable for at least 7 days in a dry environment
Lansoprazole	Zoton	Wyeth	4	Probably stable for up to 4 weeks in a compliance aid which offers a barrier against moisture*	Nifedipine	Adalat Retard and capsules	Bayer	1	Very light sensitive
Lansoprazole orodispersible	Zoton Fastab	Wyeth	1	Highly moisture sensitive*	Nifedipine	Adalat LA	Bayer	1	Very light sensitive and will significantly degrade very quickly; moisture can affect release mechanism
Levothyroxine	-	APS	2		Nifedipine	Coracten SR/XL	Celltech	2	
Levothyroxine	-	Alpha	2		Nimodipine	Nimotop	Bayer	4	Should be stable for 7 days
Lisinopril	Zestril	Astrazeneca	2		Mogadon	Valeant	Valeant	2	
Lisinopril	Carace	BMS	2		Nizatidine	Axid	Lilly	4	Probably stable for up to 4 weeks
Lisinopril/ hydrochlorothiazide	Carace plus	BMS	2		Norethisterone	Uioflan	Pfizer	2	
Lisinopril/ hydrochlorothiazide	Zestoretic	Astrazeneca	2		Nystatin	Nystan	BMS	1	Powder is hygroscopic
Lithium	Priadel	SS	4	Probably stable for 7 days	Olanzapine	Zyprexa	Lilly	4	Probably stable for up to 4 weeks; sensitive to light; wear gloves if breaking or dividing the tablets due to potential contact dermatitis
Loperamide	Imodium	Janssen-Cilag	1	Moisture sensitive and could change colour	Olanzapine Velotabs	Zyprexa Velotabs	Lilly	1	Particularly fragile/brittle — may disintegrate due to moisture in the air
Lopinavir/ritonavir	Kaletra	Abbott	2		Olsalazine sodium tablets and capsules	Dipentum	Celltech	2	
Losartan	Cozaar	MSD	2		Omeprazole capsules	-	Generics (UK)	1	Hygroscopic
Medroxyprogesterone acetate	Farlural	Pfizer	2		Omeprazole capsules	Losec	Astrazeneca	5	Stable for 14 days at room temperature (25–30C) and relative humidity up to 75%
Medroxyprogesterone acetate	Provera	Pfizer	2		Omeprazole MUPS	Losec MUPS	Astrazeneca	5	Stable for 3 months at 25C and relative humidity of 60%
Megestrol	Megace	BMS	2		Orphenadrine	Disipal	Yamanouchi	2	
Mefenazine HCl	Ebixa	Lundbeck	2		Oxybutynin	Cystin	SS	2	
Mefenazine HCl	Mobic	BI	4		Oxybutynin	Diltropan	SS	2	
Mesalazine	Asacol	P&G	1	Tablet coating is moisture and light sensitive	Oxybutynin XL	Lyrinel XL	Janssen-Cilag	1	Hygroscopic; packaged in high density polyethylene bottles with a desiccant
Methionine	-	Celltech	2		Pancreatin	Creon	Solvay	2	
Mefenazine	Glucophage	Merck	2		Paracetamol	-	Alpha	4	Probably stable for up to 28 days
Methotrexate	Maxtrex	Pfizer	1	Cytotoxic	Paracetamol/codeine caplet/capsules	Solpador	SS	2	
Methoxyphenol HCl	Ritalin	Cephalon UK	2		Paracetamol/codeine effervescent tablets	-	SS	1	
Methoxyphenol HCl	Concerta XL	Janssen-Cilag	1	Packaged with a desiccant					
Methoxyphenol HCl	Equasym	Celltech	2						
Metolazone	Metenix 5	Borg	3	Protect from light					
Metoprolol tartrate	Betaloc SA	Astrazeneca	2						

The stability of drugs in compliance aids, based on information provided by manufacturers (paracetamol/metoclopramide to valsartan)

Generic name	Brand name	Company	Code	Additional information	Generic name	Brand name	Company	Code	Additional information
Paracetamol/ metoclopramide	Paramax	SS	2		Sibutramine	Reducil	Abbott	2	
Paroxetine	Seroxat	GSK	2		Simvastatin	Zocor	MSD	2	
Penicillamine	Distamine	Lilly	2		Sotalol	Beta-cardone	Celltech	2	
Pergolide	Celance	Lilly	1	Unstable — light sensitive and extremely hygroscopic (notably the 50µg strength) Probably stable for 8 days Probably stable for 8 days	Sotalol	Sotacor	BMS	2	
Perindopril	Coversyl	Servier	4		Spiromolactone	-	IVAX	3	Protect from light
Perindopril/indapamide	Coversyl Plus	Servier	4		Spiromolactone/ furosemide	-	Alpharma	2	
Phenylethanolamine	Epanutin/Infatab	Pfizer	2		Stavudine	Zerit	BMS	2	
Piroxicam	Feldene	Pfizer	2		Sulfasalazine	Salazopyrim/EVEEC	Pfizer	2	
Piroxicam dispersible	Feldene Melt	Pfizer	1		Sulpiride	Dolmatil	SS	2	
Potassium chloride	Slow K	Alliance	4	Moisture sensitive May absorb water; probably stable in an airtight compliance aid for 14 days	Sulpiride	Sulpiril	Pfizer	2	
Pravastatin	Lipostat	BMS	2		Tacrolimus	Prograf	Fujisawa	5	Stable for 3 months at 30C and 75% humidity Known to be light labile
Prazosin	Hypovase	Pfizer	2		Tamoxifen	Nolvadex	AstraZeneca	3	
Prednisolone	-	APS	2		Tamoxifen	-	APS	2	
Prednisolone EC	Deltacortril	Pfizer	2		Tamoxifen	-	Generics (UK)	3	Sensitive to light
Prochlorperazine maleate	Buccastem	Reckitt Benckiser	2		Tamsulosin	Flomax SR	Yamanouchi	2	
Propafenone	Arythmol	Abbott	2		tegatur with uracil	Uftoral	BMS	1	Cytotoxic
Propranolol HCl	Inderal/Half Inderal	AstraZeneca	2		Terazosin	Hytrin	Abbott	2	
Propylthiouracil	-	Celltech	1		Terbinafine	Lamisil	Novartis	2	
Pyridostigmine	Mestinon	Valeant	2	Store in a brown bottle with a desiccant Probably stable for up to 7 days	Terbutaline sulphate	Bricanyl	AstraZeneca	2	
Quetiapine	Seroquel	AstraZeneca	4		Testosterone	Restandol	Organon	1	Very sensitive to moisture and becomes "sticky" if removed from packaging
Quinapril	Accupro	Pfizer	2		Tetrabenazine	Xenazine 25	Cambridge	2	
Quinine bisulphate	Kinidin	AstraZeneca	2		Theophylline	Slo-Phyllin	Merck	2	
Quinine sulphate	-	Alpharma	4	Probably stable for up to 7 days	Theophylline	Uniphyllin	Napp	2	
Rabeprozole	Pariet	Janssen-Cilag	1		Theophylline	Nuelin SA	3M	2	
Raloxifene	Evista	Lilly	2	Hygroscopic	Theophylline/ephedrine	Franol/Plus	SS	2	
Ramipril tablets and capsules	Tritace	Sanoofi Aventis	2		Thioridazine	Melleril	Novartis	2	
Ranitidine	-	Generics (UK)	1	Hygroscopic and may turn brown	Thiamine	Benerva	Roche	4	
Ranitidine	Zantac	GSK	1	Hygroscopic and degrades in the presence of water	Thiagabine	Gabitril	Cephalon UK	2	
Reboxetine	Edronax	Pfizer	2		Tiudronic acid	Skelid	SS	2	
Ribavirin	Rebetol	Schering Plough	2		Timolol maleate	Betim	Valeant	2	
Risedronate sodium	Actonel	P&G	2		Timolol maleate/ bendroflumethiazide	Prestim	Valeant	2	
Risperidone	Risperdal	Janssen-Cilag	2	Not known to be hygroscopic or need a drying agent during storage	Tizanidine HCl	Zanaflex	Zeneus Pharma	4	
Ritonavir	Novir	Abbott	2	Refrigeration by patient not required if used within 30 days	Toferanone	Detrusitol/ XL	Pfizer	2	
Ropinrole	Requip	GSK	5	Stable for up to 28 days below 25C and at 60% relative humidity	Topiramate	Topamax	Janssen-Cilag	1	Hygroscopic; hydroxyates and becomes unstable with water
Rosuvastatin	Crestor	AstraZeneca	2		Tiramadol	Zydol	Pfizer	2	
Salbutamol	Volmax	A&H/(GSK)	1	Hygroscopic	Trandolapril	Gopten	Abbott	2	
Salbutamol	Ventmax SR	Trinity	4	Probably stable for 4 weeks	Tranexamic acid	Cyklokapron	Pfizer	2	
Saquinavir	Invirase	Roche	3	Store in the dark	Trazodone	Molipaxin	Sanoofi Aventis	2	
Saquinavir	Fortovase	Roche	3	Probably stable for 3 months out of the refrigerator; store in the dark	Trimipramine	Surmontil	Sanoofi Aventis	2	
Selegiline HCl	Zelapar	Zeneus Pharma	1	Hygroscopic	Tri-potassium di-citratobismuthate	De-Noltab	Yamanouchi	2	
Sema (semnosides)	Senokot	Reckitt Benckiser	1	Can absorb moisture	Valdecoxib	Bextra	Pfizer	2	Hygroscopic
Serflindole	Serfloect	Lundbeck	3	Very light sensitive	Valproate sodium EC/ crushable tablets	Epilim	SS	1	Hygroscopic
Sertraline	Lustral	Pfizer	4		Valproate sodium chrono	Epilim chrono	SS	1	Hygroscopic
					Valproic acid	Depakote	SS	2	
					Valsartan	Diovan	Novartis	2	

The stability of drugs in compliance aids, based on information provided by manufacturers (vancomycin to zuclopenthixol)

Generic name	Brand name	Company	Code	Additional information
Vancomycin	Vancocin Matrigel	Lilly	4	Probably stable for up to 4 weeks
Vardenafil	Levitra	Bayer	4	Should be stable for 7 days
Venlafaxine	Efexor	Wyeth	1	Moisture sensitive*
Venlafaxine XL	Efexor XL	Wyeth	4	Probably stable for 7 days*
Verapamil HCl	Univer	Zeneus Pharma	4	
Verapamil HCl	Securon/SR/ Half Securon SR	Abbott	2	
Verapamil HCl/ trandolapril	Tarka	Abbott	2	
Warfarin	-	Goldshield	2	
Zafirlukast	Accolate	AstraZeneca	5	Stable for 30 days at 60-80% relative humidity
Zaleplon	Somata	Wyeth	2	*
Zidovudine	Retrovir	GSK	2	
Zidovudine/amivudine	Combivir	GSK	2	
Zolmitriptan	Zomig	AstraZeneca	2	
Zolpidem	Slinocot	SS	2	
Zopiclone	Zimovane	Sanofi Aventis	2	Protect from light
Zopiclone	-	IVAX	3	2mg stable for 14 days; other strengths stable for 4 weeks
Zuclopenthixol	Clopixol	Lundbeck	4	

KEY TO MANUFACTURERS: BJ, Boehringer Ingelheim; BSM, Bristol-Myers Squibb; GSK, GlaxoSmithKline; MSD, Merck Sharp & Dohme; P&G, Procter & Gamble; SS, Sanofi Synthelabo

Key to stability codes

1. Do not put into a compliance aid.
2. No stability data available, therefore company does not recommend putting in a compliance aid. (Refer to SPC for additional stability information.)
3. No stability data available, therefore company does not recommend putting in a compliance aid. Reason for concern is stated, eg, light-sensitive. Individual pharmacists must accept responsibility for putting in a compliance aid. Risks can be minimised by additional safeguards, eg, use of a black bag.
4. No stability data available, but it is probably suitable to put in a compliance aid.
5. Stability data available in an alternative container, but not necessarily in a compliance aid.
6. Stability data available which state that it is suitable to put in a compliance aid.

DISCLAIMERS: It is important to note that the individual manufacturers do not endorse the practice of transferring medicines from the original packs to compliance aids as it may be outside the terms of their product licences. For the majority of manufacturers any information they provide is based on anecdotal evidence or in-house studies as no formal studies would have been carried out. *The product information provided in this article has been provided by the marketing authorisation holders for these products. The marketing authorisation holders only recommend that their products are stored in accordance with the summary of product characteristics for each product and that storage of products in any other way is entirely at the pharmacist's own risk.