وزارة الصحة
Ministry of Health

Automatic Substitution

Purpose

- To ensure proper automatic therapeutic substitution/interchange within the approved therapeutic and pharmacological class

Definitions

- **Therapeutic Substitution/interchange:** The substitution within the same therapeutic class (Therapeutically equivalent) with the same indication. Both medications should be approved by SFDA.
- **Pharmaceutical equivalence:** Refers to two drug products with the same active ingredient(s), same route of administration, same dosage form, same strength and same conditions of use, but they may differ in characteristics such as shape, scoring configuration, release mechanisms, packaging, excipients (including colors, flavors, preservatives), expiration time, and, within certain limits, labeling.
- **Therapeutic equivalence:** Drug products meeting the following criteria are therapeutically equivalent and can be substituted with the full expectation that the substituted product shall produce the same therapeutic effect as the prescribed product:
  - Is from the same therapeutic class
  - Is from the same pharmacological class
  - Approved by local regulator as safe and effective for the same indication
  - They are adequately labeled
  - There is well documented dosing conversion between the medication that is going to be substituted and the therapeutically equivalent medication

Equipment/Materials

- MOH Formulary (Available online and as drug database in the HIS system)
- List of approved Automatic Substitution (Appendix A)
- Automatic Substitution Workflow (Appendix B)

Policy

- The pharmacist may apply the automatic substitution of existing medication to the MOH Formulary using the approved list from PTC.
- Automatic substitution is only allowed for medications that are within the same approved therapeutic and pharmacological class and have the same exact indication.
- This policy applies to patients under the care of providers at MOH.
- Automatic substitution is only allowed after exhausting all efforts to secure the stock of the prescribed medication according to the out-of-stock policy.

Procedure

Procedures	Explanation
1. The need for automatic change	1.1. Automatic substitution is only allowed in cases where there are: 1.1.1. Documented shortage of the original medication and after following the out-of-stock policy. 1.1.2. After clarifying with the prescribing physician. 1.1.3. Based on clinical pharmacist recommendation. 1.2. Once the original medication becomes a vailable, the patient should be switched back to the originally prescribed medication.
2. The dispensing pharmacist shall	2.1. Counsel the patient or his or her representative on the situation and the recommended substitution to ensure no drug allergies or previous adverse reactions. 2.2. Obtain patient or representative approval to substitute. 2.3. Substitute according to the approved list (Appendix A). 2.4. Record therapeutic interchange in the system, stating what and why the actual interchange occurred, what date it was implemented, and any recommended monitoring.

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Appendix A
List of approved Automatic Substitution

1. **Cardiovascular:**

ACE Inhibitors				
Generic Name	**Dose Equivalents (mg/day)**			
Short-acting				
Captopril	**75**	**150**	**300**	**450**
Intermediate-acting				
Benazepril	5	10	20	40
Enalapril	**5**	**10**	**20**	**40**
Moexipril	7.5	15	22.5	30
Quinapril	5	10	20	40
Ramipril	**2.5**	**5**	**10**	**20**
Long-acting				
Lisinopril	5	10	20	40
Fosinopril	5	10	20	40
Perindopril	**4**	**8**	**12**	**16**
Trandolapril	1	2	4	8

Captopril is short-acting and should be dosed 2-3 times daily. It also can't be substituted in case used in pediatrics.
Enalapril and benazepril are intermediate-acting and should be dosed 1-2 times daily.
Lisinopril is long-acting and should be dosed once daily

Angiotensin Receptor Blockers				
Generic Name	**Dose Equivalents (mg/day)**			
Losartan	**25**	**50**	**100**	**100**
Candesartan	4	8	16	32
Eprosartan	200	400	600	800
Irbesartan	75	150	300	300
Olmesartan	**5**	**10**	**20**	**40**
Telmisartan	**20**	**40**	**80**	**80**
Valsartan	**40**	**80**	**160**	**320**

Calcium Channel Blockers (Dihydropyridines)			
Generic Name	**Dose Equivalents (mg/day)**		
Amlodipine	**2.5**	**5**	**10**
Felodipine	2.5	5	10
Isradipine	5	10	20
Nicardipine	60	90	120
Nifedipine	**30**	**60**	**90**
Nisoldipine, extended release	17	25.5	34

Cardioselective Beta Blockers in hypertension				
Generic Name	**Dose Equivalents (mg/day)**			
Atenolol	**25**	**50**	**100**	**N/A**
Metoprolol Tartrate	**50**	**100**	**200**	**400**

Beta Blockers in heart failure		
Generic Name	**Dose Equivalents (mg/day)**	
Bisoprolol	**5**	**10**
Carvedilol	**25**	**50**

Nitroglycerin Sublingual	
Generic Name	**Dose Equivalents**
Nitroglycerin 0.4 mg/actuation spray	1 to 2 sprays every 5 minutes for a maximum of 3 sprays in 15 minutes
Nitroglycerin 0.4 mg tablet	**0.4 mg every 5 minutes for a maximum of 3 tablets in 15 minutes**

Nitroglycerin spray will be maintained on formulary as a uterine relaxant; however, for the management of angina, it will be interchanged with nitroglycerin sublingual tablets.

2. **Dyslipidemia:**

Drug	HMG-CoA Reductase Inhibitor Dose Equivalents (mg/day)					
Atorvastatin			**10**	**20**	**40**	**80**
Fluvastatin	20	40	80			
Lovastatin	10	20	40	80		
Pravastatin	10	20	40	80	80	
Rosuvastatin			**5**	**10**	**20**	**40**
Simvastatin	5	10	20	40	80	
Simvastatin/ezetimibe			10/10	20/10	40/10	80/10

3. **2nd generation Antihistamines**

Generic Name	Dose Equivalents (mg/day)		
Cetirizine	**2.5**	**5**	**10**
Desloratadine	N/A	5	5
Fexofenadine	60	120	180
Loratadine	5	10	10

4. Gastrointestinal

Drug	Equivalent doses (mg/day)	
Proton Pump Inhibitors		
Oral		
Esomeprazole	**20**	**40**
Lansoprazole	15	30
Omeprazole	**20**	**40**
Pantoprazole	20	40
Rabeprazole	20	20
IV		
Esomeprazole	40	80
Omeprazole	**20**	**40**
Pantoprazole	40	80
H_2 Blockers		
Oral		
Cimetidine		600-1200
Famotidine	**20**	**40**
Nizatidine	150	300
Ranitidine	**150**	**300**
IV		
Cimetidine		900-1200
Famotidine	20	**40**
Ranitidine	**50 -100**	**150-200**

Cimetidine is short-acting and should be dosed 3 times daily.
Nizatidine and Ranitidine are intermittent-acting and should be dosed 2 times daily.

5. Antibiotics

Carbapenems		
Generic Name	**Dose Equivalents (mg/day)**	
Meropenem	**2000**	**3000**
Doripenem	1500	3000
Imipenem/cilastatin	**2000**	**3000**

Imipenem is not to be substituted in pediatrics.
Doripenem is not recommended as substitution in case of pneumonia.

Cephalosporins				
Generic Name	**Dose Equivalents (mg/day)**			
IV				
Ceftriaxone	**1000**	**2000**	**3000**	**4000**
Cefotaxime	**3000**	**6000**	**9000**	**12000**
Oral				
Cephradine	**1000**	**2000**		
Cephalexin	**1000**	**2000**		

Ceftriaxone is the preferred third generation cephalosporin in adult patients. Cefotaxime is available for use in neonates and for orders written by Infectious Diseases faculty.
Usual adult dosing for ceftriaxone is 1-2 gm every 12-24 hours (max: 4 gm/day), usual adult dosing for cefotaxime is 1-2 gm every 6-8 hours (max: 12 gm/day).
Cephradine and Cephalexin should be dosed 4 times a daily.

***Formulary agent in bold (As reflected in Micromedex).**

Appendix B

Automatic Substitution Workflow