**S1 Supporting Tables for** ***Cost resulting from anti-tuberculosis drug shortages in the United States: a hypothetical cohort study.***

This supplement provides additional details of the model structure and calculation of model inputs and includes the following tables:

Table A. Alternative regimens a patient could receive in the setting of a medication adverse event, by regimen number

Table B. Alternative regimens a patient could receive in the setting of a medication adverse event, by adverse event

Table C. Medical tests for routine medication monitoring

Table D. Procedures and frequency of procedure after adverse events

**Table A. Alternative regimens a patient in the hypothetical cohort could be changed to in the setting of a medication adverse event.a**

|  |  |  |
| --- | --- | --- |
| **Regimen** | **Medications** b | **Duration medication given (months)** |
| 1 | INH RIFEMBPZA | 6 622 |
| 2 | RIFEMBPZA | 666 |
| 3 | INH EMBMFXPZA | 1212122 |
| 4 | EMBPZAMFXAMK  | 1818186 |
| 5 | INH RIF | 99 |
| 6 | RIFEMBMFX | 12122 |
| 7 | INH PZAEMB | 999 |
| 8 | INH RIFPZA | 662 |
| 9 | RIFEMBMFX | 999 |
| 10 | EMBMFXAMKCS | 181866 |
| 11 | RIFPZAMFX | 999 |
| 12 | INH EMBMFX AMK | 1818182 |
| 13 | INH MFX PZA | 12122 |
| 14 | INHPZAMFXAMK | 1818182 |
| 15 | INH EMBPZA | 18182 |
| 16 | EMB MFX CSAMK | 1818186 |
| 17 | PZA MFX CSAMK | 1818186 |
| 18 | PZA EMBCSLNZAMK | 181818186 |
| 19 | PZA EMBMFX LNZPAS | 1818181818 |
| 20 | EMBPZAAMKPAS  | 1818618 |
| 21 | PZA EMBMFX LNZCS | 1818181818 |
| 22 | PZAMFXAMK | 18186 |
| 23 | RIFINH EMB | 992 |
| 1. Treatment regimens were based on literature and consultations with TB treatment experts. [[1-11](#_ENREF_1)]
2. Drug abbreviations: INH - isoniazid, RIF - rifampin, PZA - pryazinamide, EMB - ethambutol, MFX - moxifloxacin, AMK - amikacin, CS - cycloserine, LNZ - linezolid, PAS – para-aminosalicylic acid
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**Table B. Alternative treatment regimens a patient can be changed to change due to an adverse event**

|  |  |
| --- | --- |
| **Medication-related adverse event** | **New regimen and duration for each drug**a, b |
| Initial Regimen: Standard Therapy |
| INH |  |
| Moderate Hepatitis | RIF 6 - EMB 6 - PZA 6 |
| Severe Hepatitis | RIF 12 - EMB 12 - MFX 2 |
| Moderate other event | RIF 6 - EMB 6 - PZA 6 |
| RIF |  |
| Moderate Hepatitis | INH 12 - EMB 12 - MFX 12 - PZA 2 |
| Severe Hepatitis | EMB 18 - MFX 18 - CS 18 - AMK 6 |
| Moderate other event | INH 9 - PZA 9 - EMB 9 |
| PZA |  |
| Moderate Hepatitis | INH 9 - RIF 9 |
| Severe Hepatitis | RIF 12 - EMB 12 - MFX 2 |
| Moderate other event | INH 9 - RIF 9 |
| EMB  Vision impairment (any) | INH 6 - RIF 6 - PZA 2 |
|  |  |
| Initial Regimen: No INH regimen |
| RIF |  |
| Moderate or hepatitis | PZA 18 - EMB 18 - MFX 18 - AMK 6 |
| Severe Hepatitis | EMB 18 - MFX 18 - CS 6 - AMK 6 |
| Moderate other event | PZA 18 - EMB 18 - MFX 18 - AMK 6 |
| PZA  Adverse event (any) | RIF 9 - EMB 9 - MFX 9 |
| EMB  Vision impairment (any) | PZA 9 - RIF 9 - MFX 9 |
|  |  |
| Initial Regimen: No RIF regimen |
| INH  Adverse event (any) | PZA 18 - EMB 18 - MFX 18 - AMK 6 |
| PZA  Adverse event (any) | INH 18 - EMB 18 - MFX 18 - AMK 2 |
| EMB |  |
| Mild vision impairment | INH 12 - MFX 12 - PZA 2 |
| Moderate vision impairment | INH 18 - PZA 18 - MFX 18 - AMK 2 |
| MFX  Adverse event (any) | INH 18 - EMB 18 - PZA 2 |
|  |  |
| Initial Regimen: No INH or RIF regimen |
| PZA |  |
| Hepatitis – moderate or severe | EMB 18 - MFX 18 - CS 18 - AMK 6 |
| Moderate other event | EMB 18 - PZA 18 - AMK 6 - PAS 18 |
| EMB |  |
| Mild vision impairment | PZA 18 - MFX 18 - AMK 6 |
| Moderate vision impairment | PZA 18 - MFX 18 - CS 18 - AMK 6 |
| MFX  Adverse event (any)  | PZA 18 - EMB 18 - LNZ 18 - CS 18 - AMK 6 |
| AMK  Adverse event (any) | PZA 18 - EMB 18 - MFX 18 - LNZ 18 - PAS 18 |
|  |  |
| Initial regimen: no PZA regimen |
| INH  Any adverse event | RIF 9 - EMB 9 - MFX 9 |
| RIF |  |
| Hepatitis – moderate or severe | INH 18 - EMB 18 - MFX 18 - AMK 2 |
| Severe Hepatitis | EMB 18 - MFX 18 - CS 18 - AMK 6 |
| Moderate other event | INH 18 - EMB 18 - MFX 18 - AMK 2 |
| EMB  Vision impairment (any) | INH 6 - RIF 6 - PZA 2 |
| 1. Treatment regimens were based on literature and consultations with TB treatment experts. [[1-11](#_ENREF_1)]
2. Drug abbreviations: INH - isoniazid, RIF - rifampin, PZA - pryazinamide, EMB - ethambutol, MFX - moxifloxacin, AMK - amikacin, CS - CS, LNZ - linezolid, PAS – para-aminosalicylic acid
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**Table C. Medical Tests Associated with Routine Monitoring of Medication Side Effectsa,b**

|  |  |  |
| --- | --- | --- |
| Drug Name | Medical Test | Frequency  |
| INH | Hepatic function panel | baseline |
| AMK | Assay of creatinine | monthly |
| AMK | Electrolyte panel | monthly |
| AMK | Assay of magnesium | monthly |
| AMK | Assay of calcium | monthly |
| RIF | Hepatic function panel | monthly |
| EMB | Visual acuity screen | monthly |
| EMB | Color vision examination | monthly |
| PZA | Hepatic function panel | monthly |
| PZA | Uric acid | monthly |
| PAS | Hepatic function panel | monthly |
| PAS | Thyroid function panel | baseline |
| LNZ | Complete blood count | baseline |
| LNZ | Complete blood count | monthly |
| 1. Treatment regimens were based on literature and consultations with TB treatment experts. [[1-3](#_ENREF_1), [5](#_ENREF_5), [6](#_ENREF_6), [8](#_ENREF_8), [12](#_ENREF_12), [13](#_ENREF_13)]
2. Drug abbreviations: INH - isoniazid, RIF - rifampin, PZA - pryazinamide, EMB - ethambutol, MFX - moxifloxacin, AMK - amikacin, CS - CS, LNZ - linezolid, PAS – para-aminosalicylic acid
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**Table D. Procedures and frequency of procedure conducted for drug-specific adverse eventsa**

|  |  |  |
| --- | --- | --- |
| Adverse Event**b** | Procedure | Estimated Quantity |
| **INH** |
| Mild hepatitis |   |   |
|   | Office or outpatient visit for established patient | 1 |
|   | Hepatic function panel | 2 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
| Moderate hepatitis |   |   |
|   | Office or outpatient visit for established patient | 2 |
|   | Hepatic function panel | 3.5 |
|   | Acute hepatitis panel | 1 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
| Severe hepatitis |   |   |
|   | Liver transplantation | 1 |
| Mild other |   |   |
|   | Office or outpatient visit for established patient | 2 |
|   | Complete blood count | 1 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
|   | Electrolyte panel | 1 |
| Moderate other |   |   |
|   | Office or outpatient visit for established patient | 3.5 |
|   | Complete blood count | 1 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
|   | Electrolyte panel | 1 |
|  |  |  |
| **RIF** |
| Mild hepatitis |   |   |
|   | Office or outpatient visit for established patient | 1 |
|   | Hepatic function panel | 2 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
| Moderate hepatitis |   |   |
|   | Office or outpatient visit for established patient | 2 |
|   | Hepatic function panel | 3.5 |
|   | Acute hepatitis panel | 1 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
| Severe hepatitis |   |   |
|   | Liver transplantation | 1 |
| Mild other |   |   |
|   | Office or outpatient visit for established patient | 2 |
|   | Hepatic function panel | 2 |
|   | Complete blood count | 1 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
|   | Topical cream | 1 |
| Moderate other |   |   |
|   | Office or outpatient visit for established patient | 3.5 |
|   | Hepatic function panel | 3.5 |
|   | Complete blood count | 3.5 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
|   | TB inpatient hospital day | 1 |
|  |  |  |
| **EMB** |
| Mild vision |   |   |
|   | Office or outpatient visit for established patient | 1 |
|   | Eye exam for a new patient | 1 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
| Moderate vision |   |   |
|   | Office or outpatient visit for established patient | 2 |
|   | Eye exam for a new patient | 2 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
|  |  |  |
| **PZA** |
| Mild hepatitis |   |   |
|   | Office or outpatient visit for established patient | 1 |
|   | Hepatic function panel | 2 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
| Moderate hepatitis |   |   |
|   | Office or outpatient visit for established patient | 2 |
|   | Hepatic function panel | 3.5 |
|   | Acute hepatitis panel | 1 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
| Severe hepatitis |   |   |
|   | Liver transplantation | 1 |
| Mild other |   |   |
|   | Office or outpatient visit for established patient | 1 |
|   | Hepatic function panel | 2 |
|   | Uric acid | 1 |
|   | Complete blood count | 1 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
|   | Topical cream for rash | 1 |
| Moderate other |   |   |
|   | Office or outpatient visit for established patient | 2 |
|   | Hepatic function panel | 3.5 |
|   | Uric acid  | 2 |
|   | Complete blood count | 1 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
|  |  |  |
| **AMK** |
| Mild nephrotoxicity |   |   |
|   | Office or outpatient visit for established patient | 2 |
|   | Comprehensive metabolic panel | 2 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
| Moderate nephrotoxicity |   |   |
|   | Office or outpatient visit for established patient | 3.5 |
|   | Comprehensive metabolic panel | 5.5 |
|   | Therapeutic drug monitoring | 1 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
| Severe nephrotoxicity |   |   |
|   | Office or outpatient visit for established patient | 5.5 |
|   | Comprehensive metabolic panel | 7.5 |
|   | Office consultation (nephrology) | 1 |
|   | Hemodialysis | 90 |
|   | TB inpatient hospital day | 1 |
| Mild hearing |   |   |
|   | Office or outpatient visit for established patient | 2 |
|   | Audiogram | 1 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
| Moderate hearing |   |   |
|   | Office or outpatient visit for established patient | 3.5 |
|   | Audiogram | 2 |
|   | Comprehensive metabolic panel | 1 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
| Mild other |   |   |
|   | Office or outpatient visit for established patient | 2 |
|   | Audiogram | 1 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
| Moderate other |   |   |
|   | Office or outpatient visit for established patient | 3.5 |
|   |  Audiogram | 2 |
|   | Comprehensive metabolic panel | 1 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
|  |  |  |
| **MFX** |
| Mild tendinopathy |   |   |
|   | Office or outpatient visit for established patient | 3.5 |
|   | Hepatic function panel | 1 |
|   | Comprehensive metabolic panel | 1 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
|   | Prescription for non-steriodal anti-inflammatory medication | 1 |
| Moderate tendinopathy |   |   |
|   | Office or outpatient visit for established patient | 4.5 |
|   | Hepatic function panel | 1 |
|   | Aspirate joint | 1 |
|   | Comprehensive metabolic panel | 1 |
|   | Complete blood count | 1 |
|   | Uric acid  | 1 |
|   | Office consultation (rheumatology) | 1 |
|   | Ankle MRI | 1 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
|   | Physical therapy evaluation | 2 |
| Mild other |   |   |
|   | Office or outpatient visit for established patient | 1 |
|   | Hepatic function panel | 1 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
| Moderate other |   |   |
|   | Office or outpatient visit for established patient | 2 |
|   | Hepatic function panel | 1 |
|   | Comprehensive metabolic panel | 1 |
|   | Ankle MRI | 1 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
|   | Routine ECG with at least 12 leads; with interpretation and report | 1 |
| Severe other |   |   |
|   | Office or outpatient visit for established patient | 3.5 |
|   | Hepatic function panel | 1 |
|   | Electrolyte panel | 1 |
|   | Ankle Magnetic resonance imaging (MRI) | 1 |
|   | Ankle radiograph | 1 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
|   | Routine ECG with at least 12 leads; with interpretation and report | 1 |
|   | Office consultation (surgery) | 0 |
|   | TB inpatient hospital day | 1 |
|  |  |  |
| **LNZ** |
| Mild neuropathy |   |   |
|   | Office or outpatient visit for established patient | 2 |
|   | Complete blood count | 1 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
|   | Electrolyte panel | 1 |
| Moderate neuropathy |   |   |
|   | Office or outpatient visit for established patient | 3.5 |
|   | Complete blood count | 1 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
|   | Electrolytes panel | 1 |
| Severe neuropathy |   |   |
|   | Office or outpatient visit for established patient | 3.5 |
|   | Complete blood count | 1 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
|   | Electrolyte panel | 1 |
| Mild myelosuppresion |   |   |
|   | Office or outpatient visit for established patient | 2 |
|   | Complete blood count | 3.5 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
|   | Electrolyte panel | 1 |
| Moderate myelosuppresion |   |   |
|   | Office or outpatient visit for established patient | 2 |
|   | Complete blood count | 4.5 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
|   | Electrolyte panel | 1 |
| Severe myelosuppresion |   |   |
|   | Office or outpatient visit for established patient | 4 |
|   | Complete blood count | 6.5 |
|   | TB inpatient hospital day | 1 |
|   | Electrolyte panel | 1 |
| Mild vision |   |   |
|   | Office or outpatient visit for established patient | 1 |
|   | Eye exam for a new patient | 1 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
| Moderate vision |   |   |
|   | Office or outpatient visit for established patient | 2 |
|   | Eye exam for a new patient | 2 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
|  |  |  |
| **PAS** |
| Mild gastrointestinal symptoms  |
|   | Office or outpatient visit for established patient | 2 |
|   | Hepatic function panel | 2 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
|   | Electrolyte panel | 2 |
| Moderate gastrointestinal symptoms  |
|   | Office or outpatient visit for established patient | 2 |
|   | Hepatic function panel | 2 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
|   | Electrolyte panel | 2 |
| Severe gastrointestinal symptoms  |
|   | Office or outpatient visit for established patient | 3.5 |
|   | Hepatic function panel | 2 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
|   | TB inpatient hospital day | 1 |
|   | Electrolyte panel | 3.5 |
| Mild hypothyroidism |   |
|   | Office or outpatient visit for established patient | 1 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
| Mild hepatitis |   |
|   | Office or outpatient visit for established patient | 1 |
|   | Hepatic function panel | 2 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
| Moderate hepatitis |   |
|   | Office or outpatient visit for established patient | 2 |
|   | Hepatic function panel | 3.5 |
|   | Acute hepatitis panel | 1 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
| Severe hepatitis |   |
|   | Liver transplantation | 1 |
|  |  |  |
| **CS** |
| Mild central nervous system symptoms  |
|   | Office or outpatient visit for established patient | 2 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
|   | Therapeutic drug monitoring | 1 |
| Moderate central nervous system symptoms  |
|   | Office or outpatient visit for established patient | 3.5 |
|   | Office or outpatient visit for established patient (nurse) | 1 |
|   | Therapeutic drug monitoring | 1 |
| 1. Treatment regimens were based on literature and consultations with TB treatment experts. [[1-3](#_ENREF_1), [5](#_ENREF_5), [6](#_ENREF_6), [8](#_ENREF_8), [12](#_ENREF_12), [13](#_ENREF_13)]
2. Drug abbreviations: INH - isoniazid, RIF - rifampin, PZA - pryazinamide, EMB - ethambutol, MFX - moxifloxacin, AMK - amikacin, CS - CS, LNZ - linezolid, PAS – para-aminosalicylic acid
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