Interim advice for countries including a pharmacovigilance component in tuberculosis proposals to Global Fund Round 10

1. Rationale for including pharmacovigilance in the proposal

Access to anti-TB medication has increased markedly in recent years and a scale-up in the provision of treatment for MDR-TB patients is expected in the coming years. Drug toxicities, intolerance and drug-drug interactions may jeopardize the successful implementation of such treatment programmes. Adverse reactions to anti-TB medication are relatively common but only scarcely reported in many settings. Adherence to treatment remains problematic in TB care and interruptions associated to adverse reactions to medication are known to be often to blame.

All proposals to the Round 10 for TB treatment programmes, and especially those targeting patients with TB/HIV or MDR-TB, should consider inclusion of pharmacovigilance (PV) to anti-TB drugs.

WHO has defined pharmacovigilance as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects (AE) or any other drug-related problem. Pharmacovigilance is an arm of patient care. It aims at getting the best outcome of treatment with medicines. No one wants to harm patients, but unfortunately, because of many different factors, any medicine will sometimes do this. Good pharmacovigilance will identify the risks in the shortest possible time after the medicine has been marketed and will help to establish/identify risk factors. When communicated effectively, this information allows for intelligent, evidence-based prescribing with potential for preventing many adverse reactions and will ultimately help each patient to receive optimum therapy at a lower cost to the health system.

The objectives for having PV for TB would be
- strengthened patient safety through the early detection and mitigation of adverse reactions
- improved effectiveness of TB programmes by ensuring that more patients complete their treatment as indicated
- better TB programme efficiency and drug forecasting
- strengthened health system through improved monitoring of patients' treatment
- increased knowledge on drug safety profiles (especially for new drugs)

2. Situation analysis

The situation analysis should include information on the TB epidemiological features relevant to PV as well as a situation background (see ANNEX).

3. Steps in setting up anti-TB/PV system

The steps should follow logically from the situation analysis. If a structure is already in place, then it may need to be reinforced. Sometimes, the system may need to be started. The situation assessment will determine if the establishment or revision of a national anti-TB/PV plan is required. Mapping of existing activities related to anti-TB/PV - procurement plans, staff training, monitoring and evaluation - is important.
3.1) National planning

- Where there is no pre-established PV system in the country
  1. Contact the WHO and International Drug Monitoring Programme (see below)
  2. Get the necessary technical assistance
  3. Prepare a pilot phase based on few sentinel sites
  4. Establish clear objectives and methodologies
  5. Identify and consult with implementing partners, stakeholders in countries and other countries with established ARV/PV system
  6. Prepare norms and standards, reporting methodologies and support, training plans, guidelines for implementation and policies for both drug policy and TB programmes.

- Where PV exists in the country but not in the anti-TB/PV programme
  1. Same as above + review and evaluation of existing data
  2. Consider stimulating passive reporting
  3. Review the project objectives and methodologies
  4. Consider introducing, in a phased manner, methods that complement passive reporting within TB cohort management

- Where PV exists in the country within the anti-TB/PV programme
  1. Evaluation of the programme
  2. Strengthening of key points
  3. Review the project objectives and methodologies
  4. Consider expanding the programme to other units that do not have established programmes

3.2) Policy and guidelines
  1. Establish a national expert working group
  2. Establish linkages with the International Drug Monitoring Centre
  3. Prepare:
     a. national policy including resource planning, training
     b. national anti-TB/PV network and reporting forms
     c. national guidelines on reporting of AEs to anti-TB drugs, analysis of data and integration in national policies and guidelines on training

3.3) Proposed activities
  1. Staff recruitment
  2. Training, initial and refreshment training of the IT, for programme managers and services providers
  3. Identify areas for technical assistance and procure the expertise
  4. Set up the communication network and mechanisms.
  5. Provide necessary tools forms, registers, communication tools
  6. Start implementing at delivery level
  7. Update and manage information through appropriate means of communication: newsletters, letters, mails, web posting; ensure a feedback system to providers; to the regulatory authorities; pharmaceutical industry;
  8. Monitor evaluate prepare reports; adapt and update the PV programme.
  9. Integrate results of PV in treatment programme management.
3.4) Some key indicators
1. Number of reports of AEs linked to anti-TB drugs sent to national database (baseline value, annual reports by centre)
2. Number of TB treatment units reporting AEs accurately of existing TB units
3. Number of new TB treatment units beginning to report AEs
4. Number of programme managers, health workers trained in anti-TB/PV
5. Number of national or regional registries established for anti-TB/PV

3.5) Costing the activities.
1. Number and type of staff to be recruited
2. Number of trainings to be done
3. Technical assistance to be provided
4. Supervision, expert evaluation of ongoing work, logistics
5. Normative tools to be created, updated or adapted
6. Components of the communication network
7. Production and dissemination of necessary tools, forms, registers, websites, bulletins, publications, other communication tools
8. IT needs (hardware, software)
9. Other equipment for the pilot sites
10. Cohort studies
11. Medication for AEs

3.6) Key implementing partners to be considered
1. Stop TB Department and QSM at WHO/HQ
2. WHO Collaborating Centre for International Drug Monitoring, Uppsala, Sweden
3. Cohort surveys implementers
4. Academicians and researchers
5. Other agencies (eg, MSH-SPS)

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1 WHO will issue specific guidance on cohort event monitoring for TB in late 2010. In the meantime the reader is referred to the relevant instructions in "WHO.A practical handbook on the pharmacovigilance of antimalarial medicines" (malaria.who.int/docs/diagnosisandtreatment/Malaria-PharmaVigil.pdf)
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Contacts at Global Fund, Geneva
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Online resources
1) The safety of medicines in public health programmes. (www.who.int/medicines/areas/quality_safety/safety_efficacy/Pharmacovigilance_B.pdf)

2) Safety Monitoring of Medicinal Products: Guidelines for Setting Up and running a pharmacovigilance centre (www.who.int/medicinedocs/en/d/Jh2934e/)

3) A practical handbook on the pharmacovigilance of antimalarial medicines. World Health Organization, 2007 (malaria.who.int/docs/diagnosisandtreatment/Malaria-PharmaVigil.pdf)

ANNEX

Components for a situation analysis

EPIDEMIOLOGY
- Indicators of TB among the general population (notification, incidence, mortality)
- Frequency of HIV-associated TB and MDR-TB
- Number and profile of treatment sites
- Number of people on TB-treatment
- Outcomes of TB treatment, in particular information on adherence to treatment and information on adverse effects, particularly life-threatening ones.

PRIORITY TARGET POPULATIONS
- Patients on long term treatment, particularly MDR-TB
- Patients with important co-morbidity, such as HIV-associated TB
- Other patients on multiple medication or using new drugs
- Other vulnerable groups (eg, extremes of life, known drug-intolerance)

TB CARE SERVICES
- National (governmental) services: primary, secondary and tertiary levels
- TB units likely to act as pilot sites
- Other services implementers (NGOs, private sector)
- Laboratory capacity to monitor drug toxicities
- PV network in country, in the region.
- Training

PV SETUP IN THE COUNTRY
- Existence of a national PV programme and database.
- Whether the country is a member of WHO's Programme for International Drug Monitoring and if it sends reports
- Number, type and quality of reported adverse events: known and unknown.
- Existing capacity in-country and identified needs.
- Existence of any activities specific to PV in TB.
- If cohort surveys and specific studies and research on adverse events linked to the use of anti-TB drugs are currently undertaken in the country.
- The need for implementing a new anti-TB/PV programme, or for strengthening and sustaining existing ones.
- Computer based data management (existing resources and gaps; software and hardware)
- Laboratory resources

NORMS & STANDARDS
- Reporting forms and reporting guidelines for TB monitoring and for PV
- Which methodologies are in place (spontaneous reporting, cohort monitoring, registers)
- Management of adverse events: guidelines for service providers
- Training tools

HUMAN RESOURCES
- Programme managers
- Regulatory authorities
- Experts in PV among pharmaceutical/clinical staff
- Other potential partners in programme implementation
- Service providers, including laboratory technicians
- IT personnel
- Training needs in country and abroad
- Integration of PV into national training curricula