RECOVERY EU Pharmacy Briefing

(Based on Core Protocol V27.0 2023-09-13 and EU Region-Specific Appendix V1.0 2024-01-24)

Contents

1 Introduction

RECOVERY is an open-label platform trial evaluating treatments for patients hospitalised with influenza or community-acquired pneumonia (CAP) caused by other pathogens. Several previous treatments have been evaluated in RECOVERY, and the IMPs being evaluated in the EU are listed in the table below (treatment comparisons "H", "I" and "M" from the core protocol). All IMPs in the EU are supplied, labelled and accounted for as if given as part of routine care, without any trial specific procedures. Prescriptions should be written by one of the patient's attending doctors in the same manner as for usual care, with no additional documentation. Only adults (aged ≥18 years) are eligible in the EU.

Table 1: IMPs in RECOVERY

Medicine	Formulation	Source	Trial accountability logs	Prescribed	Trial specific labelling
Randomisation Part H (oseltamivir comparison – patients with influenza)					
Oseltamivir	Oral capsule, oral suspension	Hospital pharmacy stock used for routine care	No (accountability as for routine care)	Yes	No
Randomisation Part I (corticosteroid comparison – patients with influenza)					
Dexamethasone	Oral tablet, oral suspension, intravenous ampoules	Hospital pharmacy stock used for routine care	No (accountability as for routine care)	Yes	No
Prednisolone (alternative for pregnant/ breastfeeding women)	Oral tablets, oral suspension	Hospital pharmacy stock used for routine care	No (accountability as for routine care)	Yes	No
Hydrocortisone (alternative for pregnant/ breastfeeding women)	Intravenous ampoules	Hospital pharmacy stock used for routine care	No (accountability as for routine care)	Yes	No
Randomisation Part M (corticosteroid comparison – patients with community-acquired pneumonia)					
Dexamethasone	Oral tablet, oral suspension, intravenous ampoules	Hospital pharmacy stock used for routine care	No (accountability as for routine care)	Yes	No
Prednisolone (alternative for pregnant/ breastfeeding women)	Oral tablets, oral suspension	Hospital pharmacy stock used for routine care	No (accountability as for routine care)	Yes	No
Hydrocortisone (alternative for pregnant/ breastfeeding women)	Intravenous ampoules	Hospital pharmacy stock used for routine care	No (accountability as for routine care)	Yes	No

In each comparison, patients are randomly allocated in a 1:1 ratio to the trial treatment or usual care without that trial treatment. Participants may be allocated to >1 trial treatment if they enter >1 comparison (i.e. both oseltamivir as well as corticosteroids for influenza). If participants are allocated to 'usual care' they do not require a prescription (there is no placebo).

Example SmPCs for the IMPs are available on the trial website (recoverytrial.net), which provide trial Reference Safety Information (section 4.8). For specific information about the formulation used at your site (e.g. storage, excipients, expiry), refer to the relevant SmPC for that formulation.

2 Dexamethasone

2.1 Initial supply and re-ordering

Dexamethasone will be sourced by the local pharmacy procurement team via their standard procedures. The locally available formulation can be used.

2.2 Storage

As per SmPC. No temperature excursion reporting required to the trial team. Follow local SOPs to manage temperature excursions.

2.3 Dispensing quantities

The regime is identical for **Randomisation Part I** (corticosteroids for influenza) and **Randomisation Part M** (corticosteroids for CAP):

Dexamethasone administered by mouth, feeding tube or intravenously.

Duration	10 days, stopped on discharge from hospital if this happens sooner
Dose	6mg
Frequency	Once daily

Note, an alternative corticosteroid with less fetal/infant exposure should be used in pregnant or breastfeeding women (this can be either prednisolone orally or hydrocortisone intravenously as described below).

2.4 Returns and Destructions

Any unused stock should be disposed of in the usual manner. No approval from sponsor is required.

2.5 FAQs

How is dexamethasone to be prescribed as there are different salts available?
To be prescribed as dexamethasone base

Is the dose the same for oral and IV for dexamethasone despite differences in bioavailability?
Yes, the dose will be as the base for both IV and oral.

How should the oral dose be taken?
Dexamethasone should ideally be taken with or after food to minimise irritation to the gastrointestinal tract.

Our normal hospital practice is to dissolve dexamethasone 2mg tablets instead of using soluble tablets or oral liquid, is this permitted?
Yes. If sites cannot source the soluble tablets or liquid, then the 2mg tablets can be dissolved in 10mL of water. There are no issues with this going down a fine bore nasogastric tubes[1].

Is IV dexamethasone to be given as an IV bolus or infusion?
Either is acceptable, treating clinician to decide.

[1] Handbook of Drug Administration via Enteral Feeding Tubes ISBN 9780857111623

3 Prednisolone

3.1 Initial supply and re-ordering

Prednisolone will be sourced by the local pharmacy procurement team via their standard procedures. The locally available formulation can be used.

3.2 Storage

As per SmPC. No temperature excursion reporting required to the trial team. Follow local SOPs to manage temperature excursions.

3.3 Dispensing quantities

Pregnant and breastfeeding women should receive *either* prednisolone *or* hydrocortisone instead of dexamethasone (if it's necessary to change the route of administration, women can switch between prednisolone and hydrocortisone, but the treatment end date should remain the same). The regime is identical for **Randomisation Part I** (corticosteroids for influenza) and **Randomisation Part M** (corticosteroids for CAP):

Prednisolone administered by mouth or feeding tube.

Duration 10 days, stopped on discharge from hospital if this happens sooner
Dose 40mg
Frequency Once daily

3.4 Returns and Destructions

Any unused stock should be disposed of in the usual manner. No approval from sponsor is required.

4 Hydrocortisone

4.1 Initial supply and re-ordering

Hydrocortisone will be sourced by the local pharmacy procurement team via their standard procedures. The locally available formulation can be used.

4.2 Storage

As per SmPC. No temperature excursion reporting required to the trial team. Follow local SOPs to manage temperature excursions.

4.3 Dispensing quantities

Pregnant and breastfeeding women should receive *either* prednisolone *or* hydrocortisone instead of dexamethasone (if it's necessary to change the route of administration, women can switch between prednisolone and hydrocortisone, but the treatment end date should remain the same). The regime is identical for **Randomisation Part I** (corticosteroids for influenza) and **Randomisation Part M** (corticosteroids for CAP):

Hydrocortisone sodium succinate administered intravenously.

Duration 10 days, stopped on discharge from hospital if this happens sooner
Dose 80mg
Frequency Twice daily

4.4 Returns and Destructions

Any unused stock should be disposed of in the usual manner. No approval from sponsor is required.

5 Oseltamivir

5.1 Initial supply and re-ordering

Oseltamivir will be sourced by the local pharmacy procurement team via their standard procedures. The locally available formulation can be used.

5.2 Storage

As per SmPC. No temperature excursion reporting required to the trial team. Follow local SOPs to manage temperature excursions.

5.3 Dispensing quantities

Oseltamivir administered by mouth or feeding tube.

Duration	5 days (10 days if the patient is immunosuppressed in opinion of their doctor). If the participant is discharged before the course is complete, they should be provided with medication to complete the course at home.	
Dose	Participants weighing >40 kg	75mg
	Participants weighing 23-40kg	60mg
Frequency	eGFR ≥30 ml/min/1.73m^2	twice daily
	eGFR 10-29 ml/min/1.73m^2	once daily
	eGFR <10 ml/min/1.73m^2	single dose on day 1 (including immunosuppressed)

Note the renal dosing adjustment in RECOVERY differs from the SmPC, as it is based on the UK Renal Drug Database regime.

5.4 Returns and Destructions

Any unused stock should be disposed of in the usual manner. No approval from sponsor is required.

5.5 FAQs

Are parenteral routes available?

No. If a patient becomes unable to take oseltamivir via an enteral route there is no alternative in the trial. If the clinical team wish to continue treatment with a parenteral NAI (e.g. zanamivir) this would be done at their discretion and is not part of the trial protocol.