BEST PRACTICE: MANAGEMENT OF ORPHAN DRUG DESIGNATION APPLICATIONS AND MARKETING AUTHORISATIONS FOR ORPHAN DRUGS

1 Revision History

When Ennov releases a new version of Ennov InSight, they issue Release Notes which explain the new features and updates. The Ennov Business Consulting Team reviews the Release Notes against each Best Practice to determine any impact to the document:

- Impact = Release notes-documented upgrade changes this Best Practice
- No Impact = Release notes-documented upgrade changes do not affect this Best Practice

When Release Notes impact Best Practice documentation, Ennov recommends that clients review the entire Release Notes for a full understanding of all changes associated with this Best Practice documentation.

Software Version	Release/ Revision Date	Summary of Change(s) (Refer to Release Notes for Full Description)
v7.3	19 Sep 2024	Reissued with additional guidance for management of Marketing Authorisation Applications for products with Orphan Drug status. Guidance applies from software version v7.1 onwards. Updated Best Practice for Ennov rebranding.
v7.1	13-Jan-2022	Update Best Practice for 7.1 - Impact
v7.0	30-Apr-2021	Update Best Practice for 7.0 - No Impact
N/A	13-Apr-2021	Update Best Practice for Calyx Rebranding – No Impact
v6.2 CHF6	21-Oct-2020	Update Best Practice for v6.2 CHF6 – No Impact
v6.2 CHF5	03-Aug-2020	Update Best Practice for v6.2 CHF5 – No Impact
v6.2 CHF4	28-Feb-2020	Update Best Practice for v6.2 CHF4 – No Impact
v6.2 CHF3	27-Jun-2019	Update Best Practice for v6.2 CHF3 – No Impact
v6.2 CHF2	15-Feb-2019	Update Best Practice for v6.2 CHF2 – No Impact

2 Contents

3 Document Purpose

The purpose of this document is to provide a Best Practice for managing:

a. Orphan Drug Designation (ODD) Applications
b. Marketing Authorisation Applications for product(s) with an ODD status

ODD Products are intended to treat an 'orphan disease'. The definition of an Orphan Drug differs from region-to-region, and is defined by the Health Authority. Typically, the Product must be intended for the treatment, prevention or diagnosis of a disease or condition with a prevalence below the limit set by the Health Authority.

4 Data Administration Activities

4.1 Application Category

A new Application Category should be created and named Orphan Drug Designation (ODD).

4.2 Application Type

A new Application Type should be created named Orphan Drug Designation. This should be mapped to the Default Application Type (Entity XML Type) and to the Orphan Drug Designation Application Category; countries assigned should be all countries appropriate for the Orphan Drug Designation submission.

4.3 Product Family

Product Family should follow standard Ennov InSight Best Practice.

It is important to note that the Active Ingredient(s) are no longer editable once a Component or Product Detail Set has been created. It is therefore best practice to not create a Component or Product Detail Set until the point of Marketing Authorisation Application. This will allow for changes in Active Ingredient – for example, if the INN has not been determined yet.

The indication(s) should be added to the Product Family before the Orphan Drug Designation Application is created. The indication should then be reviewed and amended as necessary before the Marketing Authorisation Application is created.

4.4 Product and Component

Product details, such as dosage form or active ingredient strength, may not be known at the time of application for the Orphan Designation. If the dosage form and active ingredient strength is known at the time of application for the ODD, the Product should be created following standard Ennov InSight Best Practice. Note that, as stated above, the Component should not be created until the point of Marketing Authorisation Application.

If either dosage form or active ingredient strength are not known at the time of application for the ODD, a Product may be created without this information. This Product should only be used for Orphan Drug Designation Applications. It is best practise to include 'ODD', 'Orphan Drug Designation' or a similar reference in either the Product Name or Product Code, to help users select the appropriate Product. A new Product should be created when the Marketing Authorisation Application is planned, following Ennov InSight Best Practice.

Example 1

An application for ODD status is granted for the use of Budesonide as an effervescent tablet to be dissolved in the mouth. No strengths are referenced in the application.

- *Product Name: Budesonide*
- *Product Code: ODD*
- *Product Strength Measures/Units: not populated*
- *Product Dose Form: Effervescent tablet*

- *Product Route of Administration: Oral use*

Example 2

An application for ODD is granted for the of Fedratinib. No dosage form or strengths are referenced in the application.

- *Product Name: Fedratinib*
- *Product Code: ODD*
- *Product Strength Measures/Units: not populated*
- *Product Dose Form: not populated*
- *Product Route of Administration: not populated*

Example 3

An application for ODD is made for Glycerol phenylbutyrate 1.1 mg/ml Oral liquid. As the dosage form and active ingredient strength are known, the Product is created following Ennov InSight Best Practice.

4.5 Reference

A new Reference Type should be created named Orphan Designation. A new Reference Status value 'Active' should be created for this Reference Type.

5 Orphan Drug Designation Application Process

Orphan Drug Designation is granted by the Health Authority following an application by the MAH/Sponsor with reference to (a) specific indication(s). Multiple applications may be made for a single Product Family in the same region/country: for example, to apply for ODD status for further indications.

It is best practice to capture all ODD applications on a single application, so that there is one Orphan Drug Designation Application per Product Family per country/region. All subsequent activities, such as annual report submissions, will also be captured on this single application.

This approach is recommended as it makes it easy to identify all ODDs for the Product Family in that country/region and avoids creating duplicate Events to record submission of multiple initial ODDs on one date or multiple annual reports on one date.

It is also possible to capture each individual ODD application as a separate application, so that there is one Orphan Drug Designation Application per ODD applied for. Subsequent activities, such as annual reports, will then be captured under the application for that ODD. Where multiple applications are made simultaneously, for example when applying for multiple ODDs at the same time, an Event will need to be created on each Application.

5.1 Initial Orphan Drug Designation Application

The Orphan Drug Designation application should be captured in Ennov InSight as follows:

1. Create an Application within the appropriate Product Family with the following attributes:
    a. Reviewing Country: <as appropriate>
    b. Application Code: <as appropriate>
        i. Multiple Application Codes may be separated by a comma (e.g. 'EMA/OD/012/01, EMA/OD/012/02')
    c. Application Name: <Product Family Name> ODD <Country or EU procedure> <RMS / Rapp (if appropriate)>
        i. If separate applications are to be created for each ODD, add a brief summary of the indication at the end of the Application Name (e.g. 'Graft-versus-Host', or 'Post-polycythaemia vera myelofibrosis')
    d. Application Type: Orphan Drug Designation
    e. Procedure Type: <as appropriate>
    f. Registration Type: Package Set Registration
    g. Associated Products:
        i. Associate the Product(s) for which the Orphan Drug Designation is being made
    h. Countries: (Only For EU CP procedure Type)
        i. Select all of the appropriate countries.
    i. Complete other fields as required by your organization.

Application Attributes

Add entity to Favorites

Family Name:	Fedratinib
Reviewing Country:	European Union
Region(s):	Regulatory Region - European Union
UUID:	01fbc35b-3de9-4602-b470-9a612da2e742
Applicant ID:	
Internal Code:	
Application Code:	EMA/OD/069/10
Application Name:	Fedratinib ODD EMA
Legal Status of Supply:	
Legal Basis:	
Application Type:	Orphan Drug Designation

2. Create an Event with the following attributes:
    a. Event Name: follow organisation naming convention, including a brief reference to the indication(s) applied for (e.g.: 'Initial Application: Graft-versus-Host', 'Initial Application: Post-polycythaemia vera myelofibrosis and post-essential thrombocythaemia myelofibrosis')
    b. Associated Products: (associate the Product(s) for which the ODD application is being made)
    c. Variation Number: <agency reference for the ODD application(s)>
    d. Complete other fields as required by your organization.

Event Attributes

Add entity to Favorites | Application: Fedratinib ODD EMA » Event: Initial Application:...

Application Code:	EMA/OD/069/10, EMA/OD/092/10, EMA/OD/084/10
Application Name:	Fedratinib ODD EMA
Application Internal Code:	
Project Name:	
Closed:	No
Event Code:	
Event Name:	Initial Application: Treatment of primary myelofibrosis
Action Type:	
Event Type:	New Application
Secondary Event Type:	
Timeline/Event Plan Used:	
Variation Number:	EMA/OD/069/10

3. Create a Sequence as required by your organization.
4. Create an Assembly as required by your organization. This is not required for EMA applications, where the submission is made via the IRIS portal.
5. Record submission information following Ennov InSight Best Practice.
6. Once approval is received close and approve the Event.

Where the Health Authority make information on Orphan Designation information publicly available it is useful to link to this public record (e.g. the Community Register of Orphan Medical Products in the EU).

7. Create a Reference on the Application:
    a. Reference Name: <Orphan Designation number>

b. Type: Orphan Designation
c. Reference Status: Active
d. Reference Status Date: Date the Orphan Designation was granted
e. Reference Link: URL. Copy and paste the URL of the public Orphan Designation record.
f. Origination: <brief summary of the indication>

View Reference

Add entity to Favorites | Application: Fedratinib ODD EMA » Reference: EU/3/10/794

Application Name:	Fedratinib ODD EMA
Reference Name:	EU/3/10/794
Entity Association:	Application
Entity Name:	Fedratinib ODD EMA
Type:	Orphan Designation
Content:	
Participant:	
Reference Status:	Active
Reference Status Date:	01-Oct-2010
Reference Link Type:	URL
Reference Link:	https://ec.europa.eu/health/documents/community-register/html/o794.htm
Origination:	Treatment of primary myelofibrosis

This will produce a list of the ODDs on the Reference tab of the Application, with links to the public register.

Products | Events | Sequences | Countries | Registrations | Product Detail Sets | Medicinal Products | Medicinal Product Actions | IDMP | Tasks | Activities | Workflows | **References** | Notifications | Submitted Views | Approved Views

Reference Name	Type	Content	Status	Status Date	Origination	Action
EU/3/10/794	Orphan Designation		Active	01-Oct-2010	Treatment of primary myelofibrosis	
EU/3/10/810	Orphan Designation		Active	15-Aug-2024	Treatment of post-essential thrombocythaemia myelofibrosis	
EU/3/10/811	Orphan Designation		Active	15-Aug-2024	Treatment of post-polycythaemia vera myelofibrosis	

5.2 Adding further ODD applications to the Application

Guidance is provided for the Best Practice approach of using a single Application per Product Family per country/region.

1. Update the Application:
   a. Application Code: append further Application Code(s), separating them with a comma.
   b. If necessary, associate further Product(s) to the Application.

Application Attributes

Add entity to Favorites

Family Name:	Fedratinib
Reviewing Country:	European Union
Region(s):	Regulatory Region - European Union
UUID:	01fbc35b-3de9-4602-b470-9a612da2e742
Applicant ID:	
Internal Code:	
Application Code:	EMA/OD/069/10, EMA/OD/092/10
Application Name:	Fedratinib ODD EMA

2. Complete steps 2 onwards above.

6 Marketing Authorisation Applications for Orphan Drugs

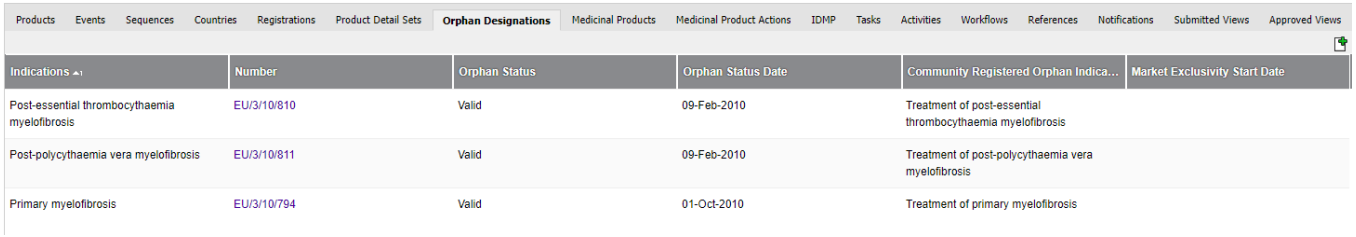
When a Marketing Authorisation Application/NDA or similar application is made, the Orphan Drug status of the Product may have implications for the application process. It is therefore best practice to record when a Marketing Authorisation Application includes Product(s) with ODD status.

1. Create Application:
    a. Orphan Drug: Yes
    b. Complete all other fields as usual, following Ennov InSight Best Practice.
2. For EU applications:
    a. Populate the Orphan Designations tab as described below.
3. It is useful to be able to cross-reference the MAA/NDA to the related Orphan Drug Designation application. Create a Reference:
    a. Reference Name: Application Name of the Orphan Drug Designation Application
    b. Type: Orphan Designation
    c. Reference Status: Active
    d. Reference Status Date: Date the Orphan Designation was granted
    e. Reference Link: URL. Copy and paste the URL of the Orphan Drug Designation Application.

6.1 Orphan Designations tab

Ennov InSight allows the capture of additional information related to the Orphan Designation in order to comply with IDMP requirements. This information is captured on the Orphan Designation tab on the Application. Currently, this is available only on EU MAA applications.

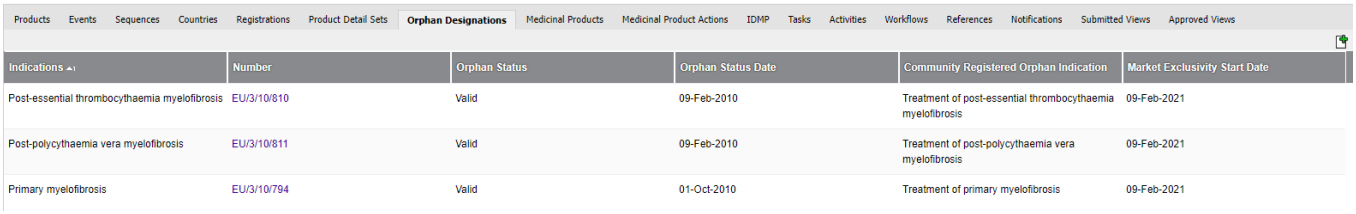
1. Navigate to the Application. The Orphan Designations tab will be visible.
2. Click 'Create' to add information on the Orphan Designation(s) relevant to this application. Each Orphan Designation should be added separately.
    a. Indications: Select the indication(s) covered by the Orphan Designation
    b. Number: Orphan Designation number
    c. Orphan Status: Valid
    d. Orphan Status Date: Date that the Designation was granted
    e. Community Registered Orphan Indication: The indication that is listed on the Union Register of Medicinal Products
    f. Where multiple products are associated with the application and have been granted different ODDs, this may be captured in the Description (e.g. 'Solution for Injection only').
        i. Add detail to describe how this would be used
3. The Orphan Designation information will be visible in the Orphan Designation tab.



Products | Events | Sequences | Countries | Registrations | Product Detail Sets | **Orphan Designations** | Medicinal Products | Medicinal Product Actions | IDMP | Tasks | Activities | Workflows | References | Notifications | Submitted Views | Approved Views

Indications	Number	Orphan Status	Orphan Status Date	Community Registered Orphan Indica...	Market Exclusivity Start Date
Post-essential thrombocythaemia myelofibrosis	EU/3/10/810	Valid	09-Feb-2010	Treatment of post-essential thrombocythaemia myelofibrosis	
Post-polycythaemia vera myelofibrosis	EU/3/10/811	Valid	09-Feb-2010	Treatment of post-polycythaemia vera myelofibrosis	
Primary myelofibrosis	EU/3/10/794	Valid	01-Oct-2010	Treatment of primary myelofibrosis	

4. Upon approval of the MAA, populate the Market Exclusivity Start Date.



Products | Events | Sequences | Countries | Registrations | Product Detail Sets | **Orphan Designations** | Medicinal Products | Medicinal Product Actions | IDMP | Tasks | Activities | Workflows | References | Notifications | Submitted Views | Approved Views

Indications	Number	Orphan Status	Orphan Status Date	Community Registered Orphan Indication	Market Exclusivity Start Date
Post-essential thrombocythaemia myelofibrosis	EU/3/10/810	Valid	09-Feb-2010	Treatment of post-essential thrombocythaemia myelofibrosis	09-Feb-2021
Post-polycythaemia vera myelofibrosis	EU/3/10/811	Valid	09-Feb-2010	Treatment of post-polycythaemia vera myelofibrosis	09-Feb-2021
Primary myelofibrosis	EU/3/10/794	Valid	01-Oct-2010	Treatment of primary myelofibrosis	09-Feb-2021