APAC e-Labeling Session

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ePI is a result of international collaboration

FHIR ePI was developed by and is maintained by an international collaboration experts from Gravitate Health, HL7's Vulcan Accelerator, EMA, Uppsala Monitoring Centre (UMC) / Global IDMP Working Group (GIDWG)

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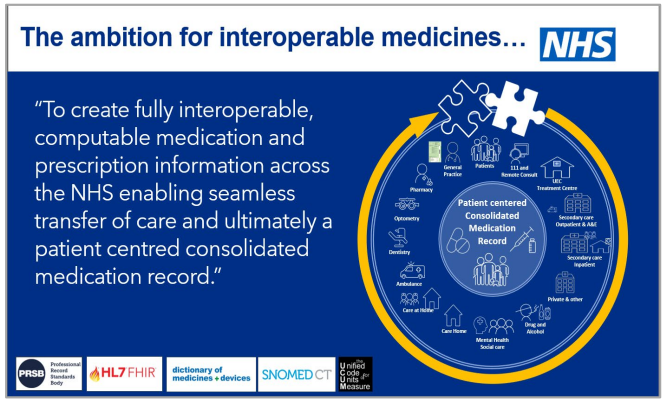
Healthcare use of FHIR

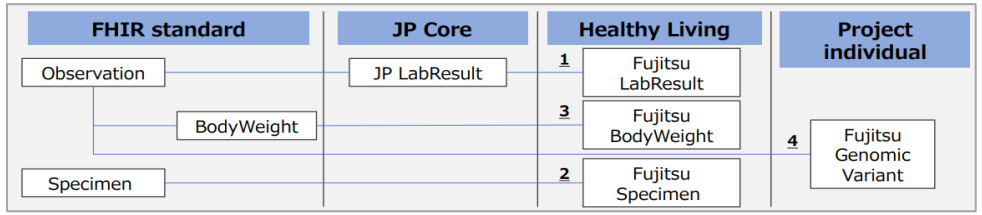
- FHIR is becoming the technical foundation for national healthcare systems.
- FHIR is the foundation for EMA's regulatory content strategy (e.g., IDMP, application forms, ePI, drug shortages).
- Opportunity to adapt FHIR to regulatory use cases like ePI, CMC, AEs, Trials.
- Opportunity to make ePI interoperable with EHR, and ePrescription systems.

USA

UK



Japan



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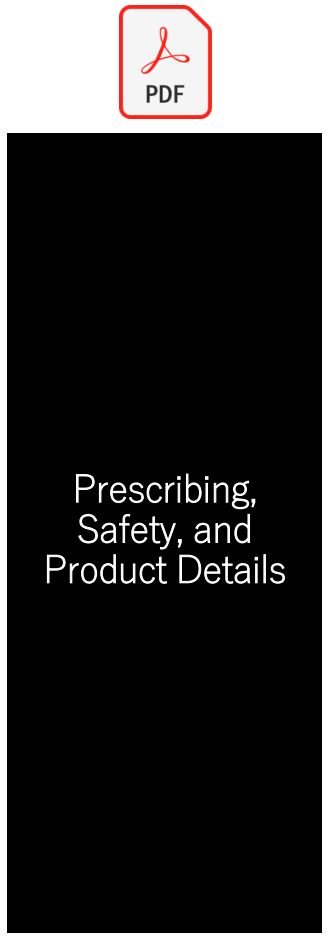
Un-structured vs. Structured



- Prescribing Information (Composition)
  - Section 1
  - Section 2
    - Indication 1
      - Semi-structured Text
      - Structured indication (SNOMED, ICD, MedDRA)
      - Version
      - Status
    - Indication 2
    - Warning 1
    - Warning 2
    - Posology 1
    - Posology 2
      - Semi-structured Text
      - Structured dose instructions
      - Version
      - Status
    - Side effect 1
    - Side effect 2
  - Section 3
  - Section 4
  - Section 5
  - Section 6
- Encoded Images (SVG)
- Medicinal Product
- Organization
- Regulated Authorization
- Manufactured Item
- Administrable Product
- Packaging
- Ingredients
- Clinical Use Definition
- Medication Statement

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Types of ePI

Recommended starting point

In development

ePI Type 1: Label Template Only	ePI Type 2: Product Details	ePI Type 3: Clinical Details	ePI Type 4: Full Structure

• Semi-structured text (Local template section headings, text, tables, bullets, images)
• Document metadata (language, date, identifier, version)
	• Type 1 and product details
	  ○ Product Name
	  ○ Ingredients
	  ○ Packaging
	  ○ Strength
	  ○ Manufactured
	  ○ Administrable dose forms
	  ○ Organization details
		• Type 1, 2, and clinical details
		  ○ Indication
		  ○ Interactions
		  ○ Contraindication
		  ○ Undesirable Effects
		  ○ Warnings
		  ○ Population demographics
			• Label content is made of structured components (E.g., Adverse event data is structured, and AE frequency tables are auto-generated)
			• Maximum personalization capability
			• Structured dose instructions

Simple search & analysis by section headings and text

Intermediate to advanced search & analysis; interoperability with ePrescription & EHRs; personalization

Auto-generate label template; interoperable with Generative AI

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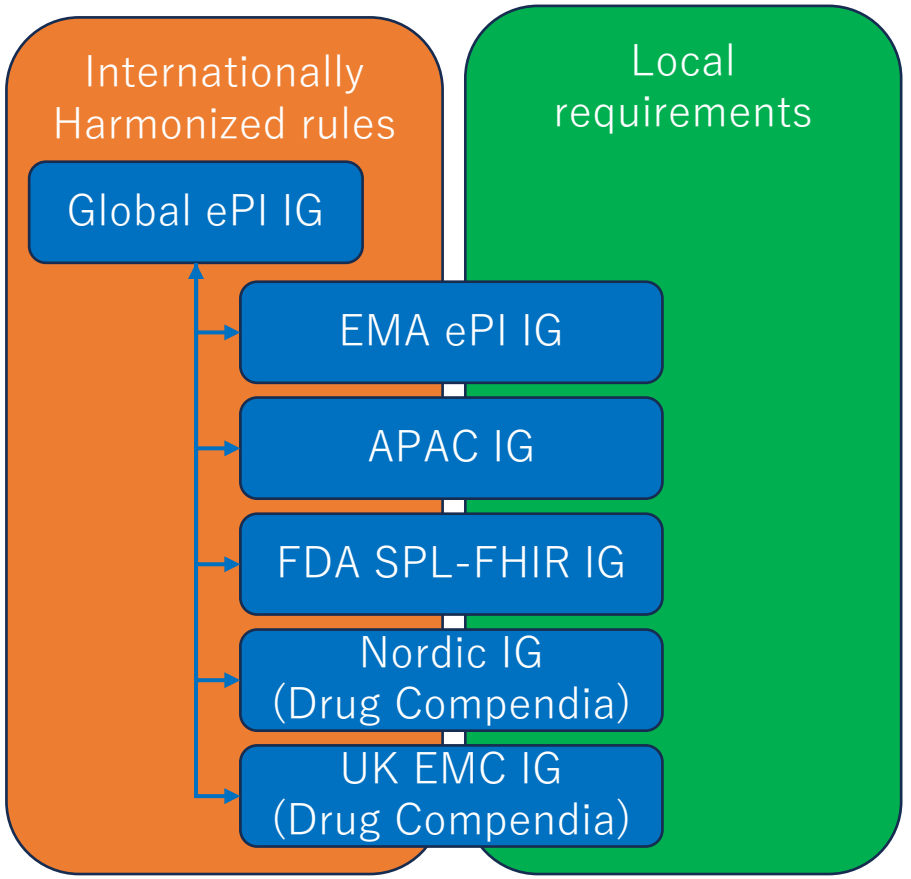
ePI Implementation Guide Hierarchy

- The Gravitate Health/Vulcan ePI Core IG provides guidance and compliance rules common to all jurisdictions (e.g., technical style guide; XML structure; validation).
- Regional or country specific IGs provide guidance and compliance rules unique to this jurisdiction (e.g.,local terminology and identifiers; local label template section headings; local business validation rules).
- Global and country specific IGs are maintained in sync and through open collaboration under HL7 (e.g., transparent sharing of lessons learned and improvements).



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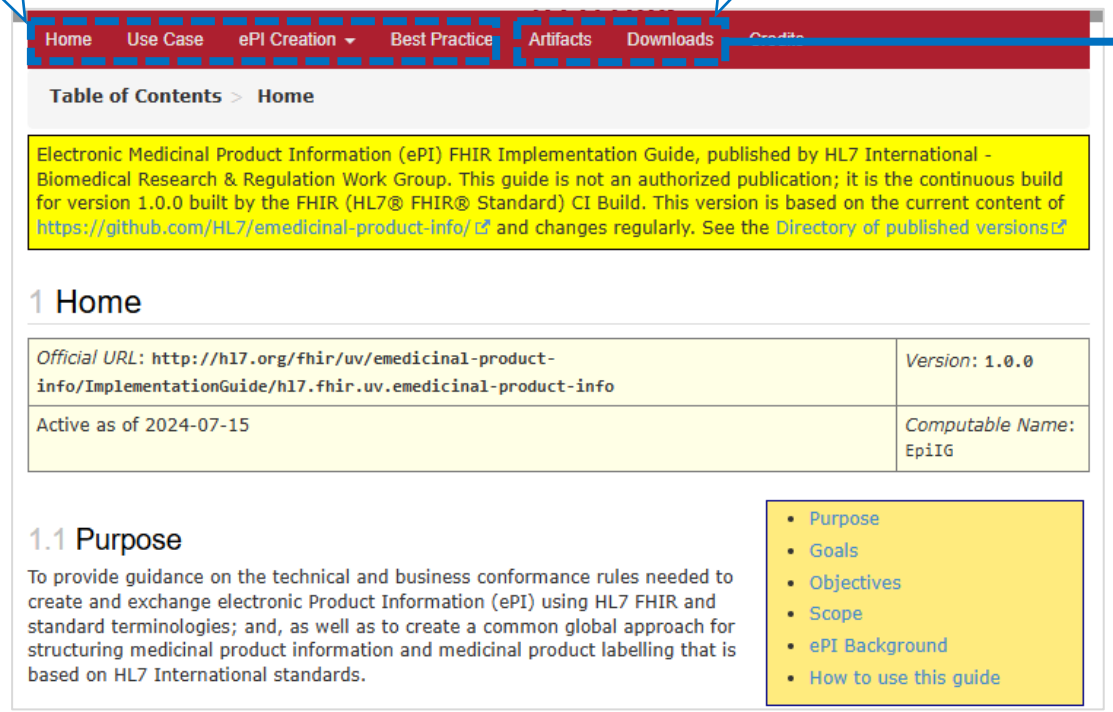
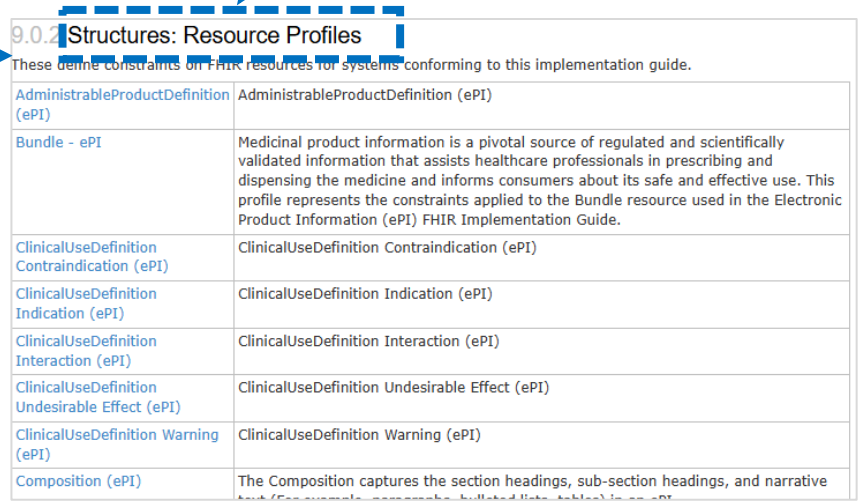
Implementation Guide Overview

Business guidance

Technical guidance

Compliance rules defining how to build an ePI using resources





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Potential ePI Use Cases

- **Personalization:** tailor ePI content to fit patient or healthcare professional's needs. E.g. , confirm if any ingredients are known allergens or a known effect.
- **Interactions:** Compare ePIs to confirm if the patient's current medications have drug:drug, drug:food interactions.
- **Contraindications:** Confirm if any of the patient's conditions are contraindicated with this medication.
- **Drug shortages:** Use ePI's product information (e.g., unique IDs for pack, drug, or manufacturer) to quickly find other drugs in the same class or category.
- **Advanced search:** Host all ePIs in a central portal (like EMA's) to facilitate content search.
- **Cross-border travel:** Allow HCPs or patients to identify the same or similar drug in another country.
- **Distribution:** Use packaging details in the ePI (e.g., product and pack identifiers) to facilitate supply chain ordering or tracking.
- **eHealth interoperability:** Reuse structured ePI content in apps like EHR, ePrescription, Apple Health or Google Health apps.

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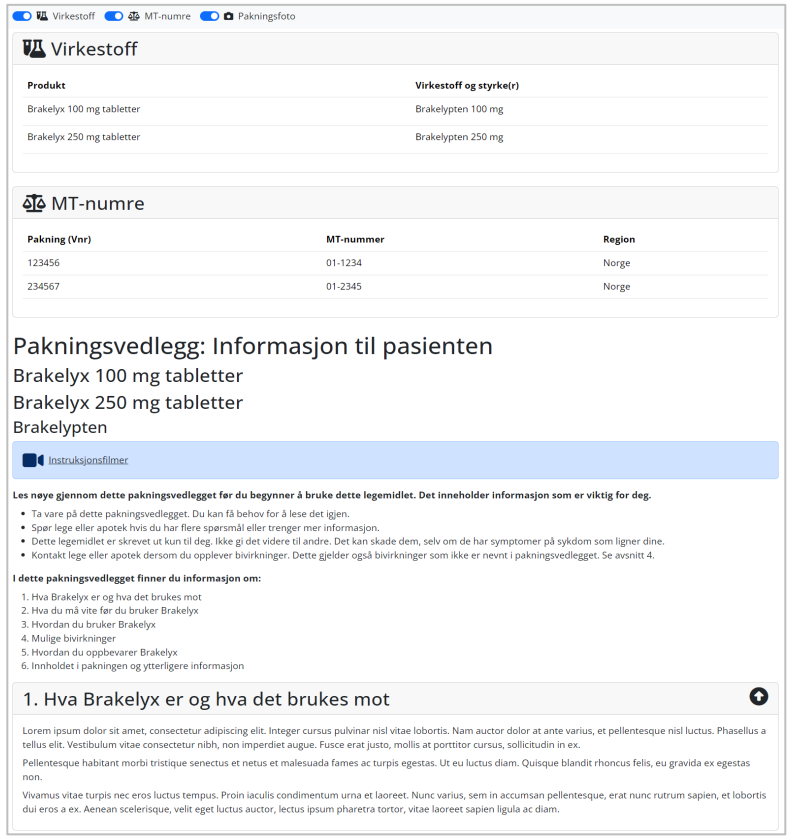
Use case: Easier to read web style content



Virkestoff MT-numre Pakningsfoto

Virkestoff

Produkt	Virkestoff og styrke(r)
Brakelyx 100 mg tabletter	Brakelypten 100 mg
Brakelyx 250 mg tabletter	Brakelypten 250 mg

MT-numre

Pakning (Vnr)	MT-nummer	Region
123456	01-1234	Norge
234567	01-2345	Norge

Pakningsvedlegg: Informasjon til pasienten

Brakelyx 100 mg tabletter
Brakelyx 250 mg tabletter
Brakelypten

Instruksjonsfilmer

Les nøye gjennom dette pakningsvedlegget før du begynner å bruke dette legemidlet. Det inneholder informasjon som er viktig for deg.

- Ta vare på dette pakningsvedlegget. Du kan få behov for å lese det igjen.
- Spør lege eller apotek hvis du har flere spørsmål eller trenger mer informasjon.
- Dette legemidlet er skrevet ut kun til deg. Ikke gi det videre til andre. Det kan skade dem, selv om de har symptomer på sykdom som ligner dine.
- Kontakt lege eller apotek dersom du opplever bivirkninger. Dette gjelder også bivirkninger som ikke er nevnt i pakningsvedlegget. Se avsnitt 4.

I dette pakningsvedlegget finner du informasjon om:

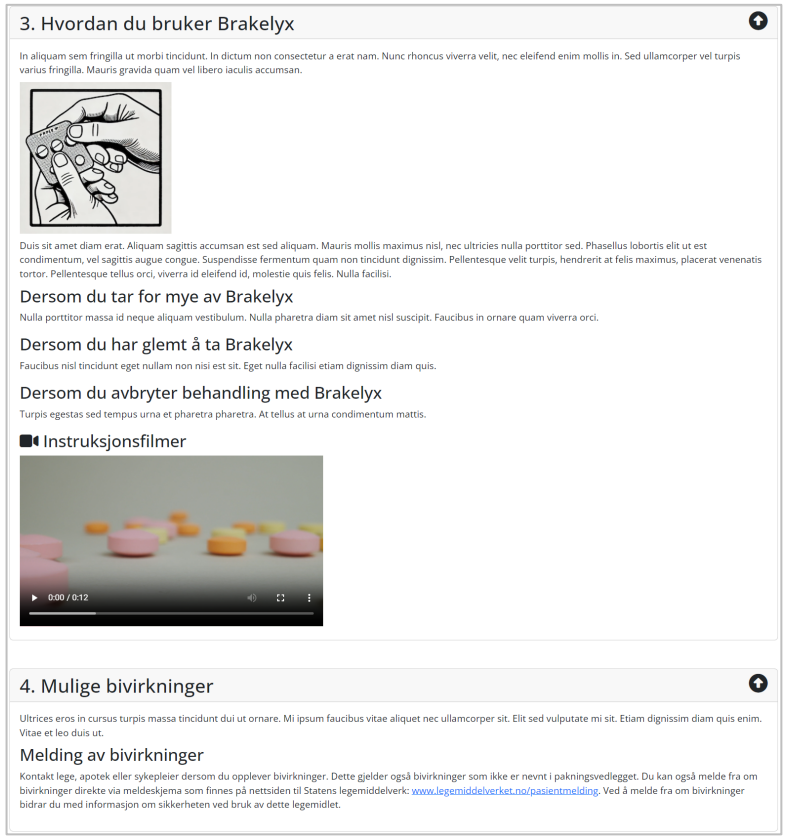
1. Hva Brakelyx er og hva det brukes mot
2. Hva du må vite før du bruker Brakelyx
3. Hvordan du bruker Brakelyx
4. Mulige bivirkninger
5. Hvordan du oppbevarer Brakelyx
6. Innholdet i pakningen og ytterligere informasjon

1. Hva Brakelyx er og hva det brukes mot

Lorem ipsum dolor sit amet, consectetur adipiscing elit. Integer cursus pulvinar nisl vitae lobortis. Nam auctor dolor at ante varius, et pellentesque nisl luctus. Phasellus a tellus elit. Vestibulum vitae consectetur nibh, non imperdiet augue. Fusce erat justo, mollis at porttitor cursus, sollicitudin in ex.

Pellentesque habitant morbi tristique senectus et netus et malesuada fames ac turpis egestas. Ut eu luctus diam. Quisque blandit rhoncus felis, eu gravida ex egestas non.

Vivamus vitae turpis nec eros luctus tempus. Proin iaculis condimentum urna et laoreet. Nunc varius, sem in accumsan pellentesque, erat nunc rutrum sapien, et lobortis dui eros a ex. Aenean scelerisque, velit eget luctus auctor, lectus ipsum pharetra tortor, vitae laoreet sapien ligula ac diam.



3. Hvordan du bruker Brakelyx

In aliquam sem fringilla ut morbi tincidunt. In dictum non consectetur a erat nam. Nunc rhoncus viverra velit, nec eleifend enim mollis in. Sed ullamcorper vel turpis varius fringilla. Mauris gravida quam vel libero iaculis accumsan.

Duis sit amet diam erat. Aliquam sagittis accumsan est sed aliquam. Mauris mollis maximus nisl, nec ultricies nulla porttitor sed. Phasellus lobortis elit ut est condimentum, vel sagittis augue congue. Suspendisse fermentum quam non tincidunt dignissim. Pellentesque velit turpis, hendrerit at felis maximus, placerat venenatis tortor. Pellentesque tellus orci, viverra id eleifend id, molestie quis felis. Nulla facilisi.

Dersom du tar for mye av Brakelyx

Nulla porttitor massa id neque aliquam vestibulum. Nulla pharetra diam sit amet nisl suscipit. Faucibus in ornare quam viverra orci.

Dersom du har glemt å ta Brakelyx

Faucibus nisl tincidunt eget nullam non nisi est sit. Eget nulla facilisi etiam dignissim diam quis.

Dersom du avbryter behandling med Brakelyx

Turpis egestas sed tempus urna et pharetra pharetra. At tellus at urna condimentum mattis.

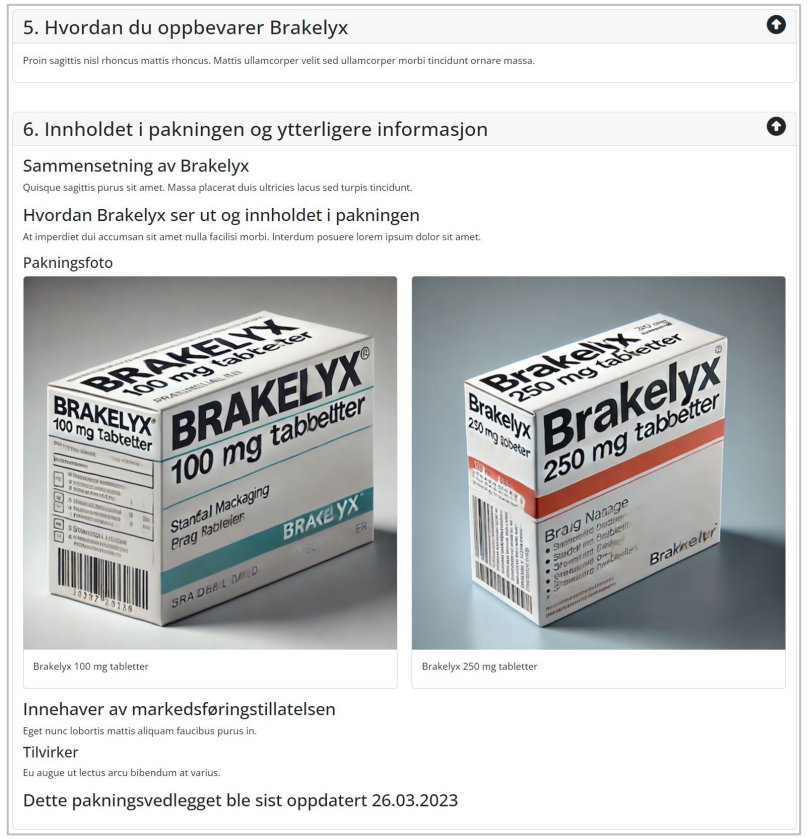
Instruksjonsfilmer

4. Mulige bivirkninger

Ultrices eros in cursus turpis massa tincidunt dui ut ornare. Mi ipsum faucibus vitae aliquet nec ullamcorper sit. Elit sed vulputate mi sit. Etiam dignissim diam quis enim. Vitae et leo duis ut.

Melding av bivirkninger

Kontakt lege, apotek eller sykepleier dersom du opplever bivirkninger. Dette gjelder også bivirkninger som ikke er nevnt i pakningsvedlegget. Du kan også melde fra om bivirkninger direkte via meldeskjema som finnes på nettsiden til Statens legemiddelverk: www.legemiddelverket.no/pasientmelding. Ved å melde fra om bivirkninger bidrar du med informasjon om sikkerheten ved bruk av dette legemidlet.



5. Hvordan du oppbevarer Brakelyx

Proin sagittis nisl rhoncus mattis rhoncus. Mattis ullamcorper velit sed ullamcorper morbi tincidunt ornare massa.

6. Innholdet i pakningen og ytterligere informasjon

Sammensetning av Brakelyx

Quisque sagittis purus sit amet. Massa placerat duis ultricies lacus sed turpis tincidunt.

Hvordan Brakelyx ser ut og innholdet i pakningen

At imperdiet dui accumsan sit amet nulla facilisi morbi. Interdum posuere lorem ipsum dolor sit amet.

Pakningsfoto

Brakelyx 100 mg tabletter

Brakelyx 250 mg tabletter

Innehaver av markedsføringstillatelsen

Eget nunc lobortis mattis aliquam faucibus purus in.

Tilvirker

Eu augue ut lectus arcu bibendum at varius.

Dette pakningsvedlegget ble sist oppdatert 26.03.2023

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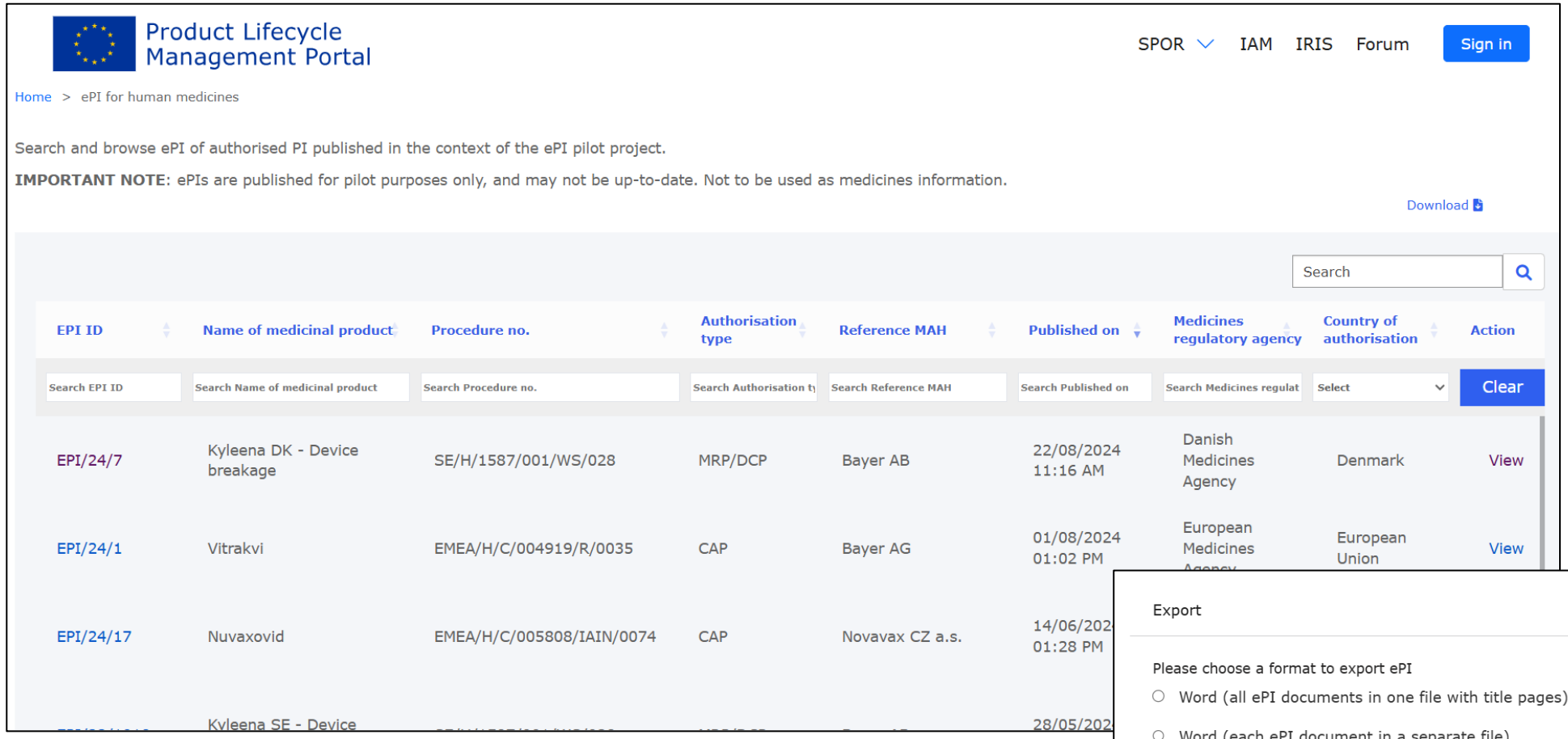
[Felleskatalogen (Norwegian national drug compendia) ePI Style sheet: nordic-epi-ig/docker at epi-styling · felleskatalogen/nordic-epi-ig]

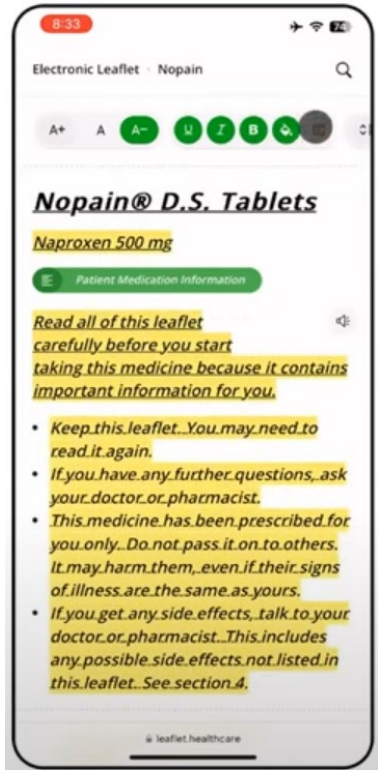
Use case: EMA's online ePI Portal



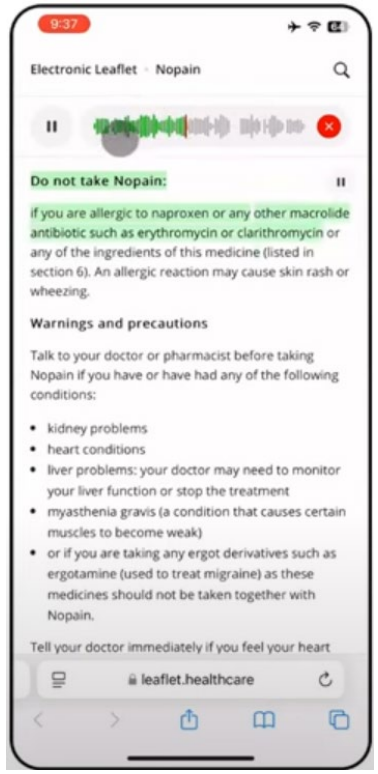
https://plm-portal.ema.europa.eu/ePIAll/

Use case: Jordan FDA's App with accessibility features

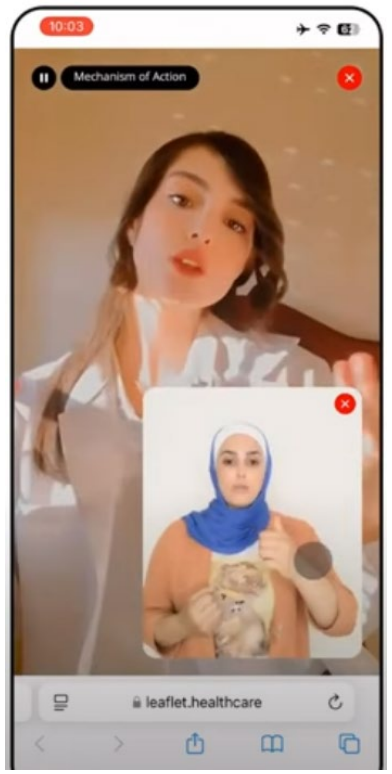
Control text size, dark mode, appearance



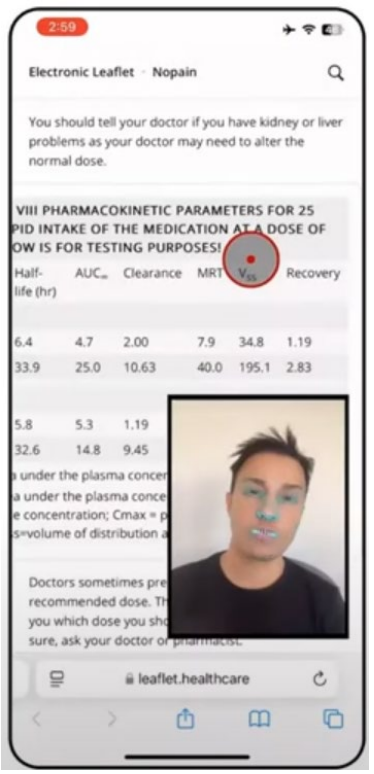
Text to speech



Sign language



Face navigation



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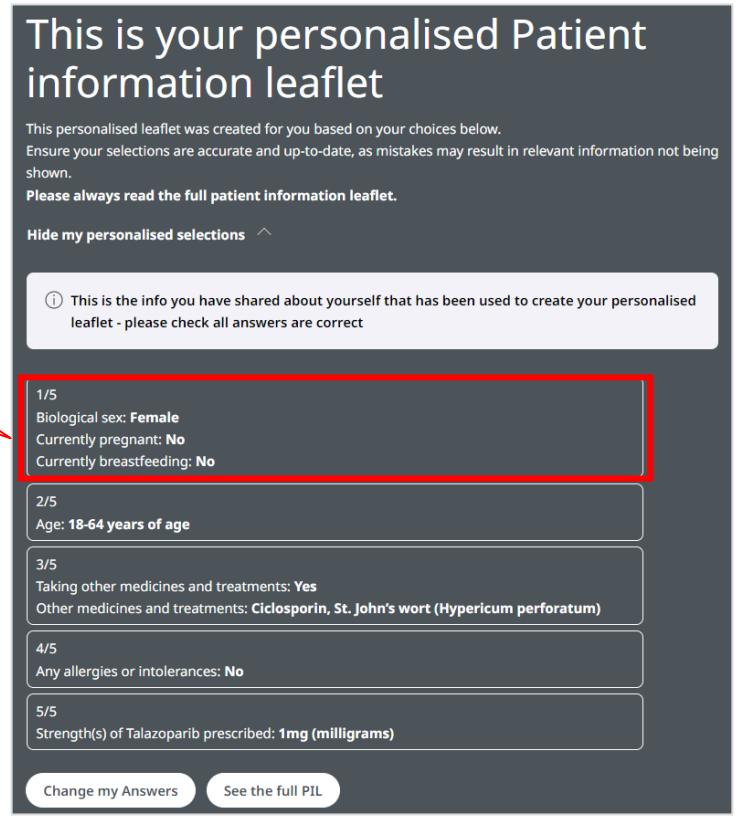
21.10.2024 | ePI on FHIR: Shaping the Future of Global Healthcare - Gravitate Health

Use case: personalization

A questionnaire helps patients personalize their ePI to only show relevant content.

Questionnaire results



Original PIL

Male and female contraception

Women who are able to become pregnant should use effective birth control (contraception) during treatment with Talzenna and for at least 7 months after the last dose of Talzenna. Since the use of hormonal contraception is not recommended if you have breast cancer, you should use two non-hormonal contraception methods.

Talk to your healthcare provider about birth control methods that may be right for you.

Men with female partners who are pregnant or able to become pregnant should use effective birth control (contraception), even after a vasectomy, during treatment with Talzenna and for at least 4 months after the last dose.

Personalized PIL

Male and female contraception

Women who are able to become pregnant should use effective birth control (contraception) during treatment with Talzenna and for at least 7 months after the last dose of Talzenna. Since the use of hormonal contraception is not recommended if you have breast cancer, you should use two non-hormonal contraception methods.

Talk to your healthcare provider about birth control methods that may be right for you.

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Future use case: ePI Type 3 / 4 - Personalized Undesirable Effects

- Rather than a “regular” Word table, the table is generated from structured data components. This will allow us to create personalized undesirable effect tables.

```
<undesirableEffect>
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        <coding>
            <system value="http://snomed.info/sct"/>
            <code value="36225005"/>
            <display value="Blood and lymphatic system disorders"/>
        </coding>
    </classification>
    <symptomConditionEffect>
        <coding>
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</undesirableEffect>
```

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<undesirableEffect>
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            <code value="36225005"/>
            <display value="Blood and lymphatic system disorders"/>
        </coding>
    </classification>
    <symptomConditionEffect>
        <coding>
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            <code value="702760002"/>
            <display value="Leukopenia"/>
        </coding>
    </symptomConditionEffect>
    <frequency value="≥10%"/>
```

Structured data styled into a table

Table 4. Adverse Reactions (≥10%) in PALOMA-2

	IBRANCE plus Letrozole (N=444)			Placebo plus Letrozole (N=222)		
Adverse Reaction	All Grades %	Grade 3 %	Grade 4 %	All Grades %	Grade 3 %	Grade 4 %
Infections and infestations						
Infections*	60[†]	6	1	42	3	0
Blood and lymphatic system disorders						
Neutropenia	80	56	10	6	1	1
Leukopenia	39	24	1	2	0	0
Anemia	24	5	<1	9	2	0
Thrombocytopenia	16	1	<1	1	0	0

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Future use case: ePI Type 3 / 4 - Structured Dose Syntax

Adults

Condition	Dose
To treat cryptococcal meningitis	400 mg on the first day then 200 mg to 400 mg once daily for 6 to 8 weeks or longer if needed. Sometimes doses are increased up to 800 mg
To stop cryptococcal meningitis from coming back	200 mg once daily until you are told to stop
To treat coccidioidomycosis	200 mg to 400 mg once daily from 11 months for up to 24 months or longer if needed. Sometimes doses are increased up to 800 mg
To treat internal fungal infections caused by *Candida*	800 mg on the first day then 400 mg once daily until you are told to stop
To treat mucosal infections affecting the lining of mouth, throat and denture sore mouth	200 mg to 400 mg on the first day then 100 mg to 200 mg once daily until you are told to stop
To treat mucosal thrush – dose depends on where the infection is located	50 mg to 400 mg once daily for 7 to 30 days until you are told to stop
To stop mucosal infections affecting the lining of mouth, throat from coming back	100 mg to 200 mg once daily, or 200 mg 3 times a week, while you are at risk of getting an infection
To treat genital thrush	150 mg as a single dose
To reduce recurrence of vaginal thrush	150 mg every third day for a total of 3 doses (day 1, 4 and 7) and then once a week for 6 months while you are at risk of getting an infection
To treat fungal skin and nail infections	Depending on the site of the infection 50 mg once daily, 150 mg once weekly, 300 to 400 mg once weekly for 1 to 4 weeks (Athlete's foot may be up to 6 weeks, for nail infection treatment until infected nail is replaced)
To stop you from getting an infection caused by *Candida* (if your immune system is weak and not working properly)	200 mg to 400 mg once daily while you are at risk of getting an infection

To treat internal fungal infections caused by *Candida*	800 mg on the first day then 400 mg once daily until you are told to stop

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  <additionalInstruction>
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      <period value="1"/>
      <periodUnit value="d"/>
    </repeat>
  </timing>
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    </coding>
  </route>
```

```
  </route>
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    </coding>
  </method>
  <doseAndRate>
    <type>
      <coding>
        <system value="http://termi
        <code value="ordered"/>
        <display value="Ordered"/>
      </coding>
    </type>
    <doseQuantity>
      <value value="4"/>
      <unit value="TAB"/>
      <system value="http://terminolo
      <code value="TAB"/>
    </doseQuantity>
  </doseAndRate>
</dosageInstruction>
```

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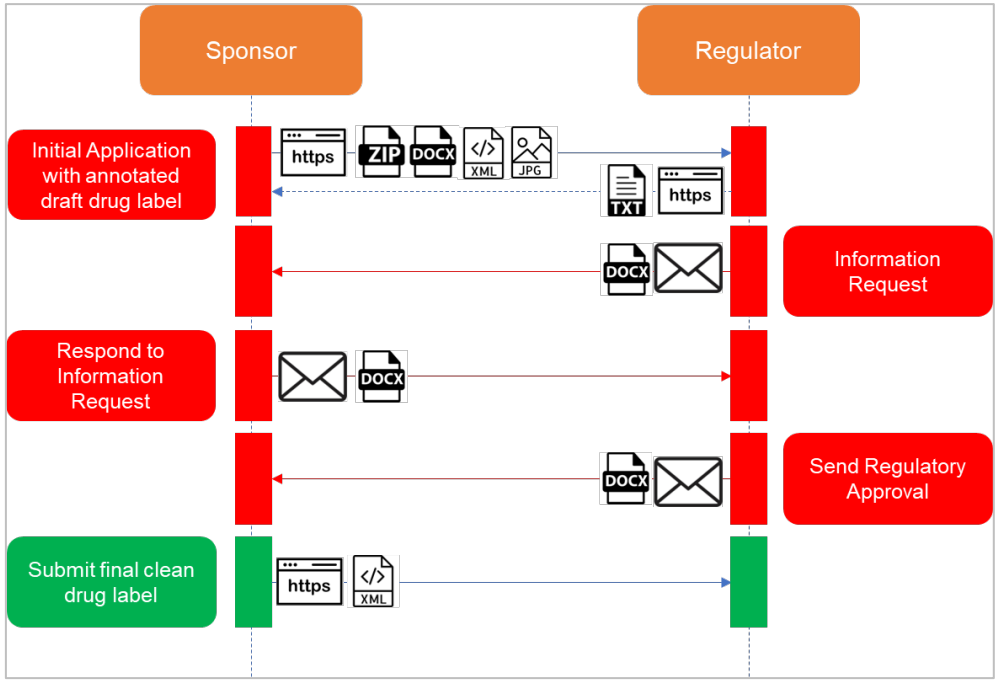
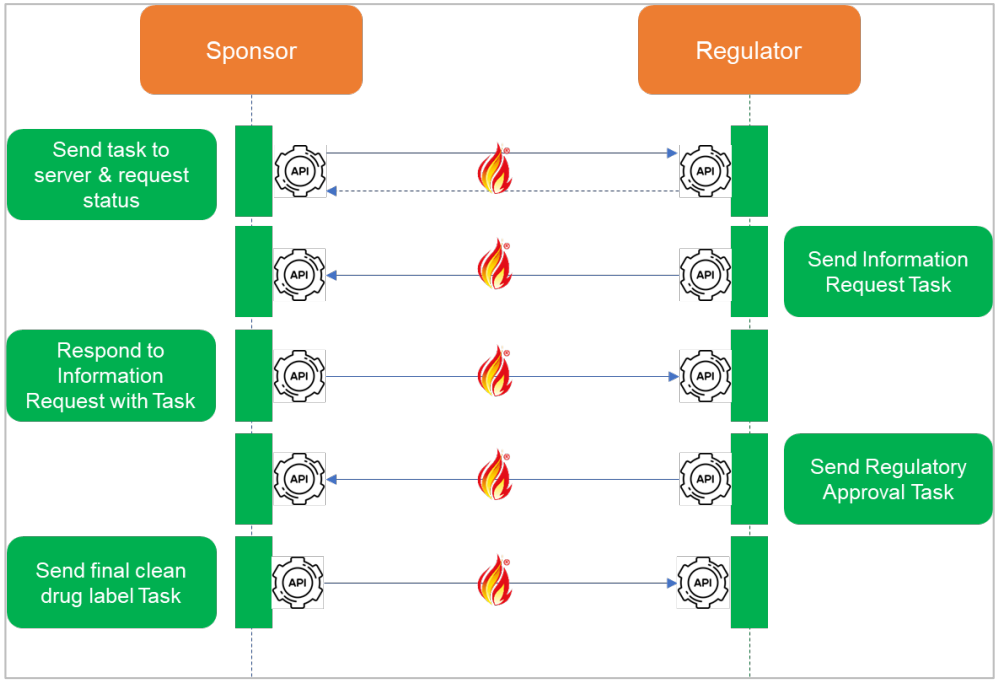
[UK's NHS FHIR Dose Syntax Implementation Guidance | Dose Syntax Implementation for FHIR]

Future use case: End-to-end FHIR Regulatory Workflow



Current State

- Workflow depends on DOCX during assessment
- Exchange via portal, email, media, manual steps
- Sponsor needs to convert between DOCX and XML



Future State

- All FHIR workflow (including assessment; no DOCX)
- Exchange via Application Program Interface (API)
- Advanced features (e.g., Subscription service)

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Lessons Learned: EMA/FDA pilots and Gravitate Health/Vulcan project work

- Recommend starting with ePI Type 2
- Remain harmonized with EMA and Vulcan Implementation Guides where possible
- Recommended roadmap:
  - Phase 1: Create a prototype ePI as a gold standard
  - Phase 2: Technical pilot
  - Phase 3: Production Pilot (Voluntary)
  - Phase 4: Production (Voluntary)
  - Phase 5: Production (Mandatory)
- Aim for a two-year timeframe to go from Phase 1 to Phase 4. Allow grace period between Phase 4 and 5 to allow industry time to get ready.
- Communicate roadmap in advance so industry has time to procure tools